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As confidentially submitted to the Securities and Exchange Commission on May 23, 2013

Registration No. 333-

# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION

**Washington, D.C. 20549**

# FORM S-1
# REGISTRATION STATEMENT

***UNDER***

***THE SECURITIES ACT OF 1933***

# AGIOS PHARMACEUTICALS, INC.

**(Exact name of registrant as specified in its charter)**

| **Delaware** | **2834** | **26-0662915** |
|---|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(Primary Standard Industrial Classification Code Number)** | **(I.R.S. Employer Identification No.)** |

**38 Sidney Street, 2nd Floor**
**Cambridge, MA 02139**
**(617) 649-8600**
**(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)**

**David P. Schenkein, M.D.**
**Chief Executive Officer**
**Agios Pharmaceuticals, Inc.**
**38 Sidney Street, 2nd Floor**
**Cambridge, MA 02139**
**(617) 649-8600**
**(Name, address, including zip code, and telephone number, including area code, of agent for service)**

***Copies to:***

| **Steven D. Singer, Esq.** | **Richard D. Truesdell, Jr., Esq.** |
|---|---|
| **Cynthia T. Mazareas, Esq.** | **Davis Polk & Wardwell LLP** |
| **Wilmer Cutler Pickering Hale and Dorr LLP** | **450 Lexington Avenue** |
| **60 State Street** | **New York, NY 10017** |
| **Boston, MA 02109** | **Telephone: (212) 450-4000** |
| **Telephone: (617) 526-6000** | |

**Approximate date of commencement of proposed sale to the public:** As soon as practicable after this Registration Statement is declared effective.

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

| | | | |
|---|---|---|---|
| Large accelerated filer | ☐ | Accelerated filer | ☐ |
| Non-accelerated filer | ☒ (Do not check if a smaller reporting company) | Smaller reporting company | ☐ |

**CALCULATION OF REGISTRATION FEE**

| **Title of each Class of Securities to be Registered** | **Proposed Maximum Aggregate Offering Price(1)** | **Amount of Registration Fee(2)** |
|---|---|---|
| Common Stock, $0.001 par value per share | $ | $ |

(1) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.
(2) Calculated pursuant to Rule 457(o) based on an estimate of the proposed maximum aggregate offering price.

**The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.**

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**The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.**

**Subject to completion, dated , 2013**

**Prospectus**

# Shares


## Common stock

Agios Pharmaceuticals, Inc. is offering shares of its common stock. This is our initial public offering, and no public market currently exists for our shares. We intend to apply to have our common stock listed on The NASDAQ Global Market under the symbol "AGIO." We anticipate that the initial public offering price will be between $ and $ per share.

We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012, and as such, have elected to comply with certain reduced public reporting requirements.

**Investing in our common stock involves risks. See "Risk factors" beginning on page 9 of this prospectus.**

| | Per share | Total |
|---|---|---|
| Public offering price | $ | $ |
| Underwriting discounts | $ | $ |
| Proceeds, before expenses, to Agios Pharmaceuticals, Inc. | $ | $ |

We have granted the underwriters the right to purchase up to an additional shares of common stock, to cover over-allotments. The underwriters can exercise this right at any time within 30 days after the date of this prospectus.

Celgene, our cancer metabolism strategic alliance partner, has agreed to purchase $ million of our common stock in a separate private placement concurrent with the completion of this offering at a price per share equal to the public offering price. The sale of such shares will not be registered under the Securities Act of 1933, as amended. The closing of this offering is not conditioned upon the closing of the concurrent private placement to Celgene.

**Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the accuracy or adequacy of this prospectus. Any representation to the contrary is a criminal offense.**

The underwriters expect to deliver the shares of common stock to investors on or about , 2013.

**J.P. Morgan** **Goldman, Sachs & Co.**

**Cowen and Company** **Leerink Swann**

**The date of this prospectus is , 2013.**

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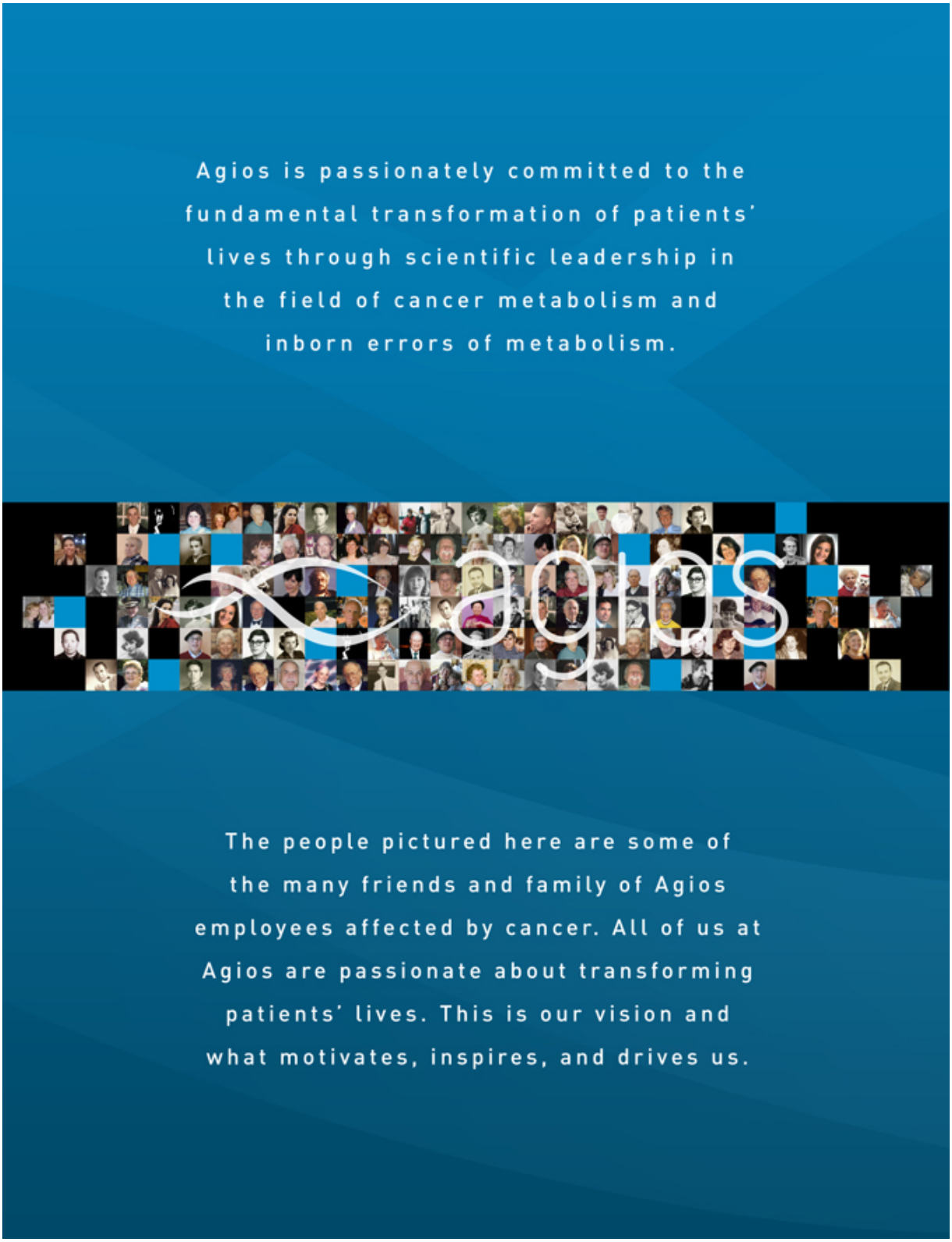

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We have not authorized anyone to provide you with any information other than that contained in this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of shares of our common stock.

**Until , 2013 (25 days after the commencement of this offering), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.**

For investors outside the United States: We have not and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

## Prospectus summary

*This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, especially the "Risk factors" section beginning on page 9 and our consolidated financial statements and the related notes appearing at the end of this prospectus, before making an investment decision.*

### Overview

We are a biopharmaceutical company passionately committed to applying our scientific leadership in the field of cellular metabolism to transform the lives of patients with cancer and inborn errors of metabolism, or IEMs, which are a subset of orphan genetic metabolic diseases. Metabolism is a complex biological process involving the uptake and assimilation of nutrients in cells to produce energy and facilitate many of the processes required for cellular division and growth. We believe that dysregulation of normal cellular metabolism plays a crucial role in many diseases, including certain cancers and IEMs. We believe Agios is a first mover in using cellular metabolism, an unexploited area of biological research with disruptive potential, as a platform for developing potentially transformative medicines. Our singular focus is to apply our expertise in cellular metabolism to develop innovative small molecule treatments for cancer and IEMs. We intend to apply our deep understanding of metabolism, coupled with our ability to create medicines that can inhibit or activate metabolic enzymes, to fundamentally change the way cancer and IEMs are treated. We have identified and validated novel and druggable targets in both cancer and IEMs.

Our two most advanced cancer programs are targeting mutations in the enzymes isocitrate dehydrogenase 1 and 2, referred to as IDH1 and IDH2. Both program targets are genetically validated and represent two of the most promising metabolic targets in cancer biology, as concluded by the leading scientific journal *Nature* in 2011. Extensive publications led by Agios scientists validate our belief that these mutations are initiating and driving events in many cancers. These two otherwise normal metabolic enzymes are mutated in a wide range of cancers, including both solid tumors and hematological malignancies. Our drug candidates are selective for the mutated forms of IDH1 and IDH2 found in cancer cells versus the normal forms of IDH1 and IDH2 found in all other cells. We expect to commence clinical trials in patients with IDH2-mutation positive cancers with AG-221, the lead candidate in our IDH2 program, by mid-2013. In the IDH1 program, we expect to commence clinical trials in patients with IDH1-mutation positive cancers with our lead development candidate, AG-120, by early 2014.

We are also focused on developing medicines to address IEMs, with a novel approach to these orphan diseases for which no effective or disease-modifying therapy is currently available. A hallmark of IEMs is abnormal cellular metabolic activity due to a genetic defect, which results in the accumulation or deficit of certain metabolites or proteins, disrupting normal metabolic functions. We apply our core capabilities in exploring cellular metabolism to identify key cellular targets in affected cells and design novel small molecules with the potential to correct the metabolic defect in patients afflicted with these diseases. We have successfully used this approach in our most advanced IEM program—pyruvate kinase deficiency, or PK deficiency, a rare form of hereditary hemolytic anemia. The disease is characterized by mild to severe forms of anemia. There are no currently available treatments other than supportive care, which includes splenectomy, transfusion support and chelation therapy. Our lead development candidate, AG-348, is a potent, orally available small molecule activator of the PKR enzyme, an isoform of PK that, when mutated, leads to PK deficiency. Our current plan is to enter clinical trials in patients with PK deficiency in 2014.

Our ability to identify, validate and drug novel targets is enabled by a set of core capabilities. Key proprietary aspects of our core capabilities in cellular metabolism include the ability to monitor numerous metabolic pathways in cells or tissues in a high throughput fashion and expertise in "flux biochemistry." This refers to the dynamic analysis of how metabolites accumulate or diminish as they are created or chemically altered by

multiple networks of metabolic enzymes. Complex mathematical modeling of metabolic pathways, enzymatic activity and the flux of metabolites through metabolic enzymatic reactions within diseased tissues allow us to identify novel disease biomarkers and targets for drug discovery.

Our understanding of metabolism within diseased tissues has enabled the development of pharmacodynamic markers and patient selection strategies for clinical development. Utilizing our approach, we identify altered metabolic pathways within abnormal cells. Altered metabolic pathways generate disease-specific metabolic fingerprints, comprising patterns of metabolite levels, that can be exploited in both discovery and development of novel therapeutics. Metabolites make ideal biomarkers because they are readily measured in the target tissues and blood. Metabolic biomarkers can identify appropriate patients for clinical trials, serve as pharmacodynamic markers to characterize medicine/target engagement in patients, and permit the monitoring of patient response to therapy. Identifying the right patient population has the potential to increase the probability of technical and clinical success, in comparison to conventional drug discovery, a benefit which will be increasingly important to the entire health care system. The clinical development strategy for all of our product candidates will always include initial study designs that allow for genetically or biomarker defined patient populations, enabling the potential for early proof of concept and a higher probability of technical success, along with accelerated clinical development and product approval.

We engage in a rigorous process that only allows the most promising programs to enter the last stage of drug discovery. We have been successful at fully validating four novel cancer targets to date with an additional ten novel targets currently in various stages of the validation process. We have also “de-validated” and terminated numerous programs, including many that have been reported in scientific journals. In our IEM portfolio, we use an equally rigorous set of validation techniques. We will only progress drug candidates forward into phase 1 trials if we have the ability to select patients who are most likely to respond to a given therapy based on genetic or metabolic biomarkers. While many factors are considered critical to maximize the probability of technical success in the drug development process, perhaps none is more important than identifying highly specific and selective molecules aimed at the best possible targets for therapy coupled with the patients most likely to respond to that therapy. Our goal is to develop increasing confidence in the target and the patient population prior to entering human clinical trials and then initiate those first human trials in a patient population that has been selected based on target dependence using a biomarker. This approach, known as personalized or precision medicine, is also designed to lead to the potential for clear proof of concept in early human trials and expedited approval timelines.

In April 2010, we entered into a collaboration agreement with Celgene focused on cancer metabolism. Under the collaboration, we are leading discovery, preclinical and early clinical development for all cancer metabolism programs. The discovery phase of the collaboration expires in April 2014, subject to Celgene’s option to extend the discovery phase for up to two additional years. Celgene has the option to obtain exclusive rights for the further development and commercialization of certain of these programs, and we will retain rights to the others. For the programs that Celgene chooses to license, we may elect to participate in a portion of the sales activities for the medicines from such programs in the United States. In addition, for certain of these programs, we may elect to retain full rights to develop and commercialize medicines from these programs in the United States. Through March 31, 2013, we have received approximately $141.2 million in payments from Celgene and $37.5 million in equity investments. We are also eligible to receive extension payments, payments upon the successful achievement of specified milestones, reimbursements for certain development expenses and royalties on any product sales. We have retained the option for exclusive rights to develop and commercialize AG-120 in the United States.

We have assembled a unique set of core capabilities at the intersection of cellular biology and metabolism, centered on the expertise of our founding scientists who are widely considered to be the thought leaders in cancer metabolism—Lew Cantley, Ph.D. (director of the Cancer Center at Weill Cornell Medical College and New York Presbyterian Hospital), Tak Mak, Ph.D. (professor of medical biophysics, University of Toronto) and Craig Thompson, M.D. (president and CEO of Memorial Sloan-Kettering Cancer Center)—as well as on the strength

of our management team, including our CEO, David Schenkein, M.D., and a group of world class scientists. We have built an exceptional team of cancer biologists, enzymologists and a core group of metabolomic experts that interrogate cellular metabolism to identify key metabolic targets and biomarkers in cancer and IEMs. Our scientists have published 11 scientific papers since 2009, including four in *Nature* and three in *Science*. We have also established an intellectual property portfolio consisting of over 100 patent applications worldwide, including multiple patent applications directed to our lead product candidates, together with trade secrets, know-how and continuing technological innovation.

**Our strategy**

We aim to build a multi-product company, based on our expertise in cellular metabolism, that discovers, develops and commercializes first- and best-in-class medicines to treat cancer and IEMs. Key elements of our strategy include:

- ***Aggressively pursuing the development of novel medicines to transform the lives of patients with cancer and IEMs.***
- ***Maintaining our competitive, first-mover advantage in the field of cellular metabolism.***
- ***Continuing to build a product engine for cancer and IEMs to generate novel and important medicines.***
- ***Building a preeminent independent biopharmaceutical company by engaging in discovery, development and commercialization of our medicines.***
- ***Maintaining a commitment to precision medicine in drug development.***

**Our guiding principles**

We aim to build a long-term company with a disciplined focus on developing medicines that transform the lives of patients with cancer and IEMs. We maintain a culture of high integrity that embraces the following guiding principles, which we believe will provide long-term benefits for all our stakeholders:

- ***Follow the science and do what is right for patients.***
- ***Maintain a culture of incisive decision-making driven by deep scientific interrogation and "respectful irreverence."***
- ***Foster collaborative spirit that includes all employees regardless of function or level.***
- ***Leverage deep strategic relationships with our academic and commercial partners to improve the quality of our discovery and development efforts.***

**Risks associated with our business**

Our business is subject to a number of risks of which you should be aware before making an investment decision. These risks are discussed more fully in the "Risk factors" section of this prospectus immediately following this prospectus summary. These risks include the following:

- We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.
- We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

- Our approach to the discovery and development of product candidates that target cellular metabolism is unproven, and we do not know whether we will be able to develop any medicines of commercial value.
- If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.
- We depend on our collaboration with Celgene and may depend on collaborations with additional third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.
- We currently do not own or license any issued patents for our key medicines or technology.
- If we are unable to obtain and maintain patent or trade secret protection for our medicines and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize medicines and technology similar or identical to ours, and our ability to successfully commercialize our medicines and technology may be adversely affected.
- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

**Concurrent private placement**

Celgene, our cancer metabolism strategic alliance partner, has agreed to purchase $ million of our common stock in a separate private placement concurrent with the completion of this offering at a price per share equal to the public offering price. The sale of such shares will not be registered under the Securities Act of 1933, as amended. The closing of this offering is not contingent upon the closing of the concurrent private placement with Celgene.

**Our corporate information**

We were incorporated under the laws of the State of Delaware in August 2007. Our executive offices are located at 38 Sidney Street, 2nd Floor, Cambridge, Massachusetts 02139, and our telephone number is (617) 649-8600. Our website address is www.agios.com. The information contained in, or accessible through, our website does not constitute part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

As used in this prospectus, unless the context otherwise requires, references to “Agios,” “we,” “us,” “our” and similar references refer to Agios Pharmaceuticals, Inc. and, where appropriate, our consolidated subsidiary. The trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

**The offering**

| | |
|---|---|
| **Common stock offered** | shares |
| **Common stock to be sold in the concurrent private placement to Celgene** | shares |
| **Common stock to be outstanding after this offering and the concurrent private placement to Celgene** | shares |
| **Option to purchase additional shares** | The underwriters have an option for a period of 30 days to purchase up to additional shares of our common stock. |
| **Use of proceeds** | We intend to use the net proceeds from this offering and the concurrent private placement as follows: approximately $ to fund clinical development of our lead product candidates in our cancer and IEM programs; approximately $ to fund research and development to advance our pipeline of preclinical product candidates; and the balance for working capital and other general corporate purposes, including potential acquisitions. See "Use of proceeds" for more information. |
| **Risk factors** | You should read the "Risk factors" section of this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock. |
| **Proposed NASDAQ Global Market symbol** | "AGIO" |

The number of shares of our common stock to be outstanding after this offering and the concurrent private placement is based on 10,441,491 shares of our common stock outstanding as of April 30, 2013, shares to be issued to Celgene in the concurrent private placement and 54,261,829 additional shares of our common stock issuable upon the automatic conversion of all outstanding shares of our preferred stock upon the closing of this offering.

The number of shares of our common stock to be outstanding after this offering excludes:

- 10,170,824 shares of common stock issuable upon exercise of stock options outstanding as of April 30, 2013 at a weighted-average exercise price of $0.81 per share;
- 303,698 shares of common stock reserved as of April 30, 2013 for future issuance under our equity incentive plans; and
- additional shares of our common stock that will be available for future issuance, as of the closing of this offering, under our 2013 stock incentive plan and our 2013 employee stock purchase plan.

Unless otherwise indicated, this prospectus reflects and assumes the following:

- the conversion of all outstanding shares of our preferred stock into an aggregate of 54,261,829 shares of our common stock, which will occur automatically immediately prior to the closing of the offering;
- no exercise of the outstanding options described above;
- the filing of our restated certificate of incorporation and the adoption of our amended and restated by-laws upon the closing of this offering;
- the issuance and sale of shares of common stock in the concurrent private placement to Celgene at the assumed public offering price; and
- no exercise by the underwriters of their over-allotment option.

**Summary consolidated financial data**

The following table summarizes our consolidated financial data. We have derived the following summary of our statement of operations data for the years ended December 31, 2011 and 2012 from our audited consolidated financial statements appearing elsewhere in this prospectus. We have derived the summary of our statement of operations data for the three months ended March 31, 2012 and 2013 and the balance sheet data as of March 31, 2013 from our unaudited consolidated financial statements appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of future results. The summary of our consolidated financial data set forth below should be read together with our consolidated financial statements and the related notes to those statements, as well as "Management's discussion and analysis of financial condition and results of operations," appearing elsewhere in this prospectus.

| | Years ended December 31, | | Three months ended March 31, | |
|---|---|---|---|---|
| (in thousands, except share and per share data) | 2011 | 2012 | 2012 | 2013 |
| **Consolidated Statement of Operations Data:** | | | | |
| Revenue | $ 21,837 | $ 25,106 | $ 6,268 | $ 6,268 |
| Operating expenses: | | | | |
| Research and development | 31,253 | 41,037 | 9,551 | 11,462 |
| General and administrative | 7,215 | 7,064 | 1,981 | 1,852 |
| Total operating costs | 38,468 | 48,101 | 11,532 | 13,314 |
| Loss from operations | (16,631) | (22,995) | (5,264) | (7,046) |
| Investment income | 132 | 69 | 26 | 8 |
| Loss before provision (benefit) for income taxes | (16,499) | (22,926) | (5,238) | (7,038) |
| Provision (benefit) for income taxes | 7,207 | (2,824) | (607) | 190 |
| Net loss | (23,706) | (20,102) | (4,631) | (7,228) |
| Cumulative preferred stock dividends | (3,100) | (7,190) | (1,798) | (1,798) |
| Net loss applicable to common stockholders | $ (26,806) | $ (27,292) | $ (6,429) | $ (9,026) |
| Net loss per share applicable to common shareholders—basic and diluted | $ (3.23) | $ (2.92) | $ (0.72) | $ (0.90) |
| Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted | 8,286,757 | 9,354,729 | 8,928,822 | 10,059,545 |
| Pro forma net loss per share applicable to common shareholders—basic and diluted(1) | | $ (0.43) | | $ (0.14) |
| Weighted-average number of common shares used in pro forma net loss per share applicable to common stockholders—basic and diluted | | 63,616,558 | | 64,321,374 |

(1) Pro forma net loss per share applicable to common shareholders gives effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 54,261,829 shares of common stock upon the closing of this offering.

| (in thousands) | As of March 31, 2013 Actual | Pro forma(1) | Pro forma as adjusted(2) |
|---|---|---|---|
| **Consolidated balance sheet data:** | | | |
| Cash, cash equivalents and marketable securities | $115,751 | $ 115,751 | $ |
| Total assets | $125,853 | $ 125,853 | $ |
| Total liabilities | $ 88,733 | $ 88,733 | $ 88,733 |
| Convertible preferred stock | $115,922 | $ — | $ — |
| Common stock | $ 10 | $ 64 | $ |
| Additional paid-in capital | $ 2,454 | $ 118,322 | $ |
| Accumulated deficit | $ (81,265) | $ (81,265) | $ (81,265) |
| Total stockholders' (deficit) equity | $ (78,802) | $ 37,120 | $ |

(1) The pro forma balance sheet data give effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 54,261,829 shares of common stock upon the closing of this offering.

(2) The pro forma as adjusted balance sheet data give effect to (i) our issuance and sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, the midpoint of the price range listed on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and (ii) our issuance and sale of shares of common stock in the concurrent private placement to Celgene at the assumed public offering price of $ per share. A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the range listed on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash, cash equivalents and marketable securities, total assets, additional paid-in capital and total stockholders' equity by approximately $ , assuming that (i) the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and (ii) the number of shares we issue and sell to Celgene in the concurrent private placement remains the same.

## Risk factors

*Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks described below, together with the other information contained in this prospectus, including our financial statements and the related notes appearing at the end of this prospectus. If any of the following risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.*

### Risks related to our financial position and need for additional capital

***We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.***

Since inception, we have incurred significant operating losses. Our net loss was $7.2 million, $20.1 million and $23.7 million for the three months ended March 31, 2013, and for the years ended December 31, 2012 and 2011, respectively. As of March 31, 2013, we had an accumulated deficit of $81.3 million. We have financed our operations primarily through private placements of our preferred stock and our collaboration with Celgene focused on cancer metabolism. We have devoted substantially all of our efforts to research and development. We have not initiated clinical development of any product candidates and expect that it will be many years, if ever, before we have a product candidate ready for commercialization. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- continue our research and preclinical development of our product candidates;
- seek to identify additional product candidates;
- initiate clinical trials for our product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control and scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts; and
- acquire or in-license other medicines and technologies.

To become and remain profitable, we must develop and eventually commercialize a medicine or medicines with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those medicines for which we may obtain marketing approval and satisfying any post-marketing requirements. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. We are currently only in the preclinical testing stages for our most advanced product candidates. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

***We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our product development programs or commercialization efforts.***

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of Celgene or other collaborators. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

We expect that the net proceeds from this offering and the concurrent private placement to Celgene, together with our existing cash, cash equivalents and marketable securities, anticipated interest income and anticipated expense reimbursements under our collaboration agreement with Celgene, will enable us to fund our operating expenses and capital expenditure requirements for at least the next months. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the success of our collaboration with Celgene;
- whether Celgene exercises either or both of its options to extend the discovery phase under our collaboration with Celgene (each of which would trigger an extension payment to us);
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval (to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of Celgene or other collaborators);
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- our ability to establish and maintain additional collaborations on favorable terms, if at all; and
- the extent to which we acquire or in-license other medicines and technologies.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

***Raising additional capital may cause dilution to our stockholders, including purchasers of common stock in this offering, restrict our operations or require us to relinquish rights to our technologies or product candidates.***

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing

arrangements. We do not have any committed external source of funds, other than our collaboration with Celgene, which is limited in scope and duration. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

***Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.***

We are an early-stage company. We were founded in the second half of 2007 and commenced operations in late 2008. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, acquiring and developing our technology, identifying potential product candidates and undertaking preclinical studies of our most advanced product candidates. All of our product candidates are still in preclinical development. We have not yet demonstrated our ability to initiate or successfully complete any clinical trials, including large-scale, pivotal clinical trials, obtain marketing approvals, manufacture a commercial scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about ten to 15 years to develop one new medicine from the time it is discovered to when it is available for treating patients. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

**Risks related to the discovery, development and commercialization of our product candidates**

***Our approach to the discovery and development of product candidates that target cellular metabolism is unproven, and we do not know whether we will be able to develop any medicines of commercial value.***

Our scientific approach focuses on using our proprietary technology to identify key metabolic enzymes in cancer, IEMs or other diseased cells in the laboratory and then using these key enzymes to screen for and identify product candidates targeting cellular metabolism.

Any medicines that we develop may not effectively correct metabolic pathways. Even if we are able to develop a product candidate that targets cellular metabolism in preclinical studies, we may not succeed in demonstrating safety and efficacy of the product candidate in human clinical trials. Our focus on using our proprietary technology to screen for and identify product candidates targeting cellular metabolism may not result in the discovery and development of commercially viable medicines to treat cancer or IEMs.

***We may not be successful in our efforts to identify or discover potential product candidates.***

A key element of our strategy is to identify and test compounds that target cellular metabolism in a variety of different types of cancer and IEMs. A significant portion of the research that we are conducting involves new

compounds and drug discovery methods, including our proprietary technology. The drug discovery that we are conducting using our proprietary technology may not be successful in identifying compounds that are useful in treating cancer or IEMs. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying appropriate biomarkers or potential product candidates; or
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be medicines that will receive marketing approval and achieve market acceptance.

Research programs to identify new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful.

If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to obtain product revenues in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

***We depend heavily on the success of our most advanced product candidates. All of our product candidates are still in preclinical development. Preclinical testing and clinical trials of our product candidates may not be successful. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.***

We have invested a significant portion of our efforts and financial resources in the identification of our most advanced product candidates, AG-221 and AG-120 for the treatment of hematological and solid tumors and AG-348 for the treatment of PK deficiency. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of these product candidates. The success of our product candidates will depend on many factors, including the following:

- successful enrollment in, and completion of, clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our medicines;
- launching commercial sales of the medicines, if and when approved, whether alone or in collaboration with others;
- acceptance of the medicines, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- a continued acceptable safety profile of the medicines following approval;
- enforcing and defending intellectual property rights and claims; and
- achieving desirable medicinal properties for the intended indications.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

***If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.***

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We or our collaborators may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate; enrollment in these clinical trials, which may be particularly challenging for some of the orphan diseases we target in our IEM program, may be slower than we anticipate; or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we might have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

If we or our collaborators are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we or our collaborators are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we or our collaborators may:

- be delayed in obtaining marketing approval for our product candidates;

- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;
- be subject to additional post-marketing testing requirements; or
- have the medicine removed from the market after obtaining marketing approval.

Product development costs will also increase if we or our collaborators experience delays in testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates, could allow our competitors to bring products to market before we do, and could impair our ability to successfully commercialize our product candidates, any of which may harm our business and results of operations.

***If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.***

We or our collaborators may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the U.S. Food and Drug Administration, or FDA, or analogous regulatory authorities outside the United States. Enrollment may be particularly challenging for some of the orphan diseases we target in our IEM program. In addition, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is also affected by other factors including:

- severity of the disease under investigation;
- availability and efficacy of approved medications for the disease under investigation;
- eligibility criteria for the study in question;
- perceived risks and benefits of the product candidate under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Our or our collaborators' inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

***If serious adverse side effects or unexpected characteristics are identified during the development of our product candidates, we may need to abandon or limit our development of some of our product candidates.***

All of our product candidates are still in preclinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. If our product candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or

subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. Many compounds that initially showed promise in early stage testing for treating cancer or other diseases have later been found to cause side effects that prevented further development of the compound.

***We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial medicines or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Under our collaboration agreement with Celgene, we have the right, exercisable during a specified period following FDA acceptance of the applicable investigational new drug application, or IND, to convert one of every three co-commercialized licensed programs into a split licensed program, for which we retain the United States rights. Our IDH2 program will not be a split licensed program. Due to the limited exercise period, we may have to choose whether a co-commercialized program will be a split licensed program before we have as much information as we would like on another co-commercialized program, including whether and when such program may receive FDA acceptance of the applicable IND. As a result of such incomplete information or due to incorrect analysis by us, we may select a split licensed program that later proves to have less commercial potential than an alternative or none at all.

***If we are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience significant delays in doing so, we may not realize the full commercial potential of our therapeutics.***

Because we are focused on precision medicine, in which predictive biomarkers will be used to identify the right patients for our drug candidates, we believe that our success may depend, in part, on our ability to develop companion diagnostics for these candidates. There has been limited success to date industrywide in developing these types of companion diagnostics. To be successful, we need to address a number of scientific, technical and logistical challenges. We have not yet initiated development of companion diagnostics. We have little experience in the development of diagnostics and may not be successful in developing appropriate diagnostics to pair with any of our therapeutic product candidates that receive marketing approval. Companion diagnostics are subject to regulation by the FDA and similar regulatory authorities outside the United States as medical devices and require separate regulatory approval prior to commercialization. Given our limited experience in developing diagnostics, we expect to rely in part or in whole on third parties for their design and manufacture. If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience delays in doing so:

- the development of our therapeutic product candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;
- our therapeutic product candidates may not receive marketing approval if safe and effective use of a therapeutic product candidate depends on an *in vitro* diagnostic; and
- we may not realize the full commercial potential of any therapeutics that receive marketing approval if, among other reasons, we are unable to appropriately select patients who are likely to benefit from therapy with our medicines.

As a result, our business would be harmed, possibly materially.

***Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.***

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our medicines for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

***If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.***

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved medicine for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to other third parties. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our medicines on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future medicines;
- the lack of complementary medicines to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market and sell any medicines that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our medicines effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

***We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.***

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the disease indications for which we are developing our product candidates, such as acute myelogenous leukemia and high risk myelodysplasia. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches, for example, in the area of IEMs. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

We are developing our initial product candidates for the treatment of cancer. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy, and cancer drugs are frequently prescribed off-label by healthcare professionals. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic products. This may make it difficult for us to achieve our business strategy of using our product candidates in combination with existing therapies or replacing existing therapies with our product candidates.

We are also pursuing product candidates to treat patients with IEMs. There are a variety of treatment options available, including a number of marketed enzyme replacement therapies, for treating patients with IEMs. In addition to currently marketed therapies, there are also a number of products that are either enzyme replacement therapies or gene therapies in various stages of clinical development to treat IEMs. These products in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain market approval.

There are also a number of product candidates in preclinical development by third parties to treat cancer and IEMs by targeting cellular metabolism. These companies include large pharmaceutical companies, including AstraZeneca plc, Eli Lilly and Company, Roche Holdings Inc. and its subsidiary Genentech, Inc., GlaxoSmithKline plc, Novartis International AG, Pfizer, Inc., and Genzyme, a Sanofi company. There are also biotechnology companies of various size that are developing therapies to target cellular metabolism, including Alexion Pharmaceuticals, Inc., BioMarin Pharmaceutical Inc., Calithera Biosciences, Inc., Cornerstone Pharmaceuticals, Inc., Forma Therapeutics Holdings LLC, and Shire Biochem Inc. Our competitors may develop products that are more effective, safer, more convenient or less costly than any that we are developing or that would render our product candidates obsolete or non-competitive. In addition, our competitors may discover

biomarkers that more efficiently measure metabolic pathways than our methods, which may give them a competitive advantage in developing potential products. Our competitors may also obtain marketing approval from the FDA or other regulatory authorities for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

***Even if we are able to commercialize any product candidates, such products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.***

The regulations that govern marketing approvals, pricing and reimbursement for new medicines vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a medicine before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a medicine in a particular country, but then be subject to price regulations that delay our commercial launch of the medicine, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the medicine in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any medicines successfully also will depend in part on the extent to which reimbursement for these medicines and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any medicine that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly approved medicines, and coverage may be more limited than the purposes for which the medicine is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that any medicine will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new medicines, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the medicine and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost

medicines and may be incorporated into existing payments for other services. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved medicines that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize medicines and our overall financial condition.

***Product liability lawsuits against us could cause us to incur substantial liabilities and could limit commercialization of any medicines that we may develop.***

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any medicines that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or medicines caused injuries, we could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or medicines that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any medicines that we may develop.

Although we maintain product liability insurance coverage, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage when we begin clinical trials and if we successfully commercialize any medicine. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

**Risks related to our dependence on third parties**

***We depend on our collaboration with Celgene and may depend on collaborations with additional third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.***

In April 2010, we entered into our collaboration with Celgene focused on cancer metabolism. The collaboration involves a complex allocation of rights, provides for milestone payments to us based on the achievement of specified clinical development, regulatory and commercial milestones, provides for additional payments upon Celgene's election to extend the term of the discovery phase and provides us with royalty-based revenue if certain product candidates are successfully commercialized. We cannot predict the success of the collaboration.

We may seek other third-party collaborators for the development and commercialization of our product candidates. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates, including our collaboration with Celgene, pose the following risks to us:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations. For example, under our collaboration with Celgene, development and commercialization plans and strategies for licensed programs will be conducted in accordance with a plan and budget approved by a joint committee comprised of equal numbers of representatives from each of us and Celgene.
- Collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities. For example, it is possible for Celgene to elect not to progress into preclinical development a product candidate that we have nominated and the joint research committee, or JRC, confirmed, without triggering a termination of the collaboration arrangement.
- Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing. For example, under our agreement with Celgene, it is possible for Celgene to terminate the agreement, upon 90 days prior written notice, with respect to any product candidate at any point in the research, development and clinical trial process, without triggering a termination of the remainder of the collaboration arrangement.
- Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our medicines or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.
- A collaborator with marketing and distribution rights to one or more medicines may not commit sufficient resources to the marketing and distribution of such medicine or medicines.

- Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation. For example, Celgene has the first right to maintain or defend our intellectual property rights under our collaboration arrangement with respect to certain licensed programs and, although we may have the right to assume the maintenance and defense of our intellectual property rights if Celgene does not, our ability to do so may be compromised by Celgene's actions.
- Disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our medicines or product candidates or that result in costly litigation or arbitration that diverts management attention and resources.
- We may lose certain valuable rights under circumstances identified in our collaborations, including, in the case of our agreement with Celgene, if we undergo a change of control.
- Collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates. For example, Celgene can terminate its agreement with us, in its entirety or with respect to any program, upon 90 days' notice and can terminate the entire agreement with us in connection with a material breach of the agreement by us that remains uncured for 60 days.
- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.

***We may seek to establish additional collaborations, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.***

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For some of our product candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. For example, during the discovery phase of our collaboration with Celgene, we may not directly or indirectly develop, manufacture or commercialize, except pursuant to the agreement, any medicine or product candidate for any cancer indication: with specified activity against certain metabolic targets except in connection with certain third party collaborations; or with specified activity against any collaboration target, or any target for which Celgene is conducting an independent program that we elected not to buy in to. Following the discovery phase until termination or expiration of the agreement, either in its entirety or with respect to the relevant program, we may not directly or indirectly develop, manufacture or

commercialize, outside of the collaboration, any medicine or product candidate with specified activity against any collaboration target that is within a licensed program or against any former collaboration target against which Celgene is conducting an independent program under the agreement.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

***We expect to rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.***

We expect to rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. We currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical testing. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

***We contract with third parties for the manufacture of our product candidates for preclinical testing and expect to continue to do so for clinical trials and for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or medicines or that such supply will not be available to us at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.***

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing and for commercial supply of any of these product candidates for which we or our collaborators obtain marketing approval. To date, we have obtained materials for AG-221 for our planned phase 1 testing from third party manufacturers. We have engaged third party manufacturers to obtain the active ingredient for AG-120 for pre-clinical and clinical testing. We do not have a long term supply agreement with the third-party manufacturers, and we purchase our required drug supply on a purchase order basis.

We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- reliance on the third party for regulatory compliance, quality assurance, and safety and pharmacovigilance reporting.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or medicines, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business and results of operations.

Any medicines that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply for bulk drug substances. If any one of our current contract manufacturer cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or medicines may adversely affect our future profit margins and our ability to commercialize any medicines that receive marketing approval on a timely and competitive basis.

**Risks related to our intellectual property**

***If we are unable to obtain and maintain patent or trade secret protection for our medicines and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize medicines and technology similar or identical to ours, and our ability to successfully commercialize our medicines and technology may be adversely affected.***

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary medicines and technology. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and medicines that are important to our business. To date, we do not own or have any rights to any issued patents that cover any of our proprietary technology or product candidates, and we cannot be certain that we will secure any rights to any issued patents with claims that cover any of our proprietary technology or product candidates.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

We may in the future license patent rights that are valuable to our business from third parties, in which event we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology or medicines underlying such licenses. We cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. If any such licensors fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our products that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties also apply to patent rights we own.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or medicines or which effectively prevent others from commercializing competitive technologies and medicines. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection.

The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore we cannot be certain that we were the first to make the inventions claimed in our owned or any licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, prior to March 2013, in the United States, the first to make the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. Beginning in March 2013, the United States transitioned to a first inventor to file system in which, assuming the other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent. We may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, revocation, reexamination,

post-grant and *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize medicines without infringing third-party patent rights.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us or otherwise provide us with any competitive advantage. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and medicines. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

***We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time consuming and unsuccessful.***

Competitors may infringe our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

***Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.***

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. We have in the past and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our medicines and technology, including interference proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third party’s intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our medicines and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us. We could be forced, including by court order, to cease developing and commercializing the infringing technology or medicine. In addition, we could be found liable for monetary damages. A finding of infringement could prevent

us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

***We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.***

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

***Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.***

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

***If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.***

In addition to seeking patents for some of our technology and medicines, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. With respect to our proprietary cellular metabolism technology platform, we consider trade secrets and know-how to be our primary intellectual property. Trade secrets and know-how can be difficult to protect. In particular, we anticipate that with respect to this technology platform, these trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel skilled in the art from academic to industry scientific positions.

We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or

independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be harmed.

**Risks related to regulatory approval of our product candidates and other legal compliance matters**

***If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.***

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by comparable authorities in other countries. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved medicine not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired.

***Failure to obtain marketing approval in international jurisdictions would prevent our medicines from being marketed in such jurisdictions.***

In order to market and sell our medicines in the European Union and many other jurisdictions, we or our third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the

FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our medicines in any market.

***Any product candidate for which we obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved.***

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such medicine, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine. The FDA closely regulates the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our medicines for their approved indications, we may be subject to enforcement action for off-label marketing.

In addition, later discovery of previously unknown problems with our medicines, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such medicines, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a medicine;
- restrictions on distribution or use of a medicine;
- requirements to conduct post-marketing clinical trials;
- warning or untitled letters;
- withdrawal of the medicines from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of medicines;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our medicines;
- product seizure; and
- injunctions or the imposition of civil or criminal penalties.

***Our relationships with customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with

third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal transparency requirements under the Affordable Care Act requires manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

***Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.***

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of

our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or Medicare Modernization Act, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payors.

More recently, in March 2010, President Obama signed into law the Affordable Care Act, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Effective October 1, 2010, the Affordable Care Act revises the definition of “average manufacturer price” for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. Substantial new provisions affecting compliance have also been enacted, which may affect our business practices with health care practitioners. We will not know the full effects of the Affordable Care Act until applicable federal and state agencies issue regulations or guidance under the new law. Although it is too early to determine the effect of the Affordable Care Act, the new law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA’s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

**Risks related to employee matters and managing growth**

***Our future success depends on our ability to retain our chief executive officer and other key executives and to attract, retain and motivate qualified personnel.***

We are highly dependent on David Schenkein, M.D., our chief executive officer, J. Duncan Higgons, our chief operating officer, and Scott Biller, Ph.D., our chief scientific officer, as well as the other principal members of our management and scientific teams. Drs. Schenkein and Biller, and Mr. Higgons are employed “at will,” meaning we or they may terminate the employment relationship at any time. We do not maintain “key person” insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also

experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, including our scientific co-founders, may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

***We expect to expand our development, regulatory and future sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expected expansion of our operations or recruit and train additional qualified personnel. Moreover, the expected physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

**Risks related to our common stock and this offering**

***After this offering and the concurrent private placement of common stock to Celgene, our executive officers, directors and principal stockholders will maintain the ability to control all matters submitted to stockholders for approval.***

Upon the closing of this offering and the concurrent private placement of common stock to Celgene, our executive officers, directors and stockholders who each owned more than 5% of our outstanding common stock before this offering will, in the aggregate, beneficially own shares representing approximately % of our capital stock. Assuming an initial offering price of $ per share, and assuming Celgene's purchase of shares in the concurrent private placement, the number of shares of our common stock beneficially owned by our executive officers, directors and stockholders who each owned more than 5% of our outstanding common stock before this offering and the concurrent private placement will, in the aggregate, equal % of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

***Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.***

Provisions in our corporate charter and our bylaws that will become effective upon the closing of this offering may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;

- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a shareholder rights plan, or so-called "poison pill," that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

***If you purchase shares of common stock in this offering, you will suffer immediate dilution of your investment.***

The initial public offering price of our common stock is substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after giving effect to this offering and the concurrent private placement to Celgene. To the extent shares are issued under outstanding options, you will incur further dilution. Based on an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, you will experience immediate dilution of $ per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the concurrent private placement at the assumed initial public offering price. In addition, purchasers of common stock in this offering will have contributed approximately % of the aggregate price paid by all purchasers of our stock but will own only approximately % of our common stock outstanding after this offering and the concurrent private placement.

***An active trading market for our common stock may not develop.***

Prior to this offering, there has been no public market for our common stock. The initial public offering price for our common stock will be determined through negotiations with the underwriters. Although we intend to apply to list our common stock on The NASDAQ Global Market, an active trading market for our shares may never develop or be sustained following this offering. If an active market for our common stock does not develop, it may be difficult for you to sell shares you purchase in this offering without depressing the market price for the shares or at all.

***If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.***

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease.

Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

***The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock in this offering.***

Our stock price is likely to be volatile. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including:

- the success of competitive products or technologies;
- results of clinical trials of our product candidates or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional product candidates or medicines;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk factors” section.

***We have broad discretion in the use of the net proceeds from this offering and the concurrent private placement of common stock to Celgene and may not use them effectively.***

Our management will have broad discretion in the application of the net proceeds from this offering and the concurrent private placement of common stock to Celgene and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses, and these financial losses could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from this offering and the concurrent private placement in a manner that does not produce income or that loses value.

***We are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.***

We are an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company for up to five years. For so long as we remain an

emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- providing only two years of audited financial statements in addition to any required unaudited interim financial statements and a correspondingly reduced "Management's discussion and analysis of financial condition and results of operations" disclosure;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In this prospectus, we have not included all of the executive compensation-related information that would be required if we were not an emerging growth company.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of reduced reporting burdens in this prospectus. In particular, we have provided only two years of audited financial statements and have not included all of the executive compensation information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

***We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.***

As a public company, and particularly after we are no longer an "emerging growth company," we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the Securities and Exchange Commission and NASDAQ have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve

compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

***Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.***

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

***A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.***

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. After this offering and the concurrent private placement of common stock to Celgene, we will have outstanding shares of common stock based on the number of shares outstanding as of , 2013. This includes the shares that we are selling in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates. Of the remaining shares, shares are currently restricted as a result of securities laws or lock-up agreements but will be able to be sold after the offering as described in the “Shares eligible for future sale” section of this prospectus. Moreover, after this offering and the concurrent private placement, holders of an aggregate of shares of our common stock will have rights, subject to some conditions, to require us to file registration statements covering their shares or, along with holders of an additional shares of our common stock, to include their shares in registration statements that we may file for ourselves or other stockholders. We also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the “Underwriting” section of this prospectus.

## Cautionary note regarding forward-looking statements

This prospectus contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this prospectus, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

- the initiation, timing, progress and results of future preclinical studies and clinical trials, and our research and development programs;
- our plans to develop and commercialize our product candidates;
- the timing or likelihood of regulatory filings and approvals;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the rate and degree of market acceptance and clinical utility of our medicines;
- our competitive position;
- our intellectual property position;
- developments and projections relating to our competitors and our industry;
- our ability to maintain and establish collaborations or obtain additional funding;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;
- our expectations related to the use of proceeds from this offering and the concurrent private placement of common stock to Celgene; and
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus, particularly in the “Risk factors” section, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.

You should read this prospectus, the documents that we reference in this prospectus and the documents that we have filed as exhibits to the registration statement of which this prospectus is a part completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

## Use of proceeds

We estimate that the net proceeds from our issuance and sale of shares of our common stock in this offering will be approximately $ million, assuming an initial public offering price of $ per share, which is the midpoint of the range listed on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that our net proceeds will be approximately $ million. We will also receive $ million from the sale of shares of common stock in the concurrent private placement to Celgene.

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share would increase (decrease) the aggregate net proceeds to us from this offering and the concurrent private placement by approximately $ million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

As of March 31, 2013, we had cash, cash equivalents and marketable securities of $115.8 million. We intend to use the net proceeds to us from this offering and the concurrent private placement, together with our existing cash resources, as follows:

- approximately $ to fund clinical development of our lead product candidates in our cancer and IEM programs;
- approximately $ to fund research and development to advance our pipeline of preclinical product candidates; and
- approximately $ for working capital and other general corporate purposes, including potential acquisitions.

This expected use of net proceeds from this offering and the concurrent private placement of common stock represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, the status of and results from clinical trials, as well as any additional collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering and the concurrent private placement.

We believe opportunities may exist from time to time to expand our current business through acquisitions or in-licenses of complementary companies, medicines or technologies. While we have no current agreements, commitments or understandings for any specific acquisitions or in-licenses at this time, we may use a portion of the net proceeds for these purposes.

Pending use of the proceeds as described above, we intend to invest the proceeds in a variety of capital preservation investments, including short-term, interest-bearing, investment-grade instruments and U.S. government securities.

## Dividend policy

We have not declared or paid any cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends to holders of common stock in the foreseeable future.

## Industry and other data

We obtained the industry, market and competitive position data in this prospectus from our own internal estimates and research as well as from industry and general publications and research, surveys and studies conducted by third parties. Industry publications, studies and surveys generally state that they have been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. While we believe that each of these studies and publications is reliable, we have not independently verified market and industry data from third-party sources. While we believe our internal company research is reliable and that our internal estimates are reasonable, neither such research nor these definitions have been verified by any independent source.

## Capitalization

The following table sets forth our cash, cash equivalents and marketable securities and capitalization as of March 31, 2013, as follows:

- on an actual basis;
- on a pro forma basis to reflect (i) the automatic conversion of all outstanding shares of our preferred stock into 54,261,829 shares of common stock upon the closing of this offering and (ii) the filing of our restated certificate of incorporation as of the closing date of this offering; and
- on a pro forma as adjusted basis to give further effect to (i) our issuance and sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, the midpoint of the price range listed on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, and (ii) our issuance and sale of shares of common stock in the concurrent private placement to Celgene at the assumed public offering price of $ per share.

Our capitalization following the closing of this offering will be adjusted based on the actual initial public offering price and other terms of the offering determined at pricing. You should read this information in conjunction with our consolidated financial statements and the related notes appearing at the end of this prospectus and the "Management's discussion and analysis of financial condition and results of operations" section and other financial information contained in this prospectus.

| | As of March 31, 2013 | | |
|---|---|---|---|
| (in thousands, except share and per share data) | Actual | Pro forma | Pro forma as adjusted(1) |
| Cash, cash equivalents and marketable securities | $115,751 | $115,751 | $ |
| Series A convertible preferred stock, par value $0.001 per share; 33,188,889 shares authorized, 33,188,889 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted | $ 32,940 | $ — | $ — |
| Series B convertible preferred stock, par value $0.001 per share; 5,190,551 shares authorized, 5,190,551 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted | 5,681 | — | — |
| Series C-1 convertible preferred stock, par value $0.001 per share; 7,395,829 shares authorized, 7,395,829 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted | 36,133 | — | — |
| Series C-2 convertible preferred stock, par value $0.001 per share; 8,486,560 shares authorized, 8,486,560 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted | 41,168 | — | — |
| Preferred stock, par value $0.001 per share; no shares authorized, issued or outstanding, actual; 25,000,000 shares authorized and no shares issued or outstanding, pro forma and pro forma as adjusted | — | — | — |
| Common stock, par value $0.001 per share; 78,300,000 shares authorized, 10,124,595 shares issued and outstanding, actual; 125,000,000 shares authorized, pro forma and pro forma as adjusted; 64,386,424 shares issued and outstanding, pro forma; shares issued and outstanding, pro forma as adjusted | 10 | 64 | |
| Additional paid-in capital | 2,454 | 118,322 | |
| Accumulated other comprehensive loss | (1) | (1) | |
| Accumulated deficit | (81,265) | (81,265) | |
| Total stockholders' (deficit) equity | (78,802) | 37,120 | |
| Total capitalization | $ 37,120 | $ 37,120 | $ |

(1) The closing of this offering is not contingent upon the closing of such concurrent private placement with Celgene. A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the range listed on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash, cash equivalents and marketable securities, additional paid-in capital, total stockholders' equity and total capitalization by approximately $ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus and in the concurrent private placement, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The table above does not include:

- 8,497,274 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2013, at a weighted-average exercise price of $0.31 per share;
- 1,991,498 shares of common stock reserved as of March 31, 2013, for future issuance under our 2007 stock incentive plan; and
- additional shares of our common stock that will be available for future issuance, as of the closing of this offering, under our 2013 stock incentive plan and our 2013 employee stock purchase plan.

## Dilution

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the initial public offering price per share and the pro forma as adjusted net tangible book value per share of our common stock after this offering.

Our historical net tangible book value as of March 31, 2013 was approximately $37.1 million, or $0.58 per share of common stock. Our historical net tangible book value is the amount of our total tangible assets less our total liabilities. Net historical tangible book value per share is our historical net tangible book value divided by the number of shares of common stock outstanding as of March 31, 2013.

Our pro forma net tangible book value as of March 31, 2013 was $ million, or $ per share of common stock. Pro forma net tangible book value gives effect to (i) the conversion of all of our outstanding convertible preferred stock into an aggregate of 54,261,829 shares of our common stock which will occur automatically upon the completion of this offering, and (ii) the sale by us in the private placement to Celgene of $ million of our common stock concurrently with the completion of this offering at the assumed public offering price of $ per share.

Pro forma as adjusted net book value is our pro forma net tangible book value, plus the effect of the sale of shares of our common stock in this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. This amount represents an immediate increase in pro forma as adjusted net tangible book value of $ per share to our existing stockholders, and an immediate dilution of $ per share to new investors participating in this offering.

The following table illustrates this dilution on a per share basis:

| | | |
|---|---|---|
| Assumed initial public offering price per share | | $ |
| Historical net tangible book value per share as of March 31, 2013 | $ 0.58 | |
| Pro forma increase in net tangible book value per share as of March 31, 2013 attributable to the conversion of convertible preferred stock and concurrent private placement described in previous paragraph | | |
| Pro forma net tangible book value per share as of March 31, 2013, before giving effect to this offering | | |
| Increase in pro forma net tangible book value per share attributable to new investors participating in this offering | | |
| Pro forma as adjusted net tangible book value per share after this offering | | |
| Dilution per share to new investors | | $ |

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value (deficit) per share after this offering by approximately $ per share and the dilution per share to investors participating in this offering by approximately $ per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

The following table summarizes, on a pro forma basis as of March 31, 2013, the total number of shares purchased from us, the total consideration paid, or to be paid, and the average price per share paid, or to be paid, by existing stockholders (including the shares of common stock purchased by Celgene in the private placement) and by new investors in this offering at an assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, before deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. As the table below

shows, new investors purchasing shares in this offering will pay an average price per share substantially higher than our existing stockholders paid.

| | Shares purchased | | Total consideration | | Average price per share |
|---|---|---|---|---|---|
| | Number | Percent | Amount | Percent | |
| Existing stockholders | | % | $ | % | $ |
| Investors participating in this offering | | | | | |
| Total | | 100% | $ | 100% | $ |

A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the total consideration paid by new investors by $ , and increase (decrease) the percentage of total consideration paid by new investors by approximately %, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and before deducting the estimated underwriting discounts and commissions and estimated offering costs payable by us.

Except as otherwise indicated, the discussion and tables above assume no exercise of the underwriters' option to purchase additional shares of our common stock in this offering and no exercise of any outstanding options. If the underwriters' option to purchase additional shares is exercised in full:

- the percentage of outstanding common stock held by existing stockholders will be reduced to % of the total number of shares of common stock to be outstanding upon completion of this offering; and
- the number of shares of common stock held by investors participating in this offering will be increased to shares, or % of the total number of shares of common stock to be outstanding upon completion of this offering.

The foregoing discussion and tables are based on the number of shares of common stock outstanding as of March 31, 2013, and excludes:

- 8,497,274 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2013, at a weighted-average exercise price of $0.31 per share;
- 1,991,498 shares of common stock reserved as of March 31, 2013 for future issuance under our 2007 stock incentive plan; and
- additional shares of our common stock that will be available for future issuance, as of the closing of this offering, under our 2013 stock incentive plan and our 2013 employee stock purchase plan.

To the extent any of these outstanding options is exercised, there will be further dilution to new investors. To the extent all of such outstanding options had been exercised as of March 31, 2013, the pro forma as adjusted net tangible book value per share after this offering would be $ , and total dilution per share to new investors would be $ .

Effective immediately upon closing of this offering, an aggregate of shares of our common stock will be reserved for issuance under our stock-based compensation plans, and these share reserves will also be subject to automatic annual increases in accordance with the terms of the plans. Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that any of these options are exercised, new options are issued under our equity incentive plans or we issue additional shares of common stock or other equity or convertible debt securities in the future, there will be further dilution to investors participating in this offering.

## Selected consolidated financial data

You should read the following selected consolidated financial data in conjunction with "Management's discussion and analysis of financial condition and results of operations" and our consolidated financial statements and the related notes appearing elsewhere in this prospectus.

The consolidated statements of operations data for the years ended December 31, 2011 and 2012 and the consolidated balance sheet data at December 31, 2011 and 2012, are derived from our audited consolidated financial statements appearing elsewhere in this prospectus. The consolidated statements of operations data for the three months ended March 31, 2012 and 2013 and the consolidated balance sheet data at March 31, 2013 are derived from our unaudited consolidated financial statements included in this prospectus. The unaudited consolidated financial statements include, in the opinion of management, all adjustments that management considers necessary for the fair presentation of the financial information set forth in those statements. Our historical results are not necessarily indicative of the results to be expected in any future period.

| (in thousands, except share and per share data) | Years ended December 31, | | Three months ended March 31, | |
|---|---|---|---|---|
| | 2011 | 2012 | 2012 | 2013 |
| **Consolidated statement of operations data:** | | | | |
| Revenue | $ 21,837 | $ 25,106 | $ 6,268 | $ 6,268 |
| Operating expenses: | | | | |
| Research and development | 31,253 | 41,037 | 9,551 | 11,462 |
| General and administrative | 7,215 | 7,064 | 1,981 | 1,852 |
| Total operating costs | 38,468 | 48,101 | 11,532 | 13,314 |
| Loss from operations | (16,631) | (22,995) | (5,264) | (7,046) |
| Investment income | 132 | 69 | 26 | 8 |
| Loss before provision (benefit) for income taxes | (16,499) | (22,926) | (5,238) | (7,038) |
| Provision (benefit) for income taxes | 7,207 | (2,824) | (607) | 190 |
| Net loss | (23,706) | (20,102) | (4,631) | (7,228) |
| Cumulative preferred stock dividends | (3,100) | (7,190) | (1,798) | (1,798) |
| Net loss applicable to common stockholders | $ (26,806) | $ (27,292) | $ (6,429) | $ (9,026) |
| Net loss per share applicable to common shareholders—basic and diluted | $ (3.23) | $ (2.92) | $ (0.72) | $ (0.90) |
| Weighted-average number of common shares used in net loss per share applicable to common stockholders—basic and diluted | 8,286,757 | 9,354,729 | 8,928,822 | 10,059,545 |
| Pro forma net loss per share applicable to common shareholders—basic and diluted(1) | | $ (0.43) | | $ (0.14) |
| Weighted-average number of common shares used in pro forma net loss per share applicable to common stockholders—basic and diluted | | 63,616,558 | | 64,321,374 |

(1) Pro forma net loss per share applicable to common shareholders gives effect to the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 54,261,829 shares of common stock upon the closing of this offering.

| (in thousands) | As of December 31, 2011 Actual | As of December 31, 2012 Actual | As of March 31, 2013 Actual | As of March 31, 2013 Pro forma(1) | As of March 31, 2013 Pro forma as adjusted(2) |
|---|---|---|---|---|---|
| **Consolidated balance sheet data:** | | | | | |
| Cash, cash equivalents and marketable securities | $179,168 | $127,976 | $115,751 | $ 115,751 | $ |
| Total assets | $194,470 | $137,008 | $125,853 | $ 125,853 | $ |
| Total liabilities | $131,330 | $ 93,110 | $ 88,733 | $ 88,733 | $ 88,733 |
| Convertible preferred stock | $115,922 | $115,922 | $115,922 | $ — | $ — |
| Common stock | $ 9 | $ 10 | $ 10 | $ 64 | $ |
| Additional paid-in capital | $ 1,121 | $ 2,005 | $ 2,454 | $ 118,322 | $ |
| Accumulated deficit | $ (53,935) | $ (74,037) | $ (81,265) | $ (81,265) | $ (81,265) |
| Total stockholders' (deficit) equity | $ (52,782) | $ (72,024) | $ (78,802) | $ 37,120 | $ |

(1) The pro forma balance sheet data give effect to the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 54,261,829 shares of common stock upon the closing of this offering.

(2) The pro forma as adjusted balance sheet data gives effect to (i) our issuance and sale of shares of common stock at an assumed initial public offering price of $ per share, the midpoint of the price range listed on the cover page of this prospectus, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us and (ii) our issuance and sale of shares of common stock in the concurrent private placement to Celgene at the assumed public offering price of $ per share. A $1.00 increase (decrease) in the assumed initial public offering price of $ per share, which is the midpoint of the range listed on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash, cash equivalents and marketable securities, total assets, additional paid-in capital and total stockholders' equity by approximately $ , assuming (i) that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us and (ii) the number of shares we issue and sell to Celgene in the concurrent private placement remains the same.

## Management's discussion and analysis of financial condition and results of operations

*You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes and other financial information included elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. You should review the "Risk factors" section of this prospectus for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.*

### Overview

We are a biopharmaceutical company passionately committed to applying our scientific leadership in the field of cellular metabolism to transform the lives of patients with cancer and inborn errors of metabolism, or IEMs, which are a subset of orphan genetic metabolic diseases. Metabolism is a complex biological process involving the uptake and assimilation of nutrients in cells to produce energy and facilitate many of the processes required for cellular division and growth. We believe that dysregulation of normal cellular metabolism plays a crucial role in many diseases, including certain cancers and IEMs. We believe Agios is a first mover in using cellular metabolism, an unexploited area of biological research with disruptive potential as a platform for developing potentially transformative medicines. Our singular focus is to apply our expertise in cellular metabolism to develop innovative small molecule treatments for cancer and IEMs. The lead product candidates in our most advanced programs are aimed at druggable targets which have undergone rigorous validation processes. Our most advanced cancer product candidates, AG-221 and AG-120, which target mutant IDH2 and IDH1, respectively, have demonstrated strong proof of concept in preclinical models and are expected to enter the clinic in mid-2013 and early 2014, respectively. The lead candidate in our IEM program, AG-348, targets pyruvate kinase and is expected to commence clinical development in 2014.

Our initial therapeutic area of focus is cancer. We are leveraging our expertise in metabolic pathways to discover, validate, develop and commercialize a pipeline of novel drug candidates. In April 2010, we entered into a collaboration agreement with Celgene focused on cancer metabolism. Under the collaboration, we are leading discovery, preclinical and early clinical development for all cancer metabolism programs. The discovery phase of the collaboration expires in April 2014, subject to Celgene's option to extend the discovery phase for up to two additional years. Celgene has the option to obtain exclusive rights for the further development and commercialization of certain of these programs, and we will retain rights to the others. For the programs that Celgene chooses to license, we may elect to participate in a portion of sales activities for the medicines from such programs in the United States. For certain of these programs, we may elect to retain full rights to develop and commercialize medicines from these programs in the United States. Through March 31, 2013, we have received approximately $141.2 million in payments from Celgene and $37.5 million in equity investments. We are also eligible to receive extension payments, payments upon the successful achievement of specified milestones, reimbursements for certain development expenses and royalties on any product sales.

Since inception, our operations have focused on organizing and staffing our company, business planning, raising capital, assembling our core capabilities in cellular metabolism, identifying potential product candidates, undertaking preclinical studies and, anticipated to begin in mid-2013, conducting a clinical trial. To date, we have financed our operations primarily through funding received from our collaboration agreement with Celgene and private placements of our preferred stock. Substantially all of our revenue to date has been collaboration revenue. Since our inception, and through March 31, 2013, we have raised an aggregate of approximately $261.2 million to fund our operations, of which approximately $141.2 million was through upfront and extension payments related to our collaboration agreement with Celgene, and approximately $120.0 million was from the issuance of preferred stock.

Since inception, we have incurred significant operating losses. Our net losses were $7.2 million, $20.1 million and $23.7 million for the three months ended March 31, 2013 and for the years ended December 31, 2012 and 2011, respectively. As of March 31, 2013, we had an accumulated deficit of $81.3 million. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and from year to year. We anticipate that our expenses will increase significantly as we commence the planned IND-enabling and clinical development activities for our lead programs AG-221, AG-120, and AG-348; continue to discover, validate and drug additional novel product candidates; expand and protect our intellectual property portfolio; and hire additional development and scientific personnel. In addition, upon the closing of this offering we expect to incur additional costs associated with operating as a public company.

**Financial operations overview**

***Revenue***

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products in the near future. All of our revenue to date has been derived from our collaboration with Celgene and funding from research grant agreements. Under our Celgene collaboration we are recognizing revenue related to the upfront license fee of $121.2 million, the implied premium of $3.1 million paid on the purchase of $8.8 million of series B convertible preferred stock and the $20.0 million extension payment received in October 2011 to extend the discovery phase until April 2014, ratably over the period over which we expect to fulfill our performance obligations, which we refer to as the performance period. As of March 31, 2013, we have not received any milestone or royalty payments under the Celgene collaboration. We expect that any revenue we generate from our collaboration agreement will fluctuate from quarter to quarter as a result of the uncertain timing and amount of milestone payments, royalties and other payments.

In the future, we will seek to generate revenue from a combination of product sales and extension payments, milestone payments, and royalties on future product sales in connection with Celgene, or other strategic relationships.

***Research and development expenses***

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, and the development of our product candidates, which include:

- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- expenses incurred under agreements with third parties, including contract research organizations, or CROs, that conduct research and development and preclinical activities on our behalf and the cost of consultants;
- the cost of lab supplies and acquiring, developing, and manufacturing preclinical study materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other operating costs.

Research and development costs are expensed as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

The following summarizes our most advanced current research and development programs.

***AG-221: lead IDH2 program***

AG-221 is an orally available, selective, potent inhibitor of the mutated IDH2 protein, making it a highly targeted therapeutic candidate for the treatment of patients with cancers that harbor IDH2 mutations. In September 2012,

AG-221 successfully completed the development candidate requirements pursuant to our Celgene collaboration and in late April 2013 substantially completed IND-enabling studies. We believe AG-221 has demonstrated a clear safety profile to advance into clinical trials and we expect to enter the clinic in mid-2013. Celgene has the exclusive option to license worldwide development and commercial rights to AG-221 and if Celgene elects this option it would be responsible for all future development and commercialization costs.

***AG-120: lead IDH1 program***

AG-120 is an orally available, selective, potent inhibitor of the mutated IDH1 protein, making it a highly targeted therapeutic candidate for the treatment of patients with cancers that harbor IDH1 mutations. In March 2013, AG-221 successfully completed the development candidate requirements pursuant to our Celgene collaboration and has initiated IND-enabling studies. We expect to enter the clinic in early 2014. Celgene has the exclusive option to license development and commercialization rights to AG-120, in which case, we have the option to retain U.S. development and commercialization rights. If Celgene exercises such option and we elect to retain U.S. rights, we and Celgene will equally fund the global development costs of AG-120 that are not specific to any particular region or country, Celgene will be responsible for development and commercialization costs specific to countries outside the United States, and we will be responsible for development and commercialization costs specific to the United States.

***AG-348: pyruvate kinase deficiency program***

Our lead IEM program relates to certain genetic defects of the pyruvate kinase enzyme causing a form of hemolytic anemia known as pyruvate kinase deficiency, or PK deficiency. AG-348 is an orally available, potent small molecule activator of the PKR enzyme, an isoform of PK that when mutated leads to PK deficiency, making AG-348 a highly targeted therapeutic candidate for the treatment of patients with PK deficiency. In May 2013, AG-348 successfully completed our internal development candidate requirements, which include two species of exploratory safety studies, and has initiated IND-enabling studies. We expect to enter the clinic in 2014. We have retained worldwide development and commercial rights to AG-348 and expect to fund the future development and commercialization costs related to this program.

***Other research and platform programs***

Other research and platform programs include activities related to exploratory efforts, target validation, lead optimization for our earlier validated programs and our proprietary metabolomics platform.

We began tracking our internal and external research and development costs on a program-by-program basis in 2011. As such, we do not have historical research and development expenditures by program prior to January 1, 2011. We use our employee and infrastructure resources across multiple research and development programs, and we allocate internal employee-related and infrastructure costs, as well as certain third party costs, to each of these programs based on the personnel resources allocated to such program. Our research and development expenses, by major program, are outlined in the table below:

| | Years ended, December 31, | | Three months ended, March 31, | |
|---|---|---|---|---|
| (in thousands) | 2011 | 2012 | 2012 | 2013 |
| IDH2 (AG-221) | $ 4,674 | $ 9,418 | $2,330 | $ 2,486 |
| IDH1 (AG-120) | 9,045 | 10,785 | 2,926 | 2,734 |
| PK deficiency (AG-348) | 3,995 | 5,005 | 1,176 | 1,200 |
| Other research and platform programs | 13,539 | 15,829 | 3,119 | 5,042 |
| Total research and development expenses | $31,253 | $41,037 | $9,551 | $11,462 |

The successful development of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to

complete the remainder of the development of these product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from AG-221, AG-120, or AG-348. This is due to the numerous risks and uncertainties associated with developing medicines, including the uncertainty of:

- establishing an appropriate safety profile with IND-enabling toxicology studies;
- successful enrollment in, and completion of clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others; and
- a continued acceptable safety profile of the products following approval.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs and timing associated with the development of that product candidate.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our product candidate development programs progress. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

***General and administrative expenses***

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, business development, legal and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities, potential commercialization of our product candidates and increased costs of operating as a public company. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. Additionally, we anticipate increased costs associated with being a public company including expenses related to services associated with maintaining compliance with exchange listing and Securities and Exchange Commission requirements, insurance, and investor relations costs.

**Critical accounting policies and estimates**

Our discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which we have prepared in accordance with United States generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and

liabilities at the date of the financial statements, as well as the reported amounts of revenues and expenses during the reporting periods. On an ongoing basis, we evaluate our estimates and judgments, including those described in greater detail below. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements included elsewhere in this prospectus, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

***Revenue recognition***

To date, our revenues have been generated primarily from our collaboration agreement with Celgene.

For multiple-element arrangements entered into prior to January 1, 2011 and not materially modified thereafter, including the Celgene agreement, we recognize revenue in accordance with Accounting Standards Codification, or ASC, 605, *Revenue Recognition*. When evaluating multiple element arrangements, we consider whether the deliverables in the arrangement should be accounted for as separate units of accounting. In making this determination we evaluate whether (1) the elements have stand-alone value, and (2) if we are able to estimate the fair value of all undelivered elements under the arrangement. Revenue is then recognized for each unit of accounting when all of the following criteria are met:

- persuasive evidence of an arrangement exists;
- delivery has occurred or services have been rendered;
- the seller's price to the buyer is fixed or determinable; and
- collectability is reasonably assured.

We concluded that there is one unit of accounting for the Celgene agreement and we are recording revenue over the period over which we expect to fulfill our performance obligations under our agreement, which we refer to as the performance period. We estimate the performance period based upon the length of the discovery phase of our agreements, and our expectations regarding the collaborator's ability and intent of exercising its option to extend the research term, as applicable, pursuant to the provisions of the respective agreement. Our estimates of our performance period may change over the course of the research term. Such a change could have a material impact on the amount of revenue we record in future periods. Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue on our consolidated balance sheets.

In January 2011, we adopted the Financial Accounting Standards Board's (FASB) Accounting Standards Update (ASU) No. 2009-13, *Multiple-Element Revenue Arrangements*, on a prospective basis, which we will apply to all revenue arrangements entered into or materially modified after the adoption date. When evaluating multiple element arrangements pursuant to ASU 2009-13, we consider whether the deliverables in the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including:

- Whether the delivered item or items have value to the customer on a standalone basis, and
- If the arrangement includes a general right of return relative to the delivered item or items, delivery or performance of the undelivered item or items is considered probable and substantially in the control of the vendor.

The arrangement consideration is then allocated to each separately identified unit of accounting based on the relative selling price of each deliverable, and the applicable revenue recognition criteria, as described above, are applied to each of the units of accounting. In the event that an element of a multiple element arrangement does not represent a separate unit of accounting, we recognize revenue from the combined element over the period over which we expect to fulfill our performance obligations or as undelivered items are delivered, as appropriate.

On January 1, 2011, we adopted ASU 2010-17, *Revenue Recognition-Milestone Method*, on a prospective basis. At the inception of each agreement that includes milestone payments, we evaluate whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the degree of certainty in achieving the milestone, the research and development risk and other risks that must be overcome to achieve the milestone, as well as the level of effort and investment required and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement. The conclusion as to whether milestone payments are substantive involves management judgment regarding the factors noted above.

We classify each of our milestones into one of three categories: (i) clinical development milestones, (ii) regulatory milestones, and (iii) commercial milestones. Clinical development milestones are typically achieved when a product candidate advances into a defined phase of clinical research or completes such phase. For example, a milestone payment may be due to us upon the initiation of a phase 3 clinical trial, which is the last phase of clinical development and could eventually contribute to marketing approval by the FDA or other regulatory authorities. Regulatory milestones are typically achieved upon acceptance of the submission for marketing approval of a product candidate or upon approval to market the product candidate by the FDA or other regulatory authorities. For example, a milestone payment may be due to us upon the FDA's acceptance of an NDA. Commercial milestones are typically achieved when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee, such as when a product first achieves global sales or annual sales of a specified amount.

We have not earned any milestone payments pursuant to the Celgene agreement to date. We have concluded that certain of the clinical development and regulatory milestones that may be received under the Celgene Agreement are substantive. Revenues from milestones, if they are nonrefundable and deemed substantive, are recognized upon successful accomplishment of the milestones. To the extent that non-substantive milestones are achieved and we have remaining performance obligations, milestones are deferred and recognized as revenue over the estimated remaining period of performance. We will recognize revenue associated with the non-substantive milestones upon achievement of the milestone if there are no undelivered elements and we have no remaining performance obligations. We will account for sales-based milestones as royalties, with revenue recognized upon achievement of the milestone.

***Income taxes***

We account for uncertain tax positions in accordance with the provisions of Topic ASC 740, *Accounting for Income Taxes.* When uncertain tax positions exist, we recognize the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of March 31, 2013, we do not have any significant uncertain tax positions.

Income taxes are recorded in accordance with ASC 740, *Accounting for Income Taxes*, which provides for deferred taxes using an asset and liability approach. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. We determine our deferred tax assets and liabilities based on differences between financial reporting and tax bases of

assets and liabilities, which are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Valuation allowances are provided, if based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

As required by ASC 740, *Income Taxes*, our management has evaluated the positive and negative evidence bearing upon the realizability of our deferred tax assets, which are comprised principally of timing differences related to the recognition of revenue under our collaboration agreement with Celgene for book versus tax purposes. During the year ended December 31, 2011, our management determined that it was more likely than not that we would realize a portion of our deferred tax assets because of our ability to carryback future losses for U.S. federal income tax purposes. As a result, we reversed approximately $10.7 million of our valuation allowance in the year ended December 31, 2011, representing the amount of deferred tax assets that will be realized in 2012 and 2013, the years available for carryback. We utilized certain of our deferred tax assets, including net operating losses, or NOLs, generated in the year ended December 31, 2012 to reduce our 2011 U.S. federal income tax liability. For the remainder of our deferred tax assets, our management has determined that it is more likely than not that we may not realize the benefit and we have recorded a valuation allowance of approximately $31.8 million at December 31, 2012.

During the years ended December 31, 2011 and 2012 and the three months ended March 31, 2012 and 2013, we had $284,000, $583,000, $38,000 and $190,000 accrued for interest and penalties related to the non-payment of U.S. federal income taxes, respectively, that are recorded in the provision (benefit) for income taxes in the statements of operations.

As of December 31, 2012, we had net operating loss carryforwards to reduce federal and state incomes taxes of approximately $0.5 million and $28.8 million, respectively. If not utilized, these carryforwards expire at various dates through 2032. At December 31, 2012, we also had available research and development tax credits for federal and state income tax purposes of approximately $27,000 and $616,000, respectively. During 2011, we conducted a study of our research and development credit carryforwards. The study resulted in an adjustment to our research and development credit carryforward, as we do not believe that these credits are more likely than not to be realized. Additionally, utilization of the NOL carryforwards and credits may be subject to annual limitations as prescribed by federal and state statutory provisions. The annual limitation may result in the expiration of NOL carryforwards prior to their utilization.

Utilization of the NOLs and tax credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future, as provided by Section 382 of the Internal Revenue Code of 1986 (Section 382), as well as similar state provisions. Ownership changes may limit the amount of NOLs and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions that increase the ownership of 5% shareholders in the stock of a corporation by more than 50 percent in the aggregate over a three-year period. During 2011, we completed a study through December 31, 2011, to determine whether any ownership change has occurred since our formation and have determined that transactions have resulted in two ownership changes, as defined by Section 382. The impact of the ownership changes was reflected in our deferred tax assets in the year ended December 31, 2011. There could be additional ownership changes in the future that could further limit the amount of NOLs and tax credit carryforwards that we can utilize.

***Accrued research and development expenses***

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and

circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include fees paid to CROs in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to CROs on our estimates of the services received and efforts expended pursuant to quotes and contracts with CROs that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could result in us reporting amounts that are too high or too low in any particular period.

***Stock-based compensation***

We apply the fair value recognition provisions of Financial Accounting Standards Board Accounting Standards Codification Topic 718, *Compensation-Stock Compensation*, which we refer to as ASC 718, to account for stock-based compensation. We recognize stock-based compensation expense related to stock options granted to employees and directors for their services on the Board of Directors based on the estimated fair value of each stock option on the date of grant, net of estimated forfeitures, using the Black-Scholes option-pricing model. The grant date fair value of awards subject to service-based vesting, net of estimated forfeitures, is recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards. In accordance with the ASC 718, stock options subject to both performance- and service-based vesting conditions are recognized using an accelerated recognition model.

We account for stock options granted to non-employees, which primarily consist of consultants and members of our scientific advisory board, using the fair value method. Stock options granted to non-employees are subject to periodic revaluation over their vesting terms and stock-based compensation expense is recognized using an accelerated recognition model.

We use the Black-Scholes option pricing model to estimate the fair value of stock option awards using various assumptions that require management to apply judgment and make estimates, including:

- the expected term of the stock option award, which we calculate using the simplified method, as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share-Based Payment*, as we have insufficient historical information regarding our stock options to provide a basis for an estimate;
- the expected volatility of the underlying common stock, which we estimate based on the historical volatility of a representative group of publicly traded biopharmaceutical companies with similar characteristics to us, including development candidates in earlier stages of drug development and areas of therapeutic focus;
- the risk-free interest rate, which we based on the yield curve of U.S. Treasury securities with periods commensurate with the expected term of the options being valued;
- the expected dividend yield, which we estimate to be zero based on the fact that we have never paid cash dividends and have no present intention to pay cash dividends; and
- the fair value of our common stock on the date of grant.

If factors change and different assumptions are used, our stock-based compensation expense could be materially different in the future.

The following table summarizes the weighted-average assumptions we used in our Black-Scholes calculations for awards to employees and non-employees:

| | Years ended December 31, | | Three months ended March 31, |
|---|---|---|---|
| | 2011 | 2012 | 2012 |
| Risk-free interest rate | 1.97% | 1.09% | 1.17% |
| Expected dividend yield | — | — | — |
| Expected term (in years) | 6.09 | 6.08 | 6.38 |
| Expected volatility | 98.60% | 97.75% | 99.51% |

Note: There were no stock options granted in the three months ended March 31, 2013.

In addition to the assumptions used in our Black-Scholes option-pricing model, the amount of stock option expense we recognize in our consolidated statements of operations includes an estimate of stock option forfeitures. Under ASC 718, we are required to estimate the level of forfeitures expected to occur and record compensation expense only for those awards that we ultimately expect will vest. Due to the lack of historical forfeiture activity, we expect to estimate our forfeiture rate based on data from our representative group of companies. Changes in the estimated forfeiture rate can have a significant impact on our stock-based compensation expense as the cumulative effect of adjusting the rate is recognized in the period the forfeiture estimate is changed. For example, if a revised forfeiture rate is higher than the previously estimated forfeiture rate, an adjustment is made that will result in a decrease to the stock-based compensation expense recognized in the consolidated financial statements. If a revised forfeiture rate is lower than the previously estimated forfeiture rate, an adjustment is made that will result in an increase to the stock-based compensation expense recognized in our consolidated financial statements. To date our forfeitures have not been material.

At March 31, 2013, the total unrecognized compensation expense related to unvested stock option awards, including estimated forfeitures, was $0.8 million, which we expect to recognize over a weighted-average period of approximately 1.8 years. We also have unrecognized stock-based compensation expense of $0.5 million related to stock options with performance-based vesting criteria that are not considered probable of achievement as of March 31, 2013; therefore we have not yet begun to recognize the expense on these awards.

**Common stock valuation**

The following table summarizes by grant date the number of shares of common stock underlying stock options granted from January 1, 2012 through April 30, 2013, as well as the associated per share exercise price, the estimated fair value per share of our common stock on the grant date and, for awards granted in September and December 2012, the retrospective fair value per share on the grant date and the related intrinsic value per common share:

| Grant dates | Number of common shares underlying options granted | Estimated fair value per common share on grant date | Retrospective fair value per share on grant date | Intrinsic value per common share |
|---|---|---|---|---|
| February 29, 2012 | 287,500 | $ 0.85 | N/A | $ — |
| March 6, 2012 | 72,500 | $ 0.85 | N/A | $ — |
| April 6, 2012 | 1,312,350 | $ 0.85 | N/A | $ — |
| June 7, 2012 | 352,500 | $ 0.85 | N/A | $ — |
| September 27, 2012 | 85,000 | $ 0.85 | $ 1.14(1) | $ 0.29 |
| December 4, 2012 | 181,000 | $ 0.85 | $ 2.10(1) | $ 1.25 |
| April 30, 2013 | 1,687,800 | $ 3.29 | N/A | $ — |

(1) The fair value of common stock at the grant date was adjusted in connection with a retrospective fair value assessment for financial reporting purposes, as described below.

The estimated fair value of common stock per share in the table above represents the determination by our board of directors of the fair value of our common stock as of the date of each grant, taking into consideration various objective and subjective factors, including the conclusions of both contemporaneous and retrospective valuations of our common stock, as discussed more fully below.

***Determination of the fair value of common stock on grant dates***

We are a private company with no active public market for our common stock. Therefore, we have periodically determined the estimated per share fair value of our common stock at various dates using contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, also known as the Practice Aid, for financial reporting purposes.

We performed contemporaneous valuations as of November 16, 2011, October 15, 2012 and April 15, 2013. In conducting the contemporaneous valuations, we considered all objective and subjective factors that we believed to be relevant for each valuation conducted, including our best estimate of our business condition, prospects and operating performance at each valuation date. Within the contemporaneous valuations performed, a range of factors, assumptions and methodologies were used. The significant factors included:

- the lack of an active public market for our common and our preferred stock;
- the prices of shares of our preferred stock that we had sold to outside investors in arm's length transactions, and the rights, preferences and privileges of that preferred stock relative to our common stock;
- our results of operations, financial position and the status of our research and preclinical development efforts, including our IDH2 and IDH1 and PK deficiency programs;
- the material risks related to our business;
- our business strategy;
- the market performance of publicly traded companies in the life sciences and biotechnology sectors, and recently completed mergers and acquisitions of companies comparable to us;
- the likelihood of achieving a liquidity event for the holders of our common stock, such as an initial public offering or sale of the company given prevailing market conditions; and
- any recent contemporaneous valuations of our common stock prepared in accordance with methodologies outlined in the Practice Aid.

The dates of our contemporaneous valuations have not always coincided with the dates of our stock option grants. In determining the exercise prices of the stock options set forth in the table above, our board of directors considered, among other things, the most recent contemporaneous valuations of our common stock and our assessment of additional objective and subjective factors we believed were relevant as of the grant date. The additional factors considered when determining any changes in fair value between the most recent contemporaneous valuation and the grant dates included our stage of research and preclinical development, our operating and financial performance and current business conditions.

There are significant judgments and estimates inherent in the determination of the fair value of our common stock, including the contemporaneous valuations. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event, the related company valuations associated with such events, and the determinations of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per share applicable to common stockholders could have been significantly different.

*Common stock valuation methodologies.* These contemporaneous valuations were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for determining the value of an enterprise, such as the cost, market and income approaches, and various methodologies for allocating the value of an enterprise to its capital structure and specifically the common stock.

We generally used the market approach, in particular the guideline company and precedent transaction methodologies, based on inputs from comparable public companies' equity valuations and comparable acquisition transactions, to estimate the equity value of our company. Additionally, if applicable, we considered company valuations implied by arm's length transactions involving sale of our securities to independent investors, taking into consideration the various rights and preferences of the equity securities transacted.

*Methods used to allocate our enterprise value to classes of securities.* In accordance with the Practice Aid, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date. The methods we considered consisted of the following:

- *Option pricing method.* The option-pricing method, or OPM, treats common stock and preferred stock as call options on the enterprise's value, with exercise prices based on the liquidation preference of the preferred stock. Under this method, the common stock has value only if the funds available for distribution to shareholders exceed the value of the liquidation preference at the time of a liquidity event (for example, merger or sale), assuming the enterprise has funds available to make a liquidation preference meaningful and collectible by the shareholders
- *Probability-weighted expected return method, or PWERM.* Under a PWERM, the value of the various equity securities are estimated based upon an analysis of future values for the enterprise assuming various future outcomes. Share value is based upon the probability-weighted present value of expected future investment returns, considering each of the possible future outcomes available to the enterprise, as well as the rights of each share class.

For each of the contemporaneous valuations described below, we used either the OPM or the PWERM to determine the estimated fair value of our common stock. The method selected was based on availability and the quality of information to develop the assumptions for the methodology.

***Contemporaneous valuation of common stock as of November 16, 2011***

Following our series C convertible preferred stock financing in November 2011 we conducted a contemporaneous valuation of our common stock as of November 16, 2011. In conducting this valuation we estimated the value of our common stock based on the price at which we sold shares of our series C convertible preferred stock in the financing. We concluded that the price paid for the series C convertible preferred stock was representative of fair value since our series C financing included significant investment from a new unrelated lead investor. We utilized the back-solve method (a form of the market approach defined in the Practice Aid) to estimate the enterprise value at November 16, 2011 that was implied by the arm's length series C transaction. In applying the back-solve method, we utilized OPM, taking into consideration the rights and preferences of the other classes of equity as well as the stock options issued and outstanding. For the OPM analysis, we estimated the time to liquidity as 1.9 years as of November 2011 which was our best estimate for a potential exit scenario for the investors. The volatility assumption was based on an analysis of guideline companies' historical equity volatility factors for a period of approximately 1.9 years, which is the term assumption. In selecting the volatility assumption, we also took into consideration the difference in stages of development between Agios and the guideline companies. Based on this analysis of the guideline companies, a volatility assumption of 50% was selected and utilized. The risk free rate assumption was based on the yield on 2-year U.S. Treasury bonds as of November 16, 2011. The exercise prices were the breakpoints representing the liquidation preferences of the preferred stock classes, the conversion features and stock option exercise values. Based on these OPM

assumptions, an implied equity value of approximately $145.4 million was determined such that the value per-share for the series C convertible preferred stock was equal to the per-share issuance price of $4.91. Based on these assumptions, the implied value per share of the common stock on a minority, marketable basis was $1.06. Because our common stock as of November 2011 was not publicly-traded or marketable, we applied a discount for lack of marketability of 20% to the calculated value. The discount for lack of marketability was based on quantitative models (put option calculation) as well as other empirical studies of restricted stock issued by publicly-traded companies and private placements by pre-IPO companies. Based on these factors, we concluded that our common stock had a fair value of $0.85 per share as of November 16, 2011.

***Stock options granted from January 2012 to September 2012***

Our board of directors granted stock options on February 29, 2012, March 6, 2012, April 6, 2012, June 7, 2012, and September 27, 2012 each having an exercise price of $0.85 per share, which our board of directors determined to be the fair value of our common stock on each grant date. In addition to the objective and subjective factors discussed above, our board of directors also considered input from management and the valuation as of November 16, 2011 in estimating the fair value of our common stock. Given the lack of clarity around a future liquidity event and the lack of significant program progression in the first nine months of 2012, our board of directors determined that no significant events or other circumstances had occurred between November 16, 2011 and September 27, 2012 that would indicate there was a change in the fair value of our common stock during that period. The nomination and approval of AG-221, our first development candidate, on September 21, 2012 by Celgene was considered an important milestone for us. However, the AG-221 program still needed to complete a series of safety studies before filing an investigational new drug application, or an IND, and was approximately 9-12 months away from starting testing in human clinical trials as of September 2012.

***Contemporaneous valuation of common stock as of October 15, 2012***

In October 2012, we conducted a contemporaneous valuation of our common stock as of October 15, 2012. In estimating our equity value as of October 15, 2012, we again relied upon the value implied by the series C convertible preferred stock financing, along with evaluating market and company-specific factors such as the stage of our research and early preclinical programs. We considered our implied equity value of approximately $145.4 million as of November 2011 as a benchmark and assessed the performance of the market (guideline companies) between November 2011 and October 2012, as well as our research and preclinical development efforts and concluded that our equity value had not materially changed. An equity value of approximately $150.0 million was assumed, indicating an increase in equity value of less than 5%. We utilized the OPM to allocate the estimated equity value of $150.0 million among the preferred and common stock. For the OPM analysis, we estimated the time to liquidity as 1.2 years which was our best estimate for a potential exit scenario for the investors and utilized a volatility rate of 50% based on an analysis of historical equity volatility factors of guideline companies over 1-year and 1.5-year periods as of October 2012. We utilized a risk-free rate of 0.21%, which was an interpolation of yields on 1-year and 2-year U.S. Treasury bonds. This OPM analysis calculated a value for the common stock of approximately $1.00 on a minority, marketable basis. Because our common stock as of October 2012 was not publicly-traded or marketable, we applied a discount for lack of marketability of 15% to the calculated value. The discount for lack of marketability was based on quantitative models (put option calculation) as well as other empirical studies of restricted stock issued by publicly-traded companies and private placement by pre-IPO companies. Based on these factors, we concluded that our common stock had a fair value of $0.85 per share as of October 15, 2012.

***Stock options granted in December 2012***

Our board of directors granted stock options on December 4, 2012, having exercise prices of $0.85 per share, which our board of directors determined to be the fair value of our common stock on the grant date. The per share exercise price determined by our board of directors was supported by the October 15, 2012 valuation, as

described more fully above, along with input from management. Our board of directors believed that this was appropriate as there continued to be a lack of clarity around a future liquidity event and a lack of significant program progression since October 1, 2012 that would indicate there was a change in the fair value of our common stock.

***Retrospective valuations of common stock as of June 7, 2012, September 27, 2012 and December 4, 2012***

In March 2013, our board of directors, based on market conditions and the growing confidence in our lead cancer metabolism program's ability to enter clinical development in mid-2013, authorized the management team to assess the feasibility of an IPO in the second half of 2013, and in late April 2013 we selected underwriters and held an organizational meeting. In connection with the preparation of the consolidated financial statements for the year ended December 31, 2012 and in preparing for a potential IPO, we reexamined, for financial reporting purposes, the valuations of our common stock as of June 7, 2012, September 27, 2012 and December 4, 2012. In connection with that reexamination, we prepared retrospective valuation reports of the fair value of our common stock for financial reporting purposes as of June 7, 2012, September 27, 2012 and December 4, 2012. We believe that the preparation of the retrospective valuations was necessary due to the fact that the timeframe and probability for a potential IPO had accelerated significantly since the time of our initial contemporaneous valuations, and that such acceleration would have a significant impact on the fair value of our common stock. We concluded that retrospective valuations for grant dates prior to June 7, 2012 were not required due to the lack of clarity and risk related to our early stage research programs and determined it would not be reasonable to assign a probability to a future IPO.

In April 2013, we conducted retrospective valuations of our common stock as of June 7, 2012, September 27, 2012 and December 4, 2012. In reassessing the fair value of our common stock, we considered our April 2013 assessment on the feasibility of an IPO in the second half of 2013. Our assessment was primarily based on external feedback, including certain current investors, and concluded that the current market conditions may be supportive of an IPO as we initiate clinical trials with our lead programs. In addition, we considered factors and events during 2012 that contributed to our increased confidence in an IPO in the second half of 2013. We specifically reviewed the timing of the nomination of our first development candidate. AG-221, our lead compound for our IDH2 program, was approved by Celgene in September 2012. This milestone allowed us to move forward into IND-enabling studies with AG-221 and based on the outcome of these studies would allow us to begin human clinical trials in mid-2013. In addition, during the fourth quarter of 2012, in our IDH2 program we generated positive preclinical efficacy data leveraging primary AML patient samples. These *ex-vivo* experiments with primary AML patient samples were later published in *Science* in April 2013.

Our retrospective valuations utilized PWERM to estimate the fair value of our common stock at June 7, 2012, September 27, 2012 and December 4, 2012. Under this method, we estimated the value of our common stock based on the probability-weighted present value of expected future investment returns considering each of four potential future liquidity events with the emphasis on the increased probability of an IPO. The four scenarios contemplated in each retrospective valuation were an IPO scenario, high and low case sale/merger scenarios and a dissolution scenario. In order to estimate expected proceeds from each potential exit scenario, we considered the last three years of historical data from the biopharmaceutical industry for both initial public offerings and merger and acquisition transactions. When reviewing the historical data we focused on a representative group of transactions involving biopharmaceutical companies with similar characteristics to us, including development candidates in early stages of drug development and similar areas of therapeutic focus. In addition, we also considered the valuation of our last private financing in November 2011. For the dissolution scenario, we used estimated proceeds equal to what we believe would be the salvage value of assets upon liquidation. We then determined the estimated timing for each exit scenario and a probability weighting, representing the likelihood of each outcome occurring relative to the others. We calculated a present value for our common stock using assumptions such as estimated proceeds from each exit scenario, expected dates for each scenario, and an appropriate risk-adjusted discount rate. We then assigned a probability weighting to each scenario, based on our estimate of the relative likelihood of occurrence of each scenario.

Within each retrospective valuation, we applied a risk-adjusted discount rate to the equity values determined for each scenario as of the future exit dates to arrive at the present value of equity under each scenario as of each valuation date. Given our stage of development at each valuation date and that we were revisiting the valuations in the context of a potential IPO, we used a discount rate of 35%. The discount rate was based on the typical venture capital rates of return for companies in the bridge/IPO stage of development, as contemplated by the Practice Aid, which we considered to be the most appropriate given our stage of development and risk profile. Finally, we applied a discount for lack of marketability to each scenario to reflect the impact on the value of our common stock due to its lack of liquidity. The discount for lack of marketability was based on quantitative models (put option calculation) as well as other empirical studies of restricted stock issued by publicly-traded companies and private placement by pre-IPO companies.

The retrospective valuation as of June 7, 2012 using PWERM, which included the probability of an IPO of 30%, a high case sale/merger scenario of 20%, a low case sale/merger scenario of 30% and a dissolution scenario of 20%, and liquidity and discount rates that are relatively consistent with those described below for the September 27, 2012 retrospective valuation, corroborated the contemporaneous valuation determined by our board of directors that was based on an OPM. As such, we did not adjust the fair value of our common stock as of June 7, 2012 for financial reporting purposes.

The following table summarizes the significant assumptions for each of the valuation scenarios used in the PWERM analysis to determine the retrospectively reassessed fair value of our common stock as of September 27, 2012 and December 4, 2012:

| Assumptions | IPO | Sale-high case | Sale-low case | Dissolution |
|---|---|---|---|---|
| **September 27, 2012 retrospective valuation** | | | | |
| Probability weighting | 40% | 10% | 30% | 20% |
| Liquidity date | 3/31/14 | 12/31/14 | 12/31/14 | 6/30/15 |
| Discount rate | 35% | 35% | 35% | 35% |
| Discount for lack of marketability | 15% | 20% | 20% | 25% |
| **December 4, 2012 retrospective valuation** | | | | |
| Probability weighting | 60% | 10% | 20% | 10% |
| Liquidity date | 12/31/13 | 12/31/14 | 12/31/14 | 6/30/15 |
| Discount rate | 35% | 35% | 35% | 35% |
| Discount for lack of marketability | 15% | 20% | 20% | 25% |

Based on the qualitative factors described above and the results of our retrospective valuation analysis, we determined that the retrospectively reassessed fair value of our common stock for financial reporting purposes at September 27, 2012 and December 4, 2012 was $1.14 and $2.10 per share, respectively. The stock-based compensation expense associated with stock options granted on September 27, 2012 and December 4, 2012 and reported in our consolidated statement of operations for the year ended December 31, 2012 reflects the retrospectively reassessed value.

***Contemporaneous valuation of common stock as of April 15, 2013***

In April 2013, we conducted a contemporaneous valuation of our common stock as of April 15, 2013. In assessing the fair value of our common stock, we considered the following factors:

- The potential for accelerated timing of an IPO due our assessment of the current market conditions;
- AG-221, our lead IDH2 compound, substantially completing IND-enabling safety studies and demonstrating a clear safety profile to advance to clinical trials;
- The nomination and acceptance by Celgene of our IDH1 development candidate, AG-120. This was our second cancer metabolism development candidate; and
- Publication of compelling preclinical experiments for IDH2.

Our contemporaneous valuation at April 15, 2013 using the PWERM included an IPO scenario, a high case sale/merger scenario, a low case sale/merger scenario and a dissolution scenario. In order to estimate expected proceeds from each potential exit scenario, we considered the last three years of historical data from the biopharmaceutical industry for both initial public offerings and merger and acquisition transactions. When reviewing the historical data we focused on a representative group of transactions involving biopharmaceutical companies with similar characteristics to us, including development candidates in early stages of drug development and similar areas of therapeutic focus. In addition we also considered the valuation of our last private financing in November 2011. For the IPO scenario, we assumed that all of our preferred shares would convert to common shares. For the high case sale/merger scenario, we assumed that the IPO did not occur, and that we have made significant progress in early clinical trials with one or more of our development candidates. For the low case sale/merger scenario, we assumed that the IPO did not occur, and that we have not made meaningful progress in early clinical trials with one or more drug candidates. For the dissolution scenario, we used estimated proceeds equal to what we believe would be the salvage value of assets upon dissolution. We then determined the estimated timing for each exit scenario and a probability weighting, representing the likelihood of each outcome occurring relative to the others.

We applied a discount rate to the equity values determined for each scenario as of the future exit dates to arrive at the present value of equity under each scenario as of April 15, 2013. Given our stage of development at April 15, 2013, we used a discount rate of 35%. The discount rate was based on the typical venture capital rates of return for companies in the bridge/IPO stage of development, as contemplated by the Practice Aid, which we considered to be the most appropriate given our stage of development and risk profile. Finally, we applied a discount for lack of marketability to each scenario to reflect the impact on the value of our common stock due to its lack of liquidity. The discount for lack of marketability was based on quantitative models (put option calculation) as well as other empirical studies of restricted stock issued by publicly-traded companies and private placements by pre-IPO companies.

The following table summarizes the significant assumptions for each of the valuation scenarios used in the PWERM analysis to determine the fair value of our common stock as of April 15, 2013:

| April 15, 2013 valuation assumptions | IPO | Sale-high case | Sale-low case | Dissolution |
|---|---|---|---|---|
| Probability weighting | 70% | 15% | 10% | 5% |
| Liquidity date | 9/30/13 | 12/31/14 | 12/31/14 | 6/30/15 |
| Discount rate | 35% | 35% | 35% | 35% |
| Discount for lack of marketability | 10% | 15% | 15% | 20% |

Based on the qualitative factors described above and the results of our contemporaneous valuation analysis, we determined that the fair value of our common stock for financial reporting purposes at April 15, 2013 was $3.29 per share.

***Stock options granted on April 30, 2013***

Our board of directors granted stock options on April 30, 2013, each having an exercise price of $3.29 per share, which our board of directors determined to be the fair value of our common stock on the date of grant. In establishing the exercise price for the grants, our board of directors considered input from management, including the contemporaneous valuation of our common stock as of April 15, 2013, as well as the objective and subjective factors outlined above.

Based on the assumed IPO price of $ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, the intrinsic value of stock options outstanding as of April 30, 2013 was $ million, of which $ million and $ million would have been related to stock options that were vested and unvested, respectively, at that date.

***JOBS Act***

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC, we intend to rely on certain of these exemptions, including without limitation, (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the PCAOB regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis. We will remain an EGC until the earlier of (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) the last day of the fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission.

**Results of operations**

***Comparison of three months ended March 31, 2012 and 2013***

The following table summarizes our results of operations for the three months ended March 31, 2012 and 2013, together with the changes in those items in dollars and as a percentage:

| | Three months ended March 31, | | | |
|---|---|---|---|---|
| (in thousands) | 2012 | 2013 | Dollar change | % change |
| Collaboration revenue | $ 6,268 | $ 6,268 | $ — | — % |
| Operating expenses: | | | | |
| Research and development | 9,551 | 11,462 | 1,911 | 20.0 |
| General and administrative | 1,981 | 1,852 | (129) | (6.5) |
| Loss from operations | (5,264) | (7,046) | (1,782) | 33.9 |
| Interest income | 26 | 8 | (18) | (69.2) |
| (Benefit) provision for income taxes | (607) | 190 | 797 | (131.3) |
| Net loss | $(4,631) | $ (7,228) | $ (2,597) | 56.1% |

*Revenue.* We recorded revenue of $6.3 million for the three months ended March 31, 2013 and 2012 associated with the Celgene agreement.

*Research and development expense.* Research and development expense increased by $1.9 million to $11.5 million for the three months ended March 31, 2013 from $9.6 million for the three months ended March 31, 2012, an increase of 20%. The increase in research and development expenses was primarily attributable to an increase of $1.0 million in external services. The increase in external services during the three months ended March 31, 2013 was primarily attributable to the following:

- approximately $0.6 million for external drug discovery efforts, primarily chemistry optimization, for our glutaminase research program;

- approximately $0.2 million for external IND-enabling preclinical studies and manufacturing activities for our lead product candidate targeting IDH2; and
- approximately $0.2 million of costs related to development candidate-enabling preclinical pharmacology and toxicology studies for our lead product candidates targeting PK deficiency and IDH1.

No such external expenses were incurred during the three months ended March 31, 2012 due to each program's early stage of research. In addition, we incurred approximately $0.7 million of additional internal research expenses related to the following:

- additional personnel costs of $0.6 million primarily from additional hires, increasing our internal headcount by 16%; and
- an increase of $0.2 million for facilities related expenses and $0.1 million for research materials related to our expanded research efforts.

*General and administrative expense.* General and administrative expenses decreased by $0.1 million to $1.9 million for the three months ended March 31, 2013 from $2.0 million for the three months ended March 31, 2012, a decrease of 7%. The decrease in general and administrative expenses was primarily attributable to decreased external legal costs of $0.1 million.

*Interest income.* Interest income decreased by $18,000 to $8,000 for the three months ended March 31, 2013, from $26,000 for the three months ended March 31, 2012, a decrease of 69%, due to a decrease in the average investment balance and a decrease in interest rates earned on investments.

*(Benefit) provision for income tax.* The (benefit) provision for income taxes increased by $0.8 million to $0.2 million for the three months ended March 31, 2013, from $(0.6) million for the three months ended March 31, 2012, a decrease of 131%. The increase in the (benefit) provision for income taxes for the three months ended March 31, 2013 was primarily attributable to penalties and interest accrued for the non-payment of U.S. federal income taxes. For the three months ended March 31, 2012, we elected to carry back a portion of our deferred tax assets, including net operating losses, generated in the three months ended March 31, 2012, resulting in a reduction of our 2011 income tax liability and a benefit for income taxes of $0.6 million.

***Comparison of years ended December 31, 2011 and 2012***

The following table summarizes our results of operations for the years ended December 31, 2011 and 2012, together with the changes in those items in dollars and as a percentage:

| (in thousands) | Years ended December 31, 2011 | 2012 | Dollar change | % change |
|---|---|---|---|---|
| Collaboration revenue | $ 21,803 | $ 25,072 | $ 3,269 | 15.0% |
| Grant revenue | 34 | 34 | — | — |
| Total revenue | 21,837 | 25,106 | 3,269 | 15.0 |
| Operating expenses: | | | | |
| Research and development | 31,253 | 41,037 | 9,784 | 31.3 |
| General and administrative | 7,215 | 7,064 | (151) | (2.1) |
| Loss from operations | (16,631) | (22,995) | (6,364) | 38.3 |
| Interest income | 132 | 69 | (63) | (47.7) |
| Provision (benefit) for income taxes | 7,207 | (2,824) | (10,031) | (139.2) |
| Net loss | $ (23,706) | $ (20,102) | $ 3,604 | (15.2)% |

*Revenue.* Revenue increased by $3.3 million to $25.1 million in 2012 from $21.8 million in 2011, an increase of 15%. The increase in revenue was the result of a full year of revenue recognized in 2012 associated with Celgene's extension payment of $20.0 million that we received in October 2011.

*Research and development expense.* Research and development expense increased by $9.8 million to $41.0 million in 2012 from $31.3 million in 2011, an increase of 31%. The increase in research and development expense was primarily attributable to an increase of $5.8 million in external services. The increase in external services in 2012 was primarily attributable to the following:

- approximately $2.9 million of costs for external development candidate-enabling preclinical pharmacology and toxicology studies and IND-enabling preclinical studies and manufacturing activities for our lead product candidate targeting IDH2;
- approximately $2.3 million of costs related to development candidate-enabling preclinical pharmacology and toxicology studies for our lead product candidates targeting PK deficiency and IDH1; and
- approximately $0.6 million of external drug discovery efforts, primarily chemistry optimization, for our glutaminase research program.

No such external expenses were incurred in 2011 due to each program's early stage of research. In addition, we incurred approximately $4.1 million of additional internal research expenses related to the following:

- additional personnel costs of $2.9 million primarily from additional hires increasing our internal headcount by 21%; and
- an increase of $1.2 million for research materials related to our expanded research efforts.

*General and administrative expense.* General and administrative expense decreased by $0.1 million to $7.1 million in 2012 from $7.2 million in 2011, a decrease of 2%. The decrease in general and administrative expense was primarily attributable to individually insignificant reductions in certain operating and professional services costs.

*Interest income.* Interest income decreased by $63,000 to $69,000 in 2012, from $132,000 in 2011, a decrease of 48%, due to a decrease in the average investment balance and a decrease in interest rates earned on investments.

*Provision (benefit) for income taxes.* During 2011, a significant portion of the upfront payment received under the collaboration agreement with Celgene was recognized as revenue for tax purposes, resulting in taxable income for 2011. Accordingly we recorded a provision for income taxes of $7.2 million for the year ended December 31, 2011. During 2012, we elected to carry back certain deferred tax assets, including our net operating losses, generated in the year ended December 31, 2012, resulting in a reduction of our U.S. federal 2011 tax liability and a benefit for income taxes of $2.8 million for the year ended December 31, 2012.

**Liquidity and capital resources**

***Sources of liquidity***

Since our inception, and through March 31, 2013, we have raised an aggregate of approximately $261.2 million to fund our operations, of which approximately $141.2 million was through upfront and extension payments related to our collaboration agreement with Celgene, and approximately $120.0 million was from the issuance of preferred stock. As of March 31, 2013, we had $115.8 million in cash, cash equivalents and marketable securities.

In addition to our existing cash, cash equivalents and marketable securities, we are eligible to earn a significant amount of milestone payments under our collaboration agreement. Our ability to earn these milestone payments and the timing of achieving these milestones is dependent upon the outcome of our research and development activities and is uncertain at this time. Our right to payments under our collaboration agreement is our only committed potential external source of funds.

***Cash flows***

The following table provides information regarding our cash flows for the years ended December 31, 2011 and 2012, and the three months ended March 31, 2012 and 2013:

| | Years ended, December 31, | | Three months ended, March 31, | |
|---|---|---|---|---|
| (in thousands) | 2011 | 2012 | 2012 | 2013 |
| Net cash used in operating activities | $(15,219) | $(49,548) | $(15,974) | $(11,981) |
| Net cash (used in) provided by investing activities | (22,360) | 23,042 | 10,389 | 4,036 |
| Net cash provided by financing activities | 77,358 | 142 | 38 | 25 |
| Net increase (decrease) in cash and cash equivalents | $ 39,779 | $(26,364) | $ (5,547) | $ (7,920) |

***Net cash used in operating activities***

The use of cash in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital. Net cash used in operating activities was $16.0 million during the three months ended March 31, 2012 compared to $12.0 million during the three months ended March 31, 2013. The decrease in cash used in operating activities in the first quarter of 2013 was driven primarily by a decrease in income taxes payable due to our ability to carry back certain of our deferred tax assets, including our 2012 net operating losses, for U.S. federal income tax purposes and to a payment of approximately $3.5 million for state income tax expense paid in the first quarter of 2012 compared to no income tax payments in the first quarter of 2013. The decrease was partially offset by an increase in net loss of $2.6 million for the three months ended March 31, 2013 as compared to the three months ended March 31, 2012.

Net cash used in operating activities was $15.2 million for the year ended December 31, 2011 compared to $49.5 million for the year ended December 31, 2012. The increase in cash used in operating activities was driven primarily by changes in components of working capital including a decrease in income taxes payable and a decrease in deferred revenue. This was partially offset by a decrease in deferred taxes and a decrease in net loss for the year ended December 31, 2012. The decrease in income taxes payable was due to a payment of approximately $3.5 million for state income tax expense and also our ability to carry back certain of our deferred tax assets, including our 2012 net operating losses, for U.S. federal income tax purposes. The decrease in deferred taxes is related to the utilization of the tax benefits during the year ended December 31, 2012. The decrease in deferred revenue was primarily due to Celgene's extension payment of $20.0 million that we received in October 2011, compared to no collaboration payments received for the year ended December 31, 2012. The decrease in net loss for the year ended December 31, 2012 was also related to revenue recognized for the Celgene extension payment.

***Net cash (used in) provided by investing activities***

Net cash provided by investing activities was $10.4 million during the three months ended March 31, 2012 compared to $4.0 million during the three months ended March 31, 2013. The cash provided by investing activities for the three months ended March 31, 2013 and 2012 was primarily the result of fewer purchases of marketable securities than the proceeds from maturities and sales of marketable securities.

Net cash used in investing activities was $22.4 million during the year ended December 31, 2011 compared to cash provided by investing activities of $23.0 million during the year ended December 31, 2012. The cash provided by investing activities for the year ended December 31, 2012 was primarily the result of fewer purchases of marketable securities than the proceeds from maturities and sales of marketable securities, partially offset by purchases of property and equipment of $1.5 million. The cash used in investing activities for the year ended December 31, 2011 was primarily the net result of more purchases of marketable securities than the proceeds from maturities and sales of marketable securities, in addition to purchases of property and equipment of $1.9 million.

***Net cash provided by financing activities***

Net cash provided by financing activities was $38,000 during the three months ended March 31, 2012 compared to $25,000 during the three months ended March 31, 2013. The cash provided by financing activities for the three months ended March 31, 2013 and 2012 was the result of proceeds received from option exercises and the issuance of common and restricted stock.

Net cash provided by financing activities was $0.1 million during the year ended December 31, 2012 compared to $77.4 million during the year ended December 31, 2011. The cash provided by financing activities for the year ended December 31, 2012 was the result of proceeds received from option exercises and the issuance of common and restricted stock. The cash provided by financing activities for the year ended December 31, 2011 was related to the issuance of 15,882,389 shares of series C convertible preferred stock in November 2011, resulting in net proceeds of $77.3 million and proceeds received from option exercises of $0.1 million.

***Funding requirements***

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate clinical trials of, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of Celgene or other collaborators. Furthermore, upon the closing of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

We expect that the net proceeds from this offering and the concurrent private placement to Celgene, together with our existing cash, cash equivalents and marketable securities, anticipated interest income and anticipated expense reimbursements under our collaboration agreement with Celgene, will enable us to fund our operating expenses and capital expenditure requirements for at least the next months. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the success of our collaboration with Celgene;
- whether Celgene exercises either or both of its options to extend the discovery phase under our collaboration agreement (each of which would trigger an extension payment to us);
- the extent to which we acquire or in-license other medicines and technologies;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval (to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of Celgene or other collaborators);
- revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- our ability to establish and maintain additional collaborations on favorable terms, if at all.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds, other than our collaboration with Celgene. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

***Contractual obligations***

The following table summarizes our significant contractual obligations as of payment due date by period at March 31, 2013:

| | Payments due by period | | | | |
|---|---|---|---|---|---|
| (in thousands) | Total | Less than 1 year | 1-3 years | 3-5 years | More than 5 years |
| Operating lease obligations(1) | $7,152 | $ 2,280 | $4,676 | $ 196 | $ — |
| Other(2) | 50 | 50 | — | — | — |
| Total contractual cash obligations | $7,202 | $ 2,330 | $4,676 | $ 196 | $ — |

(1) Represents future minimum lease payments under our non-cancelable operating lease. The minimum lease payments above do not include any related common area maintenance charges or real estate taxes.

(2) Consists of milestone payments of $25,000 each that we are required to pay to University Health Network under our license agreement upon issuance of utility patents, which we expect will occur before the end of 2013.

We enter into contracts in the normal course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes, which generally provide for termination within 30 days of notice, and therefore are cancelable contracts and not included in the table of contractual obligations above.

We have obligations to make future payments to third parties that become due and payable on the achievement of certain development, regulatory and commercial milestones. Since the achievement and timing of these milestones is not fixed and determinable, and we typically have the ability to terminate the agreements upon 60-90 days' notice, such commitments have not been included in our consolidated balance sheets or in the table of contractual obligations above.

**Off-balance sheet arrangements**

We did not have, during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable Securities and Exchange Commission rules.

**Quantitative and qualitative disclosures about market risk**

We are exposed to market risk related to changes in interest rates. As of December 31, 2012 and March 31, 2013, we had cash, cash equivalents and marketable securities of $128.0 million and $115.8 million, respectively, consisting primarily of investments in U.S. Treasuries and certificates of deposit. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term marketable securities. Our marketable securities are subject to interest rate risk and could fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio. We have the ability to hold our marketable securities until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

We are also exposed to market risk related to change in foreign currency exchange rates. We contract with CROs that are located Asia and Europe, which are denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk. As of December 31, 2012 and March 31, 2013, we had minimal or no liabilities denominated in foreign currencies.

## Business

We are a biopharmaceutical company passionately committed to applying our scientific leadership in the field of cellular metabolism to transform the lives of patients with cancer and inborn errors of metabolism, or IEMs, which are a subset of orphan genetic metabolic diseases. Metabolism is a complex biological process involving the uptake and assimilation of nutrients in cells to produce energy and facilitate many of the processes required for cellular division and growth. We believe that dysregulation of normal cellular metabolism plays a crucial role in many diseases, including certain cancers and IEMs. We believe Agios is a first mover in using cellular metabolism, an unexploited area of biological research with disruptive potential, as a platform for developing potentially transformative medicines. Our singular focus is to apply our expertise in cellular metabolism to develop innovative small molecule treatments for cancer and IEMs. The lead product candidates in our most advanced programs are aimed at druggable targets which have undergone rigorous validation processes. Our most advanced cancer product candidates, AG-221 and AG-120, which target mutant IDH2 and IDH1, respectively, have demonstrated strong proof of concept in preclinical models and are expected to enter the clinic in mid-2013 and early 2014, respectively. The lead candidate in our IEM program, AG-348, targets pyruvate kinase and is expected to commence clinical development in 2014.

Our ability to identify, validate and drug novel targets is enabled by a set of core capabilities. Key proprietary aspects of our core capabilities in cellular metabolism include the ability to measure the activities of numerous metabolic pathways in cells or tissues in a high throughput fashion and expertise in “flux biochemistry.” This refers to the dynamic analysis of how metabolites accumulate or diminish as they are created or chemically altered by multiple networks of metabolic enzymes. Complex mathematical modeling of metabolic pathways, enzymatic activity and the flux of metabolites through metabolic enzymatic reactions within diseased tissues allow us to identify novel disease biomarkers and targets for drug discovery.

Our understanding of metabolism within diseased tissues enables the development of pharmacodynamic markers and patient selection strategies for clinical development. Utilizing our approach we identify altered metabolic pathways within abnormal cells. Altered metabolic pathways generate disease-specific metabolic fingerprints, comprising patterns of metabolite levels, that can be exploited in both discovery and development of novel therapeutics. Metabolites make ideal biomarkers because they are readily measured in the target tissues and blood. Metabolic biomarkers can identify appropriate patients for clinical trials, serve as pharmacodynamic markers to characterize medicine/target engagement in patients, and permit the monitoring of patient response to therapy. Identifying the right patient population has the potential to increase the probability of technical and clinical success in comparison to conventional drug discovery, a benefit which will be increasingly important to the entire health care system. The clinical development strategy for all of our product candidates will always include initial study designs that allow for genetically or biomarker defined patient populations, enabling the potential for early proof of concept and a higher probability of technical success, along with accelerated clinical development and product approval.

We have assembled a unique set of core capabilities at the intersection of cellular biology and metabolism, centered on the expertise of our founding scientists who are widely considered to be the thought leaders in cancer metabolism—Lew Cantley, Ph.D. (director of the Cancer Center at Weill Cornell Medical College and New York Presbyterian Hospital), Tak Mak, Ph.D. (professor of medical biophysics, University of Toronto) and Craig Thompson, M.D. (president and CEO of Memorial Sloan-Kettering Cancer Center)—as well as on the strength of our management team, including our CEO, David Schenkein, M.D., and a group of world class scientists. We have built an exceptional team of cancer biologists, enzymologists and a core group of metabolomic experts that interrogate cellular metabolism to identify key metabolic targets and biomarkers in cancer and IEMs. Our scientists have published 11 scientific papers since 2009, including four in *Nature* and three in *Science*. We have also established an intellectual property portfolio consisting of over 100 patent applications worldwide, including multiple patent applications directed to our lead product candidates, together with trade secrets, know-how and continuing technological innovation.

Our initial therapeutic area of focus is cancer. We are leveraging our expertise in metabolic pathways to discover, validate, develop and commercialize a pipeline of novel drug candidates. In April 2010, we entered into a collaboration agreement with Celgene focused on cancer metabolism. Under the collaboration, we are leading discovery, preclinical and early clinical development for all cancer metabolism programs. The discovery phase of the collaboration expires in April 2014, subject to Celgene's option to extend the discovery phase for up to two additional years. Celgene has the option to obtain exclusive rights for the further development and commercialization of certain of these programs, and we will retain rights to the others. We may elect to participate in a portion of sales activities for the medicines from such programs in the United States. In addition, for certain of these programs, we may elect to retain full rights to develop and commercialize medicines from these programs in the United States. Through March 31, 2013, we have received approximately $141.2 million in payments from Celgene and $37.5 million in equity investments. We are also eligible to receive extension payments, payments upon the successful achievement of specified milestones, reimbursements for certain development expenses and royalties on any product sales.

We believe that our first-mover advantage in understanding cellular metabolism has created disruptive knowledge in biology that we can exploit for the development of transformative medicines in cancer. Because there has not previously been a systematic approach to drug discovery in this field, we have had to demonstrate significant major advances, including:

- identification of unique and specific metabolic enzymes that are altered from normal cells within cancer cells and are directly involved in the pathogenesis of cancer;
- creation of selective small molecules with drug-like properties that preferentially target disease-associated enzymes;
- achievement of pharmacologic efficacy in *in vitro* and *in vivo* models; and
- discovery of novel biomarkers that identify the appropriate patients for clinical trials.

Our two most advanced cancer programs are targeting mutations in the enzymes isocitrate dehydrogenase 1 and 2, referred to as IDH1 and IDH2. Both program targets are genetically validated and represent two of the most promising metabolic targets in cancer biology, as concluded by the leading scientific journal *Nature* in 2011. Extensive publications led by Agios scientists validate our belief that these mutations are initiating and driving events in many cancers. These two otherwise normal metabolic enzymes are mutated in a wide range of cancers, including both solid tumors and hematological malignancies. Our drug candidates are selective for the mutated form of IDH1 and IDH2 found in cancer cells versus the normal forms of IDH1 and IDH2 found in all other cells. We expect to commence clinical trials in patients with IDH2-mutation positive cancers with AG-221, the lead candidate in our IDH2 program, by mid-2013. In the IDH1 program, we expect to commence clinical trials in patients with IDH1-mutation positive cancers with our lead development candidate, AG-120, by early 2014. In our Celgene collaboration, we have retained the option for exclusive rights to develop and commercialize AG-120 in the United States.

We are also focused on developing medicines to address IEMs, with a novel approach to orphan diseases for which no effective or disease-modifying therapy is currently available. A hallmark of IEMs is abnormal cellular metabolic activity due to a genetic defect, which results in the accumulation or deficit of certain metabolites or proteins, disrupting normal metabolic functions. We utilize stringent criteria when identifying which IEMs Agios will pursue. We focus on IEMs with a common set of attributes:

- single gene, single disease (i.e., monogenic disorders);
- high unmet medical need with evidence that there is progressive disease post-birth that can be addressed with therapy; and
- an adequate number of patients for prospective clinical trials.

We apply our core capabilities in exploring cellular metabolism to identify key cellular targets in affected cells and design novel small molecules with the potential to correct the metabolic defect in patients afflicted with these diseases. We have successfully used this approach in our most advanced IEM program—pyruvate kinase deficiency, or PK deficiency, a rare form of hereditary hemolytic anemia. The disease is characterized by mild to severe forms of anemia. There are no currently available treatments other than supportive care, which includes splenectomy, transfusion support and chelation therapy. Our lead development candidate, AG-348, is a potent, orally available small molecule activator of the PKR enzyme, an isoform of PK that, when mutated, leads to PK deficiency. Our current plan is to enter clinical trials in patients with PK deficiency in 2014.

**Our strategy**

We aim to build a multi-product company, based on our expertise in cellular metabolism, that discovers, develops and commercializes first- and best-in-class medicines to treat cancer and IEMs. Key elements of our strategy include:

- ***Aggressively pursuing the development of novel medicines to transform the lives of patients with cancer and IEMs:*** We believe that our singular focus on applying our expertise in cellular metabolism to discover and develop novel treatments for cancer and IEMs will enable us to identify and develop transformative, disease-modifying therapies. Under our collaboration with Celgene, since 2010 we have identified two development candidates that we expect will enter clinical trials in mid-2013 and early 2014. We have also identified a development candidate in our IEM program that we anticipate will enter clinical trials in 2014.
- ***Maintaining our competitive, first-mover advantage in the field of cellular metabolism:*** Agios has developed core capabilities in chemistry, biology, metabolism and informatics, which have enabled us to unlock a new field of discovery in cellular metabolism. We believe that we are a leader in this field, and we are committed to maintaining and expanding our proprietary technology base to enable us to remain at the forefront of cellular metabolism research and development.
- ***Continuing to build a product engine for cancer and IEMs to generate novel and important medicines:*** We will leverage our core expertise, commitment to science and our platform technology in cellular metabolism to identify and drug novel targets in both cancer and IEMs. We will continue to invest in building this robust discovery engine as lead molecules enter the clinic to generate novel and important medicines.
- ***Building a preeminent independent biopharmaceutical company by engaging in discovery, development and commercialization of our medicines:*** We aspire to become one of the great biopharmaceutical companies. We have aggregated a group of world class scientists with renowned science and technology capabilities, which, when coupled with our strong intellectual property position, the culture of our organization and the structure of our partner relationships, enable Agios to have a meaningful impact on the discovery, development and commercialization of our potential medicines. In our collaboration with Celgene, we have retained U.S. development and commercialization rights to certain programs, and may elect to participate in a portion of sales activities in the U.S. for the medicines in all remaining programs. We retain global development and commercialization rights to our IEM programs.
- ***Maintaining a commitment to precision medicine in drug development:*** We intend to utilize our expertise in cellular metabolism to identify and validate novel disease targets and relevant biomarkers, which enables us to develop highly selective and specific drug candidates for cancer and IEMs. We then intend to use these biomarkers to rigorously select patients for clinical trials and to design studies with potential for rapid proof of concept along with accelerated clinical development and product approval timelines.

**Our guiding principles**

We aim to build a long-term company with a disciplined focus on developing medicines that transform the lives of patients with cancer and IEMs. We maintain a culture of high integrity that embraces the following guiding principles, which we believe will provide long-term benefits for all our stakeholders:

- ***Follow the science and do what is right for patients.***
- ***Maintain a culture of incisive decision-making driven by deep scientific interrogation and "respectful irreverence."***
- ***Foster collaborative spirit that includes all employees regardless of function or level.***
- ***Leverage deep strategic relationships with our academic and commercial partners to improve the quality of our discovery and development efforts.***

**Our focus—cellular metabolism**

Cellular metabolism refers to the set of life-sustaining chemical transformations within the cells of living organisms. The conversion of nutrients into energy via enzyme-catalyzed reactions allows organisms to grow and reproduce, maintain their structures, and respond to their environments. The chemical reactions of metabolism are organized into metabolic pathways, in which one chemical is transformed through a series of steps into another chemical, by a sequence of enzymes. Enzymes catalyze quick and efficient reactions, serve as key regulators of metabolic pathways, and respond to changes in the cell's environment or signals from other cells. We believe our deep understanding of metabolic pathways within normal cells enables us to identify altered metabolic pathways within abnormal cells such as in rapidly proliferating cancers and IEMs.

Fundamental differences in the metabolism of normal cells and rapidly proliferating cancer cells were first discovered by Otto Warburg more than 80 years ago—an observation that earned him the Nobel Prize. Warburg demonstrated that in contrast to normal cells, which convert nutrients, such as sugar, into energy via a process known as the Krebs cycle, cancer cells ferment their sugar into lactic acid—a process known as aerobic glycolysis. It is now known that this allows the cancer cells to generate the building blocks they need to grow rapidly. The ability of the cancer cell to "rewire" its metabolic pathways to fuel its growth and survival has spawned an entirely new field of cancer biology known as cancer metabolism or tumor metabolism. It is only in the last decade that scientists have developed sophisticated tools to interrogate and evaluate metabolism within cancer or rapidly dividing cells. Agios' founders and scientific advisors have largely driven this intense focus on studying the metabolism of cancer cells.

Cancer metabolism is a new and exciting field of biology that provides a fundamentally different approach to treating cancer. Cancers become addicted to certain fuel sources and inherently alter their cellular machinery to change how they consume and utilize nutrients. Cancer cells increase the transport of nutrients into the cell by 200-400 fold compared to normal cells while also mutating metabolic enzymes to generate metabolites that fuel growth and altering gene expression of enzymes to divert energy production. Collectively, these changes afford cancer cells the ability to generate the building blocks that drive tumor growth. Inhibiting key enzymes in cancer cell specific metabolic pathways has the potential to disrupt tumor cell proliferation and survival without affecting normal cells, thus providing a powerful new intervention point for discovery and development of novel targeted, cancer therapeutics. We believe that this is an entirely novel approach to treating cancer, and our research is directed at identifying such metabolic targets and discovering medicines against them.

Validation of the concept of cancer cell metabolic rewiring and excessive nutrient uptake comes from the widespread use of positron emission tomography, or PET, to detect cancers. This medical imaging technology relies on the uptake of nutrients, namely sugar, into cells. Patients are injected with a radioactively labeled form of sugar, which is more rapidly consumed by cancer cells given their profound requirement for nutrients relative to normal tissues. PET imaging precisely locates cancerous areas throughout the body and provides for both a diagnostic and prognostic tool throughout cancer therapy.

The metabolic rewiring of cancer cells can also be linked to specific genetic alterations in oncogenes (which are genes that transform normal cells into tumor cells) and tumor suppressor genes (which are genes that are anti-oncogenic) responsible for cell signaling. These mutations in signaling pathways can drive excessive uptake of nutrients and altered metabolic pathways, thereby causing cancer formation. This cross-talk between cell signaling and metabolism offers multiple opportunities to treat cancer by combining Agios therapies directed against metabolic enzymes with existing or emerging standards of care.

In cancer, our target universe for creating novel transformative medicines is derived from the human cellular metabolic machinery, referred to as the "metabolome," containing 2,000-3,000 cellular metabolic enzymes, from which we anticipate that there will likely be between 50-100 novel targets for oncology. This represents one of the largest unexploited new classes of important targets in oncology. The Agios team has already studied more than 50 metabolic enzymes as possible important cancer targets. With our focus on targets that are distinct in cancer versus normal cells, we believe that they are likely to fall within three broad categories:

- a mutation leading to a unique metabolic enzyme only found in cancer;
- unique isoforms of metabolic enzymes that are found in the cancer and that are different in normal cells; and
- dysregulation of an entire metabolic pathway to feed the cancer's need for a specific metabolite or nutrient.

An understanding of metabolic pathways based solely on traditional biochemistry would underestimate the pervasive role of metabolism in essentially every aspect of biology. Recent work has demonstrated that many human diseases involve altered cellular metabolism—often genetically programmed—that disrupts normal physiology and leads to severe tissue dysfunction. Another area of unmet medical need is IEMs, severe and often life-threatening inherited childhood and adult diseases caused by a defect in a metabolic enzyme or pathway. Our core capabilities to interrogate the metabolic pathway of the disease have allowed us to create potential medicines that can restore the metabolic balance and potentially lead to disease-modifying therapies for these orphan diseases. Our approach is designed to develop treatment for the "right" patient identified by the genetic and metabolic alteration marked by their inherited disease.

**Our core capabilities and science**

We believe that our capabilities in understanding both static and dynamic aspects of cellular metabolism are unique in the industry as demonstrated by our ability to identify and validate four novel, druggable targets. Among our key core capabilities to identify and validate novel enzyme targets are:

- ***Measurement of metabolites and metabolic pathways in cells and tissues using high throughput mass spectrometry.***
- ***Identification of candidate metabolic enzymes using flux biochemistry:*** In many circumstances, cancers and normal cells utilize multiple routes to produce the same metabolite. To identify the relevant target, we evaluate the kinetics of enzymes to determine the speed at which metabolites are moving along enzymatic pathways. This critically important technology is called "flux biochemistry" and is distinguished from the more conventional "static" metabolomics view. Flux biochemistry, by labeling the nutrients, allows us to create a pathway map by measuring the rate of filling and emptying of metabolic pools. This methodology, which precisely measures the rate at which a nutrient source is broken down and reassembled into cellular building blocks and biochemical energy, has been automated in a high throughput fashion at Agios. Experimental data is integrated with mathematical modeling of enzyme pathways to generate an accurate understanding of the metabolic dysregulation. This allows us to determine which enzyme is the "Achilles' Heel" of a particular cancer or IEM.
- ***Mining of genomic data emerging from the public cancer genome sequencing efforts, utilizing our state of the art genomics and bioinformatics capabilities, to identify metabolic enzymes that are mutated or amplified in tumors:*** This provides insight into novel targets for therapy while facilitating a precision medicine approach to patient selection based on the genetic defect (e.g., mutant IDH1 and IDH2).

- ***Development of a multiplexed, barcoded RNAi depletion screening strategy, enabling us to interrogate the entire metabolome in a single experiment, both in cells and in tumor bearing animals:*** This technology allows us to identify novel targets in cancers of interest.
- ***Inhibition and activation of metabolic enzymes using structure-based design from crystal structures, computational chemistry, and high throughput chemical and fragment library screening***.

**Our approach to drug discovery and development, and the utilization of precision medicine**

We intend to apply our deep understanding of metabolism, coupled with our ability to create medicines that can inhibit or activate metabolic enzymes, to fundamentally change the way cancer and IEMs are treated. We have the ability to identify and validate novel and druggable targets in both cancer and IEMs.

We begin the process to find and validate new targets by evaluating a cancer's dependency on certain nutrients or enzymes in comparison to normal cells. We then utilize a number of techniques to determine if the cancer is dependent on the identified enzyme. The candidate enzyme target is inactivated, or turned off using genetic tools, first in tissue culture and then in xenograft models, in which representative tumors have been implanted in animals. Once inactivated, we can determine if turning off the enzyme stops the growth of the cancer cells *in vitro* and slows or stops the growth of a tumor in the xenograft model. If our findings are positive, we begin the process of searching for biomarkers that will enable our precision medicine approach of identifying the right patients to be eventually treated. In the early stages of biomarker development, we create a responder hypothesis, comparing the molecular genetics and metabolite patterns between cancers that respond to treatment to those that do not respond to enzyme inhibition. The process to design a small molecule drug candidate begins by determining the crystal structure of the enzyme. We create candidate molecules using structure-based design coupled with high throughput chemical screening, searching for small molecules that can inhibit the enzyme. The decision to enter the final and most expensive part of drug discovery, which is the refinement of the small molecule product candidates, is only made when we have completed all of these critical steps. The target is then considered "validated". This rigorous process only allows the most promising programs to enter the last stage of drug discovery. Agios has been successful at fully validating four novel cancer targets to date with an additional ten novel targets currently in various stages of the validation process. We have also "de-validated" and terminated numerous programs, including many that have been reported in scientific journals.

In our IEM portfolio, we use an equally rigorous set of validation techniques. We begin with an assessment of scientific literature and disease and genomic databases, applying text and data mining techniques, to identify IEMs that are caused by a mutation in a single metabolic enzyme, referred to as monogenic disorders. We perform a full evaluation of the clinical aspects of the disease, which includes an understanding of the severity of the disease, the progression of the disease manifestations post-birth and currently available treatments. We intend to focus only on diseases of a severe nature for which there are no available effective treatments, where intervention is likely to ameliorate disease manifestations, and where there are an adequate number of patients to conduct appropriate clinical trials. We conduct a detailed mutational and structural analysis of the metabolic enzyme and the entire pathway of interest to determine the scientific feasibility of intervention using small molecules to restore metabolic balance within the diseased cell. As in our efforts to develop therapeutics for cancer, we create a crystal structure of the enzyme to begin the process of drug design. We make candidate tool molecules using structure-based design coupled with high throughput chemical screening. To fully evaluate the potential of our lead molecules to lead to disease modifying effects we strive to develop an animal model of the disease by genetically inserting the mutated enzyme into animals ("knock-in mouse model"). Agios has selected a product candidate for the treatment of PK deficiency to advance into clinical development. Drug discovery for an additional four IEMs are in various stages of research.

We will only progress drug candidates forward into phase 1 trials if we have the ability to select patients who are most likely to respond to a given therapy based on genetic or metabolic biomarkers. Our industry has been plagued by an unacceptable rate of both early and late stage clinical failures, leading to disappointments for both patients and investors. We believe that the primary reason for failure is the difficulty of demonstrating efficacy,

due to an inability to identify an appropriately defined treatable patient sub-population. While many factors are considered critical to maximize the probability of technical success in the drug development process, perhaps none is more important than identifying highly specific and selective molecules aimed at the best possible targets for therapy coupled with the patients most likely to respond to that therapy. Our goal is to develop increasing confidence in the target and the patient population prior to entering human clinical trials and then initiate those first human trials in a patient population that has been selected based on target dependence using a biomarker. This approach, known as personalized or precision medicine, is also designed to lead to the potential for clear proof of concept in early human trials and expedited approval timelines.

We believe our approach to drug discovery and development will translate into a higher probability of technical success for our programs in comparison to conventional drug discovery and will lead to transformative medicines for patients. We plan to partner closely with worldwide regulatory authorities and to utilize all available methodologies such as orphan, fast track, accelerated approval and/or breakthrough therapy designations as appropriate. We expect that conducting clinical trials with a targeted agent in the appropriate clinical population will lead to very rapid development timelines. There are now multiple examples within oncology of drugs against novel targets that have progressed from first in human trial to regulatory approval in less than five years (e.g., Gleevec®, VELCADE® and Xalkori®).

**Our development programs**

We have leveraged our core capabilities in cellular metabolism to build a research and development engine that is focused in the therapeutic areas of cancer and IEMs. This engine has permitted us to discover proprietary first-in-class orally available small molecules as potential lead product candidates for each of several novel programs in preclinical development. All of our lead programs focus on diagnostically-identified patient populations with the potential for early clinical proof of concept and accelerated approval paths.

The following table summarizes key information about our most advanced product candidates, each of which is described and discussed in further detail below:

| Product candidate | Biomarker(s) | Initial indications | Stage of development | Commercial rights |
|---|---|---|---|---|
| **Cancer metabolism programs:** | | | | |
| AG-221 (IDH2 mutant inhibitor) | Genotyping of IDH2 mutation; 2HG | All cancer patients with an IDH2 mutation in the following diseases: acute myelogenous leukemia, high risk myelodysplasia and myeloproliferative disorders, angio-immunoblastic non-Hodgkins T cell lymphoma, glioma, chondrosarcoma and other solid tumors | IND-enabling activities | Agios: milestones and royalties<br><br>Celgene: worldwide |
| AG-120 (IDH1 mutant inhibitor) | Genotyping of IDH1 mutation; 2HG | All cancer patients with an IDH1 mutation in the following diseases: glioma, chondrosarcoma, cholangiocarcinoma, acute myelogenous leukemia, high risk myelodysplasia and myeloproliferative disorders, and other hematological and solid tumors | IND-enabling activities | Agios: option on 100% of U.S. rights<br><br>Celgene: ex-U.S. rights; worldwide rights if Agios option is not exercised |
| Glutaminase (Glutaminase inhibitor) | To be determined | Cancer patients with various subsets of tumors dependent on glutaminase | Late research | Agios: if option on AG-120 U.S. rights not exercised, we retain an option on 100% of U.S. rights<br><br>Celgene: worldwide if option on AG-120 U.S. rights exercised; ex-U.S. if AG-120 U.S. rights not exercised and we exercise our option on glutaminase U.S. rights |
| **Inborn errors of metabolism programs:** | | | | |
| AG-348 (Pyruvate kinase (R) activator) | Genetic testing for mutation in the pyruvate kinase R gene | Patients with pyruvate kinase deficiency | IND-enabling activities | Agios: worldwide |
| AG-221 or other mutant inhibitor (IDH2 mutant inhibitor) | Genotyping of IDH2 mutation; 2HG | Patients with Type II D-2-hydroxyglutaric aciduria | Research | Agios: milestones and royalties<br><br>Celgene: worldwide |

**Cancer**

***Background***

In most cases of advanced cancer, the diagnosis still represents a death sentence to patients and their families.

The American Cancer Society estimates that 1.66 million new cancer cases will be diagnosed in the U.S. in 2013. According to the Society, about 580,000 Americans and 7.6 million people worldwide will die of cancer in 2013. Cancer is the second leading cause of death in the United States, exceeded only by heart disease. Lung, colon and rectal, breast, and prostate cancer are the most prevalent cancers. Causes of cancer include environmental factors such as tobacco, chemicals, radiation and diet, genetic factors, such as inherited mutations, and endogenous hormone levels, and associated medical conditions such as certain viral infections and immunodeficiency.

Cancer is a disease characterized by unregulated cell growth. Cancer typically develops when the repair of genetic material in normal cells begins to fail and genes that regulate cell growth become disrupted. Carcinogens, or cancer causing agents, such as radiation, chemicals and hormones, can trigger changes to the genetic material of a cell, and typically prompt this disruption. Cells that have been disrupted may become cancerous, leading to changes in the cells' DNA, and ultimately uncontrolled growth. Cancer cells can spread to other areas of the body, or metastasize, and form tumors, which can destroy normal tissue or organs. Risk factors for cancer include family history, age, diet, and exogenous factors, such as exposure to ultraviolet sunlight and smoking. Cancers can be classified in stages to document disease severity, measured in stages of I to IV, generally based on tumor size, involvement of lymph nodes, and metastases.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy. A cancer patient often receives treatment with a combination of these methods. Surgery and radiation therapy are particularly effective in patients in whom the disease is localized. Physicians generally use systemic drug therapies in situations in which the cancer has spread beyond the primary site or cannot otherwise be treated through surgery. The goal of drug therapy is to kill cancer cells or to damage cellular components required for rapid growth and survival of cancer cells. In many cases, drug therapy entails the administration of several different drugs in combination. Over the past several decades, drug therapy has evolved from non-specific drugs that kill both healthy and cancerous cells to drugs that target specific molecular pathways involved in cancer.

*Cytotoxic chemotherapies*

The earliest approach to cancer treatment was to develop drugs, referred to as cytotoxic drugs, that kill rapidly proliferating cancer cells through non-specific mechanisms, such as disrupting cell metabolism or causing damage to cellular components required for survival and rapid growth. While these drugs, (e.g. CYTOXAN®, Adriamycin®) have been effective in the treatment of some cancers they act in an indiscriminate manner, killing healthy as well as cancerous cells. Due to their mechanism of action, many cytotoxic drugs have a narrow dose range above which the toxicity causes unacceptable or even fatal levels of damage and below which the drugs are not effective in eradicating cancer cells.

*Targeted therapies*

The next approach to pharmacological cancer treatment was to develop drugs, referred to as targeted therapeutics, that target specific biological molecules in the human body that play a role in rapid cell growth and the spread of cancer. Targeted therapeutics are designed to preferentially kill cancer cells and spare normal cells, to improve efficacy and minimize side effects. The drugs are designed to either attack a target that causes uncontrolled growth of cancer cells because of either a specific genetic alteration primarily found in cancer cells but not in normal cells or a target that cancer cells are more dependent on for their growth in comparison to normal cells. Examples of effective targeted therapies include Herceptin®, Avastin® and Zelboraf®.

*Emerging areas*

Several new approaches to develop novel cancer treatments are underway. They include: treatment with drugs or other methods that stimulate the normal immune system to attack the cancer; antibody drug conjugates (Kadcyla™) that carry a powerful chemotherapy payload that is only released into the cancer cell; and drugs that target the proteins that coat the DNA in cancer cells (epigenetics).

We believe that interrogating altered cellular metabolism—the way cancers take up and break down their nutrients—will lead to a new wave of important cancer treatments. Further, we believe that we must utilize a precision medicine approach, which will enable us to only enroll patients in clinical trials based on a biomarker likely to predict response and benefit.

***Programs in isocitrate dehydrogenase (IDH)***

The isocitrate dehydrogenase (IDH) protein is a critical enzyme in the citric acid cycle, also known as the tricarboxylic acid, or Krebs, cycle. The Krebs cycle is centrally important to many biochemical pathways, and is one of the earliest established components of cellular metabolism. The Krebs cycle converts an essential cellular metabolite called isocitrate into another metabolite, alpha-ketoglutarate (a-ketoglutarate), both of which are critically important for cellular function and the creation of energy. In humans, there are three forms of the IDH enzyme (IDH1, IDH2, and IDH3) but only IDH1 and IDH2 appear to be mutated in cancers. IDH1 and IDH2 catalyze the same reaction but in different cellular compartments: IDH1 is found in the cytoplasm of the cell and IDH2 in the mitochondria. Tumor cells are generally observed to carry either an IDH1 or IDH2 mutation, but not both.

We have identified selective development candidates that target the mutated forms of IDH1 and IDH2 which are each found in a wide range of solid and hematological cancers. We and our collaborators have demonstrated that these mutations initiate and drive cancer growth by blocking differentiation, also referred to as maturation, of primitive cells which leads to tumor formation and maintenance. We believe that inhibition of these mutated proteins, and not their normal counterparts, may lead to clinical benefit for the subset of cancer patients whose tumors carry these mutations.

*Agios research in IDH mutations in cancer*

Academic researchers first identified mutations in either IDH1 or IDH2 in over 70% of patients with brain tumors, also known as gliomas. They also demonstrated that the mutated form of the enzyme IDH was no longer able to conduct its normal function of converting the metabolite isocitrate into alpha-ketoglutarate. Our scientists decided to examine the mutated pathway using our metabolic platform and discovered that the mutated IDH enzymes had adopted a novel “gain of function” activity that allows only the mutated IDH enzyme to produce large amounts of a metabolite called 2–hydroxygluturate, or 2HG. This discovery was the subject of the first Agios publication in the scientific journal *Nature* (Dang et al 2009), and was subsequently deemed by *Nature* to be one of the most important recent discoveries in cancer research.

We believe that the excessive levels of the metabolite 2HG produced by the tumor, fuel cancer growth and survival via multiple cellular changes that lead to a block in cell maturation, or differentiation. Recently, two published preclinical studies confirm that 2HG promotes tumorigenesis and that the effects of 2HG can be reversed with an IDH1 or IDH2 mutant specific inhibitor. 2HG is also an ideal biomarker to identify and follow cancer patients as they receive treatment with an IDH mutant specific inhibitor. In normal cells, 2HG is present at extremely low levels. However, in cancer cells that carry the IDH mutation, 2HG is produced at massively higher levels than in normal cells. It can easily be detected in samples from cancer specimens and in the blood of certain cancer patients. In patients with brain tumors it can also be imaged on an MRI.

In a cell based model it was demonstrated that the IDH1 mutation (R132H) promotes growth factor independence (i.e., transformation into cancerous cells) and blocks differentiation in hematopoietic cells. It was also demonstrated

in this model that the cell's transformation into cancer could be driven solely by the metabolite 2HG without any mutant enzyme. Lastly the transformation by IDH1 mutation was reversible with the use of an IDH1 mutant inhibitor. (*Science* Kaelin et al 2013). These results are illustrated in the graph below.

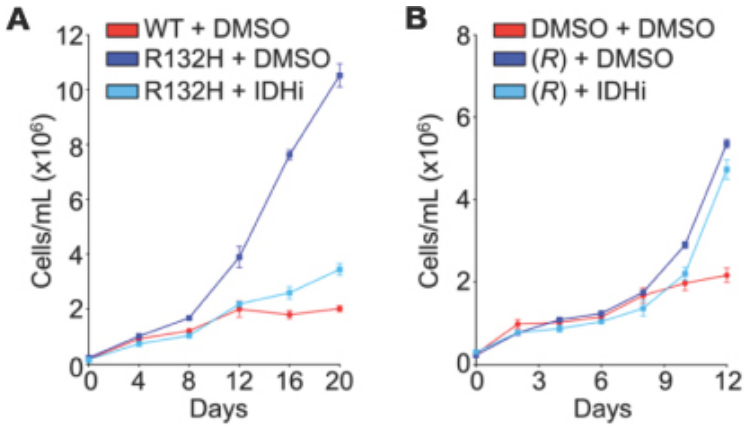
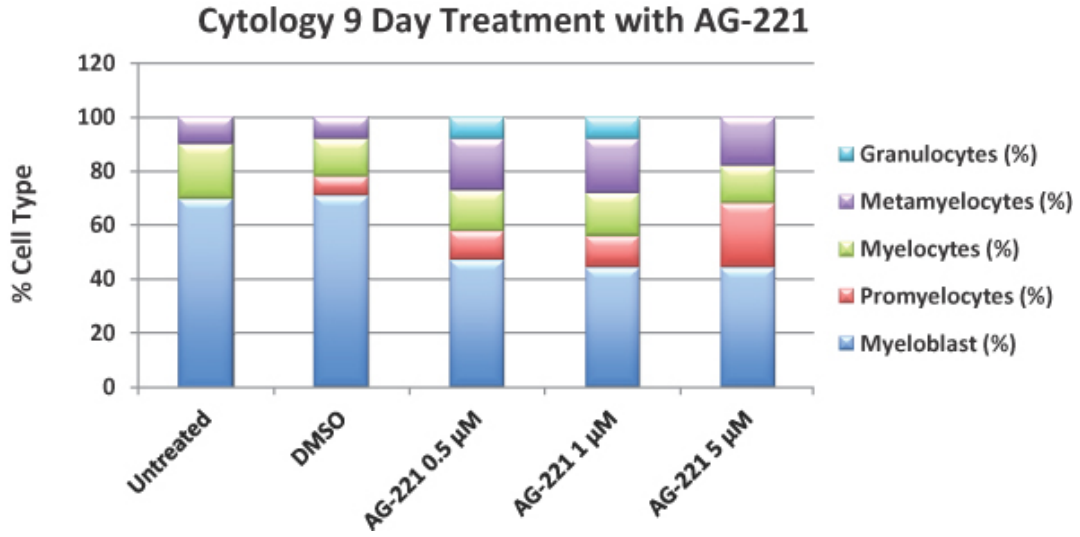



***Figure A*** demonstrates that insertion of R132H IDH1 mutation into TF-1 cells leads to growth factor independence which can be reversed by the addition of an Agios IDH1 inhibitor. ***Figure B*** demonstrates that this transformation to growth factor independence can be replicated solely by the addition of 2HG(R). As expected, the IDH1 inhibitor has no effect on the ability of exogenously administered 2HG to transform cells.

An *ex vivo* model is shown in the figure below, in which human acute myelogenous leukemia, or AML, bone marrow cells removed directly from a patient with a leukemia positive for an IDH2 mutation were maintained in short term culture. Treatment with the Agios clinical candidate at concentrations achievable *in vivo* revealed a significant decrease in leukemia cells (myeloblasts) associated with evidence that normal cell maturation is returning, as noted by the increase in normal maturing cells (promyeocytes, myeocytes, metamyelocytes and granulocytes). These data provide *ex vivo* proof of concept that inhibitors targeting mutant IDH2 could induce differentiation in cells previously destined to form undifferentiated leukemic cells.



Taken together, these data provide compelling evidence that IDH1 or IDH2 mutant inhibitors induce differentiation in both cell based models and primary patient samples. The best example of an approved treatment that can reverse the block in differentiation induced by a mutation is all trans-retinoic acid (ATRA) for the treatment of acute promyelocytic leukemia. This single agent leads to complete responses in this form of leukemia, which is driven by a genetic alteration in the retinoic acid receptor, and is proof of principle that differentiation therapy can lead to major clinical activity in patients with acute leukemia.

*Incidence of IDH mutations*

To date, IDH1 and IDH2 mutations have been found to be prevalent in both solid and hematologic tumors. Mutations in IDH1 were identified through a genome-wide mutation analysis in glioblastoma multiforme, or GBM. High throughput deep sequencing revealed the presence of mutations in either IDH1 or IDH2 in more than 70% of grade II-III gliomas and secondary glioblastomas. Subsequent sequencing efforts revealed alterations in these two genes across additional cancers, including hematologic malignancies. Mutations in IDH1 and IDH2 are generally mutually exclusive and occur at very early stages of tumor development suggesting that they can promote tumorigenesis.

- IDH2 mutations appear to be most prevalent in hematologic tumors. Among patients with AML, IDH2 mutations have been observed in 15% of adult patients. Outside of AML, IDH2 mutations are found in a subset of other hematologic and non-hematologic cancers. Sequence analysis has shown that IDH2 mutations occur in approximately 5% of patients with myelodysplastic syndrome, or MDS, or myeloproliferative neoplasms, or MPN. IDH2 mutations have also been found in several solid tumor types such as melanoma, glioma and chondrosarcoma.
- IDH1 mutations appear to be most prevalent in solid tumors. Among patients with gliomas (low grade glioma and secondary glioblastoma), IDH1 mutations have been observed in 70% of patients. Outside of gliomas, mutations have been found in a subset of other solid and hematologic cancers. Importantly, mutations in IDH1 have been identified in difficult to treat cancers such as chondrosarcoma and cholangiocarcinoma where both the treatment options and prognosis for patients are poor. IDH1 mutations have also been found in several other solid tumor types such as colon, melanoma and lung.

The following table summarizes our current estimates on the prevalence of IDH2 and IDH1 mutations in hematologic and solid tumors. We believe our estimates may expand as more cancer treatment centers screen for these IDH mutations.

| Mutation | Indications | % with IDH mutations | Estimated patients per year(1) |
|---|---|---|---|
| **IDH2** | AML | 15% | 7,200 |
| | MDS/MPN | 5% | 2,000 |
| | Angio-immunoblastic T cell NHL | 25% | 400 |
| | Others (melanoma, glioma, chondrosarcoma) | 3-5% | 1,500 |
| | **Total** | | **11,100** |
| **IDH1** | Grade II, III glioma & secondary GBM | 70% | 11,000 |
| | Chondrosarcoma | >50% | 4,600 |
| | AML | 7.50% | 3,600 |
| | MDS/MPN | 5% | 2,000 |
| | Cholangiocarcinoma | 20% | 1,600 |
| | Others (colon, melanoma, lung) | 1-2% | 8,000 |
| | **Total** | | **30,800** |

(1) Estimated U.S., Europe and Japan incidence

***AG-221: lead IDH2 program***

AG-221 is an orally available, selective, potent inhibitor of the mutated IDH2 protein, making it a highly targeted therapeutic candidate for the treatment of patients with cancers that harbor IDH2 mutations, including those with AML. Based on our established non-clinically-based target profiling, as well as non-clinical *in vitro* and *in vivo* efficacy data, there is a clear rationale to develop AG-221 in defined target populations that harbor the IDH2 gene mutation.

We have conducted exploratory pharmacology studies to develop a model of IDH mutant-induced tumorigenesis and to characterize the binding, inhibition, and selectivity of AG-221. AG-221 is a potent inhibitor of the IDH2 mutant protein. We have demonstrated in *in vitro* experiments that exposure to AG-221 reduces 2HG levels to those found in normal cells, reverses 2HG-induced histone hypermethylation, and induces differentiation in multiple leukemia cell models. Targeted inhibition of the IDH2 mutant also reversed the differentiation block in both TF-1 leukemia cells and primary AML cells derived from patients.

We have successfully completed IND-enabling studies on AG-221. The molecule has excellent pharmacological properties with a wide therapeutic index, and has demonstrated a clear safety profile to advance into clinical trials. We have obtained materials for AG-221 for our planned phase 1/2 testing from third party manufacturers. We plan to initiate phase 1/2 clinical trials in IDH2–mutation positive cancers in mid-2013. Our first clinical trial is being planned as a phase 1/2 trial in patients with advanced hematological malignancies that carry the IDH2 mutation and have correspondingly elevated 2HG levels. This multi-center, multiple ascending dose trial will primarily assess safety and tolerability for AG-221 in adults with AML or related diseases. Secondary endpoints will evaluate the pharmacokinetics and pharmacodynamics properties of AG-221 and determine if any efficacy

signals can be measured. The initial proof of mechanism will require the reduction of the metabolite 2HG in response to drug treatment. Multiple disease specific cohorts of 10-20 patients will be enrolled after a safe biologically active dose has been determined to evaluate the single-agent disease modifying activity of AG-221. We intend to conduct subsequent trials in patients with other cancers carrying the IDH2 mutation and in combination with other anti-cancer agents. We plan to pursue additional clinical studies, evaluating both single-agent as well as combination therapy in patients with serious and life-threatening hematological and solid tumors that harbor IDH2 mutation, in the most efficient manner as we seek to establish the safety and effectiveness of AG-221. The potential regulatory pathway (i.e., conventional or accelerated approval) will be determined by data emerging from the early development program.

***AG-120: lead IDH1 program***

AG-120 is an orally available, selective, potent inhibitor of the mutated IDH1 protein, making it a highly targeted therapeutic candidate for the treatment of patients with cancers that harbor IDH1 mutations. Importantly, mutations in IDH1 have been identified in difficult to treat cancers such as chondrosarcoma and cholangiocarcinoma where both the treatment options and prognosis for patients are poor. These are indications where the standard of care treatment options are limited, thus providing an opportunity for more rapid development of an IDH1 inhibitor. Based on our nonclinical *in vitro* and *in vivo* efficacy data, there is a clear rationale to develop AG-120 in defined target populations that harbor the IDH1 gene mutation.

AG-120 has completed exploratory safety studies in both rodents and primates, and has initiated manufacturing to allow for IND-enabling studies. We expect to initiate clinical trials in early 2014. Shortly thereafter, we plan to initiate multiple phase 1/2 clinical trials in both hematological and solid cancers. Our first clinical trial is being planned as a phase 1/2 trial in patients with advanced solid and hematological malignancies that carry the IDH1 mutation.

***Other programs***

In addition to our lead IDH2 and IDH1 programs, we are in earlier stages of validation and drug discovery on multiple novel programs. Our third cancer metabolism program targets the enzyme glutaminase, or GLS, which converts the nutrient glutamine into the metabolite glutamate. There appear to be multiple cancers that are dependent on this reaction for their survival and rely heavily on glutamine rather than glucose as a nutrient source. Our research has identified a means to identify the patients whose tumors are addicted to this nutrient source and the GLS enzyme. Drug discovery is currently in the late lead optimization stage. We also have a fourth validated program in drug discovery and currently have 10 targets in the early stages of validation.

**Inborn errors of metabolism**

***Background***

IEMs are a broad group of more than 600 orphan genetic diseases caused by mutations of single metabolic genes. In these disorders, the defect of a single metabolic enzyme disrupts the normal functioning of a metabolic pathway, leading to either aberrant accumulation of “upstream” metabolites which may be toxic or interfere with normal function or reduced ability to synthesize essential “downstream” metabolites or other critical cellular components. IEMs are also referred to as congenital metabolic diseases or rare genetic metabolic diseases.

The term inborn error of metabolism was coined by a British physician, Archibald Garrod (1857–1936), in the early 20th century. He is known for work that prefigured the “one gene-one enzyme” hypothesis, and his seminal text, Inborn Errors of Metabolism, was published in 1923. Traditionally, IEMs were categorized as disorders of carbohydrate metabolism, amino acid metabolism, organic acid metabolism, or lysosomal storage diseases. In recent decades, hundreds of new IEMs have been discovered and the categories have proliferated.

Most of these diseases are rare or ultra-rare orphan diseases, often with severe or life-threatening features. A disorder is considered orphan if it affects fewer than 200,000 people in the United States, or fewer than five per 10,000 people in the European Union. In a study in British Columbia, the overall incidence of IEMs was estimated to be 70 per 100,000 live births or one in 1,400 births, overall representing more than approximately 15% of single gene disorders in the population. Incidence of a single IEM can vary widely but is generally rare, usually equal to or less than one per 100,000 births. Many IEMs are likely to be under-diagnosed given the lack of available therapies or diagnostics and the rarity of the condition.

Current treatment options for these disorders are limited. Diet modification or nutrient supplementation can be beneficial in some IEMs. Several of these disorders, from a group known as lysosomal storage diseases, have been treated successfully with enzyme replacement therapy, or ERT, the therapeutic administration of a functional version of the defective enzyme. Examples of ERTs for lysosomal storage disorders include Fabrazyme® for Fabry disease, Myozome® for Pompe disease, Cerezyme® for Gaucher disease, and Elaprase® for Hunter syndrome.

Unfortunately, most mutations driving IEMs are intracellular and not amenable for treatment with enzyme replacement therapies. As a result, despite the promising progress made for patients with a small group of these diseases, the vast majority of patients with IEMs have few therapeutic options available, and the standard of care is palliative, meaning treatment of symptoms with no effect on underlying disease mechanisms. We are taking a novel small molecule approach to correct the metabolic defects within diseased cells with a goal of developing transformative medicines for patients.

***Pyruvate kinase deficiency program***

Pyruvate kinase, or PK, is the enzyme involved in the second to last reaction in glycolysis—the conversion of glucose into lactic acid. This enzyme is critical for the survival of the cell and has several tissue-specific isoforms (PKR, PKL, PKM1 and PKM2). PKR is the isoform of pyruvate kinase which is present in red blood cells. Mutations in PKR cause defects in red cell glycolysis and leads to a hematological IEM known as pyruvate kinase deficiency, or PK deficiency. Glycolysis is the only pathway available for red blood cells to maintain the production of ATP, or Adenosine-5'-triphosphate, which transports chemical energy within cells for metabolism. Accordingly, total absence of the PKR gene is not compatible with life. PK deficiency leads to a shortened life-span for red blood cells and is the most common form of non-spherocytic hemolytic anemia in humans. The disease is autosomal recessive, meaning children inherit one mutated form of PKR from one parent and the second mutated form from the other parent. Children with the disease produce PKR enzyme that has only a fraction of the normal level of activity (generally <50%). Parents of affected children have only one copy of the mutated PKR enzyme and are clinically normal.

PK deficiency is a rare disorder and disease understanding is still evolving. Several published epidemiology studies estimated prevalence of PK deficiency between three to nine diagnosed patients per million. Agios estimates that between 1,000-3,000 diagnosed patients are alive in the U.S., with similar numbers in Europe, and we believe that the disease is likely under-diagnosed. There is no unique ethnic or geographic representation of the disease. The disease manifests by mild to severe forms of anemia caused by the excessive premature destruction of red blood cells. The precise mechanism for the destruction is not well understood but is thought to result from membrane instability secondary to the metabolic defect caused by the low level of PKR enzyme. The hemolysis is "extra-vascular" in that the red blood cells are destroyed in small capillaries or organs and not spontaneously breaking open in the circulation.

The disease typically presents during early infancy with jaundice and severe anemia, which can require immediate life-saving intervention via replacement of the infant's entire blood system with a donor's blood, referred to as an exchange transfusion. Children are classified as either severe disease (hemoglobin <8gm/dl and life long need for transfusions) or moderate (hemoglobin levels of 8-10 gm/dl and intermittent or rare transfusion support). Adults also fall into two similar categories: severe, which requires chronic transfusions, often monthly,

or moderate, which requires intermittent transfusions. Both moderate and severe patients may develop a severe hemolytic crisis in the face of infections or other "stressful" situations and face life-long anemia with an impact on the quality of life.

There is no treatment for this disease other than transfusion support and the disease is life-long. The true natural history and impact of life-long hemolysis is unknown. Chronic iron overload related to transfusions and possibly the disease itself can lead to life-threatening complications. Splenectomy, which refers to removal of the spleen, can modify the symptoms of the disease in some patients but has minimal impact on the ongoing hemolysis. Agios has commissioned and initiated a natural history study that will conduct a chart review of patients with the disorder and prospectively follow a select group.

*AG-348: lead PKR program*

Our development candidate AG-348 is an orally available, potent small molecule activator of PKR. Preclinical *in vitro* data demonstrate that these activators can significantly enhance both the activity and the stability of the majority of the common PKR mutants. This degree of enzyme activation leads to a meaningful correction of the metabolic imbalance normally found within mutant cells. Red blood cells have been obtained from patients with severe and moderate PK deficiency where *ex vivo* studies have demonstrated enzyme activation and metabolic improvement. AG-348 has completed exploratory safety studies in both rodents and primates, and we will be initiating manufacturing to allow for IND-enabling studies. We expect to start phase 1/2 clinical trials in patients with PK deficiency in 2014.

We believe the clinical and regulatory strategy for our PK deficiency program has well established primary and secondary endpoints similar to that of other approved medicines developed for the treatment of hemolytic anemia.

***Type II D-2 hydroxyglutaric aciduria: IDH2 non-cancer indication***

A germline mutation in IDH2, identical to that of cancer patients, has recently been discovered in patients with an ultra-rare, extremely debilitating, and uniformly fatal, genetic neurometabolic disorder called Type II D-2 hydroxyglutaric aciduria. Type II D-2-HGA patients develop a range of medical complications, including developmental delay, seizures, hypotonia, epilepsy, cardiomyopathy, and dysmorphic features. Few affected patients survive past their teens, with the majority dying from cardiac and/or central nervous system disease.

In addition to our planned cancer development program, we will potentially evaluate the use of AG-221 for Type II D-2 HGA. We have initiated collaborations with global metabolic clinical centers to further explore the prevalence and incidence of the disease. There have been potentially 50 reported cases globally, however there is uncertainty as to the number of patients, and we are conducting a natural history study in order to better determine the incidence of the disease.

***Other preclinical IEM programs***

Our approach is to identify a series of IEMs which share the following common set of features:

- single gene defect;
- severe clinical presentation with evidence that disease damage is progressive but potentially reversible;
- adequate number of patients identified for prospective clinical trials; and
- an assessment of the target, based upon a detailed mutational, structural, and metabolomic analysis, to determine if a small molecule approach to correcting the disease is possible.

Based on the above criteria, we have started exploratory and early target validation for four programs.

**Collaboration with Celgene**

In April 2010, we entered into a Discovery and Development Collaboration and License Agreement with Celgene, focused on targeting cancer metabolism. The goal of the collaboration is to discover, develop and commercialize disease-altering therapies in oncology arising out of our cancer metabolism research platform that have achieved development candidate status on or before April 14, 2014. Celgene will have the option to extend such period through April 14, 2016. We refer to such four to six year period as the discovery phase of the collaboration. We are leading discovery, preclinical and early clinical development for all cancer metabolism programs under the collaboration. We have nominated two development candidates during the discovery phase and both development candidates have been confirmed by a joint research committee, or JRC, pursuant to the agreement—our IDH1 and IDH2 development candidates.

*Discovery programs with development candidates*. Celgene may elect to progress into preclinical development each discovery program for which we nominate and the JRC confirms a development candidate during the discovery phase. If Celgene makes such an election, we will, at our expense, conduct studies required to meet the requirements for filing an IND, or IND-enabling studies, and, following their successful completion as confirmed by the JRC, we will file an IND to commence clinical studies of such development candidate. If the FDA accepts the IND, Celgene may request that we conduct an initial phase 1 study at our expense, for which Celgene will pay us at least $5 million upon enrollment of the last patient in such study unless such program becomes a split licensed program, as described below.

Celgene may elect to convert each discovery program for which we have nominated a development candidate into a co-commercialized licensed program, the attributes of which are described below. We have the right, exercisable during a specified period following FDA acceptance of the applicable IND, to convert one of every three co-commercialized licensed programs into a split licensed program, for which we retain the United States rights, other attributes of which are further described below. Our IDH2 program will not be a split licensed program. We may elect to opt out of any split licensed program, after which such split licensed program will revert to a co-commercialized licensed program, and Celgene will have the right, but not the obligation, to commercialize medicines from such program in the United States.

We will retain our rights to the development candidate and certain other compounds from any discovery program for which we nominate and the JRC confirms a development candidate and that Celgene does not elect to progress into preclinical development or convert into a co-commercialized licensed program. In addition, if the JRC or Celgene elects not to continue collaboration activities with respect to a particular target, either we or Celgene would have the right independently to undertake a discovery program on such target and would have rights to specified compounds from such program, subject to certain “buy-in” rights granted to the other party.

*Further development and commercialization of programs*. The agreement provides for three types of licensed programs discussed above: co-commercialized licensed programs, split licensed programs, and buy-in programs. Celgene’s and our rights and obligations under each licensed program vary depending on the type of licensed program, as described below.

- *Co-commercialized licensed programs*: Celgene will lead and, following either IND acceptance by the FDA or, if Celgene requests us to conduct the initial phase 1 study, completion of such study, will fund global development and commercialization of each co-commercialized licensed program. We have the right to participate in a portion of sales activities in the United States for medicines from co-commercialized programs in accordance with the applicable commercialization plan.
- *Split licensed programs*: Celgene will lead development and commercialization outside the United States, and we will lead development and commercialization in the United States, for each split licensed program. We and Celgene will equally fund the global development costs of each split licensed program that are not specific to any particular region or country, Celgene will be responsible for development and commercialization costs specific to countries outside the United States, and we will be responsible for development and commercialization costs specific to the United States.

- *Buy-in programs*: The party that was conducting an independent program that became a buy-in program will lead the development and commercialization of such program. The party that elects to buy in to such program will be responsible for funding a portion of development costs incurred after acceptance of an IND for a buy-in program compound, and the lead party will be responsible for all other development costs and all commercialization costs for medicines from such buy-in program.

In addition, Celgene may license certain discovery programs for which we did not nominate or the JRC did not confirm a development candidate during the discovery phase and for which Celgene will lead and fund global development and commercialization. We refer to these as picked licensed programs.

*Collaboration governance*. The collaboration is managed by a set of joint committees comprised of equal numbers of representatives from each of us and Celgene. The joint steering committee, or JSC, oversees and coordinates the overall conduct of the collaboration. The JRC oversees and coordinates discovery, research and preclinical activities with respect to each discovery program during the discovery phase. A joint development committee, or JDC, for each licensed program will oversee and coordinate development (including manufacturing of clinical supply) of medicines under such licensed program. The joint commercialization committee, or JCC, will oversee the commercialization (including manufacturing of commercial supply) of medicines under the licensed programs.

*Diligence*. We and Celgene each must use commercially reasonable efforts to perform all activities for which such party is responsible under the collaboration.

*Exclusivity*. During the discovery phase, we may not directly or indirectly develop, manufacture or commercialize, except pursuant to the agreement, any product or product candidate for any cancer indication with specified activity against certain metabolic targets (except in connection with certain specified third party collaborations), or with specified activity against any collaboration target (or any target for which Celgene is conducting an independent program that we elected not to buy in to) for any indication. Following the discovery phase until termination or expiration of the agreement, either in its entirety or with respect to the relevant program, we may not directly or indirectly develop, manufacture or commercialize, outside of the collaboration, any therapeutic modality with specified activity against any collaboration target that is within a licensed program or against any former collaboration target against which Celgene is conducting an independent program under the agreement. Pursuant to the terms of the first amendment to the agreement, we have the right to develop, manufacture and commercialize outside of the collaboration certain medicines directed against PKR for certain indications, including PK deficiency, subject to specified conditions, including a right of first negotiation that Celgene may exercise if we intend to license our PKR program to any third party.

*Financial terms*. Under the terms of the agreement, we received an upfront payment of approximately $121.2 million. In addition, Celgene purchased 5,190,551 shares of our series B convertible preferred stock at a price of $1.70 per share, resulting in net proceeds to us of approximately $8.8 million. Celgene made a payment to us of $20.0 million pursuant to an October 2011 amendment in consideration of extending the discovery phase until April 14, 2014.

We may be eligible to receive up to an additional $40.0 million in extension payments to extend the discovery phase until April 2016 and up to $120.0 million in potential milestone payments payable for each licensed program other than buy-in programs. The potential milestone payments under the agreement for such licensed program are comprised of: (i) a $25.0 million milestone payment upon achievement of a specified clinical development milestone event, (ii) up to $70.0 million in milestone payments upon achievement of specified regulatory milestone events, and (iii) a $25.0 million milestone payment upon achievement of a specified commercial milestone event (for co-commercialized and certain other licensed programs only). In addition, we are eligible to receive a payment of $22.5 million upon achievement of an early clinical development milestone event for certain co-commercialized licensed programs. We are also eligible to receive a one-time payment of $25.0 million upon dosing of the last patient in a phase 2 study for the first split licensed program.

We are eligible to receive royalties at tiered, low- to mid-teen percentage rates on Celgene's net sales of medicines from licensed programs. We are also eligible to receive royalties at a fixed, mid-single digit percentage rate on net sales of medicines from certain Celgene independent programs. We may be obligated to pay Celgene royalties at tiered, low- to mid-teen percentage rates on our net sales in the United States of medicines from split licensed programs and on net sales of medicines from buy-in programs for which we are the commercializing party.

*Termination*. Celgene may terminate the agreement for convenience in its entirety or with respect to one or more programs upon ninety days written notice to us. Either we or Celgene may terminate the agreement, in its entirety or with respect to one or more programs, if the other party is in material breach and fails to cure such breach within the specified cure period; however, if such breach relates solely to a specific program, the non-breaching party may terminate the agreement solely with respect to such program. Either we or Celgene may terminate the agreement in the event of specified insolvency events involving the other party.

If Celgene terminates the agreement as a result of our uncured material breach, then certain of our rights and certain of Celgene's obligations described above would change with respect to the terminated program(s), including, for example: the licenses we granted to Celgene would become perpetual; milestone payments to which we may be entitled may be reduced or eliminated; royalties to which we may be entitled may be reduced or eliminated; we would lose the development and commercialization rights for the United States for any terminated split licensed program; and we would grant Celgene specified rights, and take specified actions, to assist Celgene in continuing the development, manufacture and commercialization of medicines for the United States from each terminated split licensed program.

If Celgene terminates the agreement for convenience or if we terminate the agreement as a result of Celgene's uncured material breach, the licenses we granted to Celgene with respect to the terminated program(s) will end, and we will have specified rights for, and Celgene will take specified actions to assist us in continuing, the development, manufacture and commercialization of medicines from each terminated program.

**Intellectual property**

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our product candidates and our core technologies, including novel biomarker and diagnostic discoveries, and other know-how, to operate without infringing on the proprietary rights of others and to prevent others from infringing our proprietary or intellectual property rights. Our policy is to seek to protect our proprietary and intellectual property position by, among other methods, filing U.S., international and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position.

We file patent applications directed to our key product candidates in an effort to establish intellectual property positions regarding new chemical entities relating to these product candidates as well as uses of new chemical entities in the treatment of diseases. We also seek patent protection with respect to biomarkers that may be useful in selecting the right patient population for therapies with our product candidates. As of April 30, 2013, we had approximately 30 pending U.S. patent applications and approximately 120 pending foreign patent applications. A significant portion of our pending patent applications pertain to our key discovery programs. Any patents that may issue from these applications would expire between 2027 and 2034.

The intellectual property portfolios for our most advanced product candidates as of April 30, 2013 are summarized below.

***Cancer metabolism***

- *IDH2:* The intellectual property portfolio for our IDH2 program contains patent applications directed to compositions of matter for AG-221 and other chemical scaffolds as well as methods of making, referred to as synthetic methods, and methods of use. As of April 30, 2013, we owned two pending U.S. patent applications as well as corresponding pending foreign patent applications, and a pending Patent Cooperation Treaty, or PCT, patent application.

- *IDH1:* The intellectual property portfolio for our IDH1 program contains patent applications directed to compositions of matter for AG-120 and multiple chemical scaffolds as well as synthetic methods and methods of use. As of April 30, 2013, we owned five pending U.S. patent applications as well as corresponding foreign patent applications, and four pending PCT patent applications.

- *GLS:* The intellectual property portfolio for our GLS program contains patent applications directed to compositions of matter for the lead series and other chemical scaffolds as well as synthetic methods and methods of use. As of April 30, 2013, we owned two pending U.S. patent applications and a pending PCT patent application.

***Inborn errors of metabolism***

- *PKR*: The intellectual property portfolio for our PKR program contains patent applications directed to compositions of matter for AG-348 and multiple chemical scaffolds as well as synthetic methods and methods of use. As of April 30, 2013, we owned seven pending U.S. patent applications as well as their corresponding foreign patent applications, and seven pending PCT patent applications.

In addition to the pending patent applications covering our most advanced product candidates, our portfolio also includes pending patent applications relating to diagnostic methods for detecting various IDH1 and IDH2 mutations and biomarkers useful for identifying patients suitable for therapies by GLS inhibitors, as well as compositions of matter and methods of use directed to modulating other metabolic targets.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or the USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug or biological product may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. See "—Government regulation—The Hatch-Waxman Act" below for additional information on such exclusivity. In the future, if and when our product candidates receive approval by the FDA or foreign regulatory authorities, we expect to apply for patent term extensions on issued patents covering those products, depending upon the length of the clinical trials for each medicine and other factors. There can be no assurance that any of our pending patent applications will issue or that we will benefit from any patent term extension or favorable adjustment to the term of any of our patents.

As with other biotechnology and pharmaceutical companies, our ability to maintain and solidify our proprietary and intellectual property position for our product candidates and technologies will depend on our success in obtaining effective patent claims and enforcing those claims if granted. However, patent applications that we may file or license from third parties may not result in the issuance of patents. We also cannot predict the breadth of claims that may be allowed or enforced in our patents. Any issued patents that we may receive in the future

may be challenged, invalidated or circumvented. For example, we cannot be certain of the priority of inventions covered by pending third-party patent applications. If third parties prepare and file patent applications in the United States that also claim technology or therapeutics to which we have rights, we may have to participate in interference proceedings in the USPTO to determine priority of invention, which could result in substantial costs to us, even if the eventual outcome is favorable to us. In addition, because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that, before any of our product candidates can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of any such patent.

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with selected consultants, scientific advisors and collaborators. The confidentiality agreements are designed to protect our proprietary information and, in the case of agreements or clauses requiring invention assignment, to grant us ownership of technologies that are developed through a relationship with a third party.

With respect to our proprietary cellular metabolism technology platform, we consider trade secrets and know-how to be our primary intellectual property. Trade secrets and know-how can be difficult to protect. In particular, we anticipate that with respect to this technology platform, these trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology, and the movement of personnel skilled in the art from academic to industry scientific positions.

**Competition**

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, development experience and scientific knowledge provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that address cancer metabolism and IEMs. There are other companies working to develop therapies in the field of cancer metabolism and IEMs. These companies include divisions of large pharmaceutical companies and biotechnology companies of various sizes.

*Cancer metabolism*. In the field of cancer metabolism, our principal competitors include AstraZeneca, Calithera Biosciences, Cornerstone Pharmaceuticals, Eli Lilly, Forma Therapeutics, GlaxoSmithKline, Novartis, Pfizer, and Roche Holdings, and its subsidiary Genentech.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates may compete with many existing drug and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates will not be competitive with them. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. In general, although there has been considerable progress over the past few decades in the treatment of cancer and the currently marketed therapies provide benefits to many patients, these therapies all are limited to some extent in their efficacy and frequency of adverse events,

and none are successful in treating all patients. As a result, the level of morbidity and mortality from cancer remains high.

In addition to currently marketed therapies, there are also a number of medicines in late stage clinical development to treat cancer. These medicines in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain market approval.

*Inborn errors of metabolism*. In the field of IEMs, our principal competitors include Alexion Pharmaceuticals, BioMarin Pharmaceutical, Genzyme, a Sanofi company, and Shire.

The most common methods for treating patients with IEMs are dietary restriction, dietary supplementation or replacement, treatment of symptoms and complications, gene therapy, organ transplant and enzyme replacement therapies. There are a number of marketed enzyme replacement therapies available for treating patients with IEMs. In some cases, these treatment methods are used in combination to improve efficacy. While our product candidates may compete with existing medicines and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates will not be competitive with them. In addition to currently marketed therapies, there are also a number of products that are either enzyme replacement therapies or gene therapies in various stages of clinical development to treat IEMs. These products in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain market approval.

Many of our competitors may have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved medicines than we do. Mergers and acquisitions in the pharmaceutical, biotechnology and diagnostic industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of all of our product candidates, if approved, are likely to be their efficacy, safety, convenience, price, the effectiveness of companion diagnostics in guiding the use of related therapeutics, the level of generic competition and the availability of reimbursement from government and other third-party payors.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize medicines that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any medicines that we may develop. Our competitors also may obtain FDA or other regulatory approval for their medicines more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic medicines. There are many generic medicines currently on the market for the indications that we are pursuing, and additional medicines are expected to become available on a generic basis over the coming years. If our therapeutic product candidates are approved, we expect that they will be priced at a significant premium over competitive generic medicines.

**Manufacturing**

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical

and clinical testing, as well as for commercial manufacture of any products that we may commercialize. To date, we have obtained materials for AG-221 for our planned phase 1/2 testing from third party manufacturers. We have engaged third party manufacturers to obtain the active ingredient for AG-120 for preclinical and clinical testing. We obtain our supplies from these manufacturers on a purchase order basis and do not have a long-term supply arrangement in place. We do not currently have arrangements in place for redundant supply for bulk drug substance. For all of our product candidates, we intend to identify and qualify additional manufacturers to provide the active pharmaceutical ingredient and fill-and-finish services prior to submission of a new drug application to the FDA.

AG-221, AG-120 and AG-348 are organic compounds of low molecular weight, generally called small molecules. They can be manufactured in reliable and reproducible synthetic processes from readily available starting materials. The chemistry is amenable to scale-up and does not require unusual equipment in the manufacturing process. We expect to continue to develop drug candidates that can be produced cost-effectively at contract manufacturing facilities.

We generally expect to rely on third parties for the manufacture of any companion diagnostics we develop.

**Government regulation**

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, import and export of pharmaceutical products, such as those we are developing.

***United States drug approval process***

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and untitled letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug for each indication;
- submission to the FDA of a new drug application, or NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, requirements and to

assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and

- FDA review and approval of the NDA.

*Preclinical studies and IND*

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

*Clinical trials*

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination at www.clinicaltrials.gov.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- *Phase 1:* The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- *Phase 2:* The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- *Phase 3:* The drug is administered to an expanded patient population in adequate and well-controlled clinical trials to generate sufficient data to statistically confirm the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and, more frequently, if serious adverse events occur. Phase 1, phase 2 and phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical

trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

*Marketing approval*

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee, currently exceeding $1.8 million, and the sponsor of an approved NDA is also subject to annual product and establishment user fees, currently exceeding $98,000 per product and $520,000 per establishment. These fees are typically increased annually.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission before accepting them for filing to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review of NDAs. Under these goals, the FDA has committed to review most such applications for non-priority products within 10 months, and most applications for priority review products, that is, drugs that the FDA determines represent a significant improvement over existing therapy, within six months. The review process may be extended by the FDA for three additional months to consider certain information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drugs or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and integrity of the clinical data submitted.

The testing and approval process requires substantial time, effort and financial resources, and each may take many years to complete. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. We may encounter difficulties or unanticipated costs in our efforts to develop our product candidates and secure necessary governmental approvals, which could delay or preclude us from marketing our products.

After the FDA's evaluation of the NDA and inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval and refuse to approve the NDA. Even if the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the

product labeling, require that post-approval studies, including phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including Risk Evaluation and Mitigation Strategies, or REMs, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

*Fast track designation*

The FDA is required to facilitate the development and expedite the review of drugs that are intended for the treatment of a serious or life-threatening condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new drug candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the filing of the IND for the product candidate. The FDA must determine if the product candidate qualifies for fast track designation within 60 days after receipt of the sponsor's request.

In addition to other benefits, such as the ability to use surrogate endpoints and have greater interactions with the FDA, the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

*Priority review*

Under FDA policies, a product candidate may be eligible for priority review, or review generally within a six-month time frame from the time a complete application is received. Products regulated by the FDA's Center for Drug Evaluation and Research, or CDER, are eligible for priority review if they provide a significant improvement compared to marketed products in the treatment, diagnosis or prevention of a disease. A fast track designated product candidate would ordinarily meet the FDA's criteria for priority review.

*Accelerated approval*

Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

*Breakthrough therapy designation*

Under the provisions of the new Food and Drug Administration Safety and Innovation Act, or FDASIA, enacted in 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough

therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

*Orphan drugs*

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same orphan indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

*Pediatric information*

Under the Pediatric Research Equity Act of 2003, as amended and reauthorized by the Food and Drug Administration Amendments Act of 2007, or the FDAAA, an NDA or supplement to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan drug designation.

*The Hatch-Waxman Act*

*Abbreviated new drug applications*

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. Generally, an ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths, dosage form and route of administration as the listed drug and has been shown to be bioequivalent through *in vitro* or *in vivo* testing or otherwise to the listed drug. ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug product, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly

referred to as “generic equivalents” to the listed drug, and can be and are often substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA’s Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval. Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product’s listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA also will not be approved until any applicable non-patent exclusivity period, such as exclusivity for obtaining approval of a new chemical entity, for the referenced product has expired. Federal law provides a period of five years following approval of a drug containing no previously approved active moiety during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph IV challenge to a listed patent, in which case the submission may be made four years following the original product approval. Federal law provides for a period of three years of exclusivity during which the FDA cannot grant effective approval of an ANDA if a listed drug contains a previously approved active moiety, but FDA requires as a condition of approval new clinical trials conducted by or for the sponsor. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Under the Best Pharmaceuticals for Children Act, federal law also provides that periods of patent and non-patent marketing exclusivity listed in the Orange Book for a drug may be extended by six months if the NDA sponsor conducts pediatric studies identified by the FDA in a written request. For written requests issued by the FDA after September 27, 2007, the date of enactment of the FDAAA, the FDA must grant pediatric exclusivity no later than nine months prior to the date of expiration of patent or non-patent exclusivity in order for the six-month pediatric extension to apply to that exclusivity period.

*Section 505(b)(2) new drug applications*

Most drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on the FDA’s previous approval of a similar product, or published literature, in support of its application.

505(b)(2) NDAs often provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the

applicant has not obtained a right of reference. If the 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. As a result, approval of a 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

*Combination products*

The FDA regulates combinations of products that cross FDA centers, such as drug, biologic or medical device components that are physically, chemically or otherwise combined into a single entity, as a combination product. The FDA center with primary jurisdiction for the combination product will take the lead in the premarket review of the product, with the other center consulting or collaborating with the lead center.

The FDA's Office of Combination Products, or OCP, determines which center will have primary jurisdiction for the combination product based on the combination product's "primary mode of action." A mode of action is the means by which a product achieves an intended therapeutic effect or action. The primary mode of action is the mode of action that provides the most important therapeutic action of the combination product, or the mode of action expected to make the greatest contribution to the overall intended therapeutic effects of the combination product.

Often it is difficult for the OCP to determine with reasonable certainty the most important therapeutic action of the combination product. In those difficult cases, the OCP will consider consistency with other combination products raising similar types of safety and effectiveness questions, or which center has the most expertise to evaluate the most significant safety and effectiveness questions raised by the combination product.

A sponsor may use a voluntary formal process, known as a Request for Designation, when the product classification is unclear or in dispute, to obtain a binding decision as to which center will regulate the combination product. If the sponsor objects to that decision, it may request that the agency reconsider that decision.

***Overview of FDA regulation of companion diagnostics***

We may seek to develop in *vitro* and *in vivo* companion diagnostics for use in selecting the patients that we believe will respond to our therapeutics.

FDA officials have issued draft guidance that, when finalized, would address issues critical to developing *in vitro* companion diagnostics, such as biomarker qualification, establishing clinical validity, the use of retrospective data, the appropriate patient population and when the FDA will require that the device and the drug be approved simultaneously. The draft guidance issued in July 2011 states that if safe and effective use of a therapeutic product depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of the diagnostic at the same time that the FDA approves the therapeutic product. The FDA has yet to issue further guidance, and it is unclear whether it will do so, or what the scope would be.

The FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to the cancer treatment to obtain Pre-Market Approval, or PMA, simultaneously with approval of the drug.

***PMA approval pathway***

A medical device, including an *in vitro* diagnostic, or IVD, to be commercially distributed in the United States must receive either 510(k) clearance or PMA approval from the FDA prior to marketing. Devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life supporting or implantable devices, or devices deemed not substantially equivalent to a previously 510(k) cleared device or a pre-amendment class III device for which PMA applications have not been called, are placed in Class III requiring PMA approval. The PMA approval pathway requires proof of the safety and effectiveness of the device to the FDA's satisfaction.

The PMA approval pathway generally takes from one to three years or even longer from submission of the application.

A PMA application for an IVD must provide extensive preclinical and clinical trial data. Preclinical data for an IVD includes many different tests, including how reproducible the results are when the same sample is tested multiple times by multiple users at multiple laboratories. The clinical data need to establish that the test is sufficiently safe, effective and reliable in the intended use population. In addition, the FDA must be convinced that a device has clinical utility, meaning that an IVD provides information that is clinically meaningful. A biomarker's clinical significance may be obvious, or the applicant may be able to rely upon published literature or submit data to show clinical utility.

A PMA application also must provide information about the device and its components regarding, among other things, device design, manufacturing and labeling. The sponsor must pay an application fee.

As part of the PMA review, the FDA will typically inspect the manufacturer's facilities for compliance with Quality System Regulation, or QSR, requirements, which impose elaborate testing, control, documentation and other quality assurance procedures.

Upon submission, the FDA determines if the PMA application is sufficiently complete to permit a substantive review, and, if so, the FDA accepts the application for filing. The FDA then commences an in-depth review of the PMA application. The entire process typically takes one to three years, but may take longer. The review time is often significantly extended as a result of the FDA asking for more information or clarification of information already provided. The FDA also may respond with a not approvable determination based on deficiencies in the application and require additional clinical trials that are often expensive and time-consuming and can substantially delay approval.

During the review period, an FDA advisory committee, typically a panel of clinicians, may be convened to review the application and recommend to the FDA whether, or upon what conditions, the device should be approved. Although the FDA is not bound by the advisory panel decision, the panel's recommendation is important to the FDA's overall decision making process.

If the FDA's evaluation of the PMA application is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the manufacturer. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Failure to comply with the conditions of approval can result in material adverse enforcement action, including the loss or withdrawal of the approval.

Even after approval of a PMA, a new PMA or PMA supplement may be required in the event of a modification to the device, its labeling or its manufacturing process. Supplements to a PMA often require the submission of the same type of information required for an original PMA, except that the supplement is generally limited to the information needed to support the proposed change from the product covered by the original PMA.

*Clinical trials*

A clinical trial is almost always required to support a PMA application. In some cases, one or more smaller Investigational Device Exemption, or IDE, studies may precede a pivotal clinical trial intended to demonstrate the safety and efficacy of the investigational device.

All clinical studies of investigational devices must be conducted in compliance with the FDA's requirements. If an investigational device could pose a significant risk to patients pursuant to FDA regulations, the FDA must approve an IDE application prior to initiation of investigational use. IVD trials usually do not require an IDE, as the FDA does not judge them to be a significant risk because the results do not affect the patients in the study. However, for a trial where the IVD result directs the therapeutic care of patients with cancer, we believe that the FDA would consider the investigation to present significant risk.

An IDE application must be supported by appropriate data, such as laboratory test results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The FDA typically grants IDE approval for a specified number of patients. A non-significant risk device does not require FDA approval of an IDE. Both significant risk and non-significant risk investigational devices require approval from IRBs at the study centers where the device will be used.

During the trial, the sponsor must comply with the FDA's IDE requirements for investigator selection, trial monitoring, reporting and record keeping. The investigators must obtain patient informed consent, rigorously follow the investigational plan and study protocol, control the disposition of investigational devices and comply with all reporting and record keeping requirements. Prior to granting PMA approval, the FDA typically inspects the records relating to the conduct of the study and the clinical data supporting the PMA application for compliance with applicable requirements.

Although the QSR does not fully apply to investigational devices, the requirement for controls on design and development does apply. The sponsor also must manufacture the investigational device in conformity with the quality controls described in the IDE application and any conditions of IDE approval that the FDA may impose with respect to manufacturing.

*Post-market*

After a device is on the market, numerous regulatory requirements apply. These requirements include: the QSR, labeling regulations, the FDA's general prohibition against promoting products for unapproved or "off label" uses, the Medical Device Reporting regulation, which requires that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if it were to recur, and the Reports of Corrections and Removals regulation, which requires manufacturers to report recalls and field actions to the FDA if initiated to reduce a risk to health posed by the device or to remedy a violation of the FDCA.

The FDA enforces these requirements by inspection and market surveillance. If the FDA finds a violation, it can institute a wide variety of enforcement actions, ranging from a public warning letter to more severe sanctions such as: fines, injunctions and civil penalties; recall or seizure of products; operating restrictions, partial suspension or total shutdown of production; refusing requests for PMA approval of new products; withdrawing PMA approvals already granted; and criminal prosecution.

***Other regulatory requirements***

Any drug manufactured or distributed by us pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval.

The FDA may impose a number of post-approval requirements, including REMs, as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the drug.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-market studies or clinical trials to assess new safety risks or imposition of distribution or other restrictions under a Risk Evaluation and Mitigation Strategy program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- consent decrees, injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off label uses, and a company that is found to have improperly promoted off label uses may be subject to significant liability.

***Additional provisions***

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving

remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

**Physician drug samples**

As part of the sales and marketing process, pharmaceutical companies frequently provide samples of approved drugs to physicians. The Prescription Drug Marketing Act, or the PDMA, imposes requirements and limitations upon the provision of drug samples to physicians, as well as prohibits states from licensing distributors of prescription drugs unless the state licensing program meets certain federal guidelines that include minimum standards for storage, handling and record keeping. In addition, the PDMA sets forth civil and criminal penalties for violations.

**Foreign regulation**

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

**New legislation and regulations**

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted or whether FDA regulations, guidance, policies or interpretations changed or what the effect of such changes, if any, may be.

**Pharmaceutical coverage, pricing and reimbursement**

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we obtain regulatory approval. Sales of any of our product candidates, if approved, will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the approved drugs for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals such as the drug candidates that we are developing and could adversely affect our net revenue and results.

Pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drug products will allow favorable reimbursement and pricing arrangements for any of our products.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. In particular, the Patient Protection and Affordable Care Act was enacted in the United States

in March 2010 and contain provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

**Our scientific founders and advisors**

***Founders***

The founders of Agios are eminent scientists and authorities in cancer who have pioneered key advances in the field of cancer metabolism. Together, they provide scientific leadership and expertise in this field.

*Lewis C. Cantley, Ph.D.* Dr. Cantley is director of the Cancer Center at Weill Cornell Medical College and New York-Presbyterian Hospital and a member of the National Academy of Sciences and American Academy of Arts and Sciences. Dr. Cantley is a foremost expert in understanding the biochemical pathways linking cancer and energy metabolism. His key contributions include:

- discovering the phosphatidylinositol-3-kinase (PI3K) signaling pathway;
- characterizing the mechanism by which PI3K is activated by growth factors and oncogenes and elucidating pathways downstream of PI3K, including the AKT/PKB signaling pathway;
- pioneering the application of fluorescence resonance energy transfer (FRET) for studying small molecule cell membrane transport; and
- discovering pyruvate kinase M2 (PKM2) as a "hub" to integrate growth factor signaling and aerobic glycolysis, an evolution in the understanding of the Warburg effect.

*Tak W. Mak, Ph.D.* Dr. Mak is professor of medical biophysics, University of Toronto; director of the Advanced Medical Discovery Institute; director of the Campbell Family Institute for Breast Cancer Research; foreign associate of the National Academy of Sciences; and fellow of the Royal Society. Dr. Mak is a preeminent researcher of the biology of the immune system, the biology of apoptosis and the pathogenesis of cancer. His key contributions include:

- discovering the T-Cell receptor;
- characterizing the tumorigenic functions of the tumor suppressor protein p53 and the kinase Chk2;
- identifying CPT1C as a tumor-specific gene product that plays an important role in the utilization of fatty acids as an alternative energy source of cancer cells; and
- discovery of the function of CTLA-4.

*Craig B. Thompson, M.D.* Dr. Thompson is president and CEO of Memorial Sloan-Kettering Cancer Center; and a member of the National Academy of Sciences, American Academy of Arts and Sciences and Institute of Medicine. Dr. Thompson is an authority in the study of how genes regulate apoptosis and metabolism and investigates their application in treating cancer. His key contributions include:

- elucidating the role of the Bcl-2 family of oncogenes in regulating cell survival;
- identifying the roles of aerobic glycolysis, fatty acid synthesis and autophagy in the metabolic adaptation by cancer cells as part of carcinogenesis; and
- proposing the concept that most oncogenes and tumor suppressors evolved to regulate cellular metabolism.

### Scientific advisors

We have assembled a world-class scientific advisory board that includes renowned experts in cancer metabolism, oncology, drug discovery and translational medicine. These advisors work in close collaboration with our scientists to identify new research directions and accelerate our target validation and drug discovery programs.

| Name | Primary affiliation |
|---|---|
| Craig B. Thompson, M.D. | Memorial Sloan-Kettering Cancer Center |
| Joan Brugge, Ph.D. | Harvard Medical School |
| Lewis C. Cantley, Ph.D. | The Cancer Center at Weill Cornell Medical College and New York-Presbyterian Hospital |
| Jeffrey Engelman, M.D., Ph.D. | Massachusetts General Hospital and Harvard Medical School |
| William G. Kaelin, Jr., M.D. | Dana-Farber Cancer Institute and Harvard Medical School |
| Tak W. Mak, Ph.D. | University of Toronto and the Campbell Family Institute for Breast Cancer Research |
| Pier Paolo Pandolfi, M.D., Ph.D. | Beth Israel Deaconess Medical Center |
| David M. Sabatini, M.D., Ph.D. | Whitehead Institute and Massachusetts Institute of Technology |
| Charles Sawyers, M.D. | Memorial Sloan-Kettering Cancer Center |
| Matthew Vander Heiden, M.D., Ph.D. | Koch Institute for Integrative Cancer Research at MIT |

### Employees

As of April 30, 2013, we had 84 full-time employees, including 41 employees with M.D. or Ph.D. degrees. Of these full-time employees, 65 employees are engaged in research and development activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

### Facilities

We occupy approximately 38,500 rentable square feet of office and laboratory space in Cambridge, Massachusetts under a lease that expires in April 2016. We believe that our facility is sufficient to meet our current needs and that suitable additional space will be available as and when needed.

### Legal proceedings

We are not currently a party to any material legal proceedings.

## Management

### Executive officers and directors

The following table sets forth the name, age and position of each of our executive officers and directors as of as of April 30, 2013.

| Name | Age | Position |
|---|---|---|
| ***Executive Officers*** | | |
| David P. Schenkein, M.D. | 55 | Chief Executive Officer and Director |
| Duncan Higgons | 58 | Chief Operating Officer |
| Scott Biller, Ph.D. | 57 | Chief Scientific Officer |
| Glenn Goddard | 42 | Vice President, Finance |
| ***Key Employees*** | | |
| Shin-San Michael Su, Ph.D. | 57 | Senior Vice President, Research & Development |
| ***Directors*** | | |
| Lewis C. Cantley, Ph.D. | 64 | Director |
| Douglas G. Cole, M.D. | 52 | Director |
| Perry Karsen | 58 | Director |
| John M. Maraganore, Ph.D. | 50 | Director |
| Robert T. Nelsen | 49 | Director |
| Kevin P. Starr | 50 | Director |
| Marc Tessier-Lavigne, Ph.D. | 53 | Director |

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.

*David P. Schenkein, M.D.* joined Agios in August 2009 as chief executive officer and a member of our board of directors and has been a hematologist and medical oncologist for more than 20 years. He currently serves as an adjunct attending physician in hematology at Tufts Medical Center and is a member of the board of directors of the Biotechnology Industry Organization, the world's largest biotechnology trade association, a position he has held since 2012. Prior to joining Agios, from March 2006 to July 2009, Dr. Schenkein was the senior vice president, clinical hematology/oncology at Genentech, Inc., a pharmaceutical company, where he was responsible for numerous successful oncology drug approvals and leading the medical and scientific strategies for its BioOncology portfolio. While at Genentech, he served as an adjunct clinical professor of medical oncology at Stanford University School of Medicine. Prior to joining Genentech, he served as the senior vice president of clinical research at Millennium Pharmaceuticals, Inc. (a wholly-owned subsidiary of Takeda Pharmaceuticals Company Limited), overseeing the clinical development and worldwide approval of VELCADE®, a first-in-class cancer therapy now approved to treat multiple myeloma and non-Hodgkins lymphoma. He currently serves on the board of directors of Foundation Medicine, Inc., bluebird bio, Inc., and Blueprint Medicines Inc., all private biopharmaceutical companies. Dr. Schenkein holds a B.A. in chemistry from Wesleyan University and an M.D. from the State University of New York Upstate Medical School. We believe that Dr. Schenkein's detailed knowledge of our company and his extensive background in the biotechnology industry, including his roles at Genentech and Millennium, provide a critical contribution to our board of directors.

*Duncan Higgons* joined Agios in May 2009 as chief operating officer. Prior to joining Agios, Mr. Higgons worked at Archemix Corporation, a privately held biopharmaceutical company, from 2006 to 2009, where he most recently served as president, chief operating officer and interim chief executive officer. Prior to Archemix, Mr. Higgons served as the chief commercial officer at TransForm Pharmaceuticals, Inc., a privately-held biotechnology company which was acquired by Johnson & Johnson Company. Mr. Higgons holds a B.Sc. in mathematics from King's College University of London and an M.Sc. in economics from London Business School.

*Scott Biller, Ph.D.* joined Agios in September 2010 as chief scientific officer, with more than 25 years of drug discovery and development experience. Most recently, from 2003 to September 2010, he was vice president and head of global discovery chemistry at the Novartis Institutes for Biomedical Research (NIBR). Prior to that, Dr. Biller held the positions of vice president, pharmaceutical candidate optimization at the Bristol Myers Squibb or BMS, Pharmaceutical Research Institute and executive director of drug discovery chemistry for the BMS research site in Lawrenceville, New Jersey. Among his other key leadership positions at BMS, Dr. Biller was the executive director of metabolic diseases chemistry. He contributed to robust pipelines at both BMS and Novartis, culminating in two medicines launched worldwide (Onglyza® for the treatment of Type 2 diabetes and Juxtapid® for familial hypercholesterolemia) and three additional drugs reaching phase 3 clinical development. Dr. Biller earned a S.B. degree in chemistry at MIT, a Ph.D. in organic chemistry at Caltech and was an NIH Postdoctoral Fellow at Columbia University in natural product synthesis.

*Glenn Goddard* joined Agios in July 2010 as vice president, finance, and brings more than 10 years of experience in emerging private and public platform-based biopharmaceutical companies. Prior to joining Agios, Mr. Goddard worked from 2004 to 2010 at Archemix, where he most recently served as the vice president of finance. During his time at Archemix he oversaw all aspects of financial operations. Prior to Archemix, he was the corporate controller of ImmunoGen, Inc., a publicly traded oncology-focused biopharmaceutical company. During his time at ImmunoGen, Mr. Goddard was responsible for external financial reporting, financial planning and tax compliance, and initiated the company's Sarbanes-Oxley compliance efforts. Earlier in his career, he was an audit supervisor within the Technology, Communication and Entertainment group of Ernst & Young, LLP and an audit manager at Feeley & Driscoll, P.C. Mr. Goddard is a graduate of Bentley College, where he earned a B.S. in accountancy, and is a certified public accountant in the Commonwealth of Massachusetts.

*Shin-San Michael Su, Ph.D.* is one of our founding scientists and has served as senior vice president, research & development since 2012. Dr. Su brings more than 20 years of organization, project management and scientific experience in the biotechnology industry to Agios. Most recently, from 2004 to 2006 he served as general director and vice president of the Biomedical Engineering Research Laboratory (BEL) at ITRI in Taiwan. Prior to that, he spent 14 years in a number of roles, concluding his tenure as program executive and vice president of the Novartis kinase collaboration for Vertex Pharmaceuticals, a publicly-traded a pharmaceutical company. Dr. Su earned his Ph.D. in biochemistry at Duke University and was a Helen Hay Whitney Fellow at Harvard University.

*Lewis C. Cantley, Ph.D.* has served as a member of our board of directors since August 2007. Dr. Cantley has served as a director of the Cancer Center at Weill Cornell Medical College and New York-Presbyterian Hospital since October 2012. Prior to that, from 1992 to 2012 Dr. Cantley was a professor of systems biology at Harvard Medical School and chief of the division of Signal Transduction at Beth Israel Deaconess Medical Center, a major teaching hospital of Harvard Medical School in Boston. From 2007 to 2012, Dr. Cantley served as director of the Cancer Center at Beth Israel Deaconess Medical Center. Dr. Cantley is a member of the American Academy of Arts and Sciences and the National Academy of Sciences, and serves on the editorial boards of the journals *Cell* and the *Journal of Cell Biology*. Dr. Cantley is the recipient of the 2005 Pezcoller Foundation-American Association for Cancer Research International Award for Cancer Research, for his leadership in the field of signal transduction, including the discovery of PI3K. Dr. Cantley received his B.S. in chemistry from West Virginia Wesleyan College, and obtained a Ph.D. in biophysical chemistry from Cornell University. Dr. Cantley's qualifications to sit on our board of directors include his position as a foremost expert in understanding the biochemical pathways linking cancer and metabolism.

*Douglas G. Cole, M.D.* has served as a member of our board of directors since December 2007. Dr. Cole has been a general partner of Flagship Ventures, where he has focused on life science investments, since 2001. He currently serves on the boards of directors of publicly-traded biopharmaceutical companies Tetraphase Pharmaceuticals, Inc. and Receptos, Inc., and on the boards of directors of several private biopharmaceutical companies, including Ensemble Therapeutics, Concert Pharmaceuticals, Inc., Quanterix Corporation, Selecta Biosciences, Inc., Avedro, Inc., and Syros Pharmaceuticals Inc. In the past five years Dr. Cole has served on the boards of Seventh Sense Biosystems, Inc., Resolvyx Pharmaceuticals, Inc., AVEO Pharmaceuticals, Inc., Zalicus, Inc. (formerly CombinatoRx), CGI Pharmaceuticals, and Morphotek Inc. Dr. Cole holds a B.A. in English from Dartmouth College and an M.D. from the University of Pennsylvania School of Medicine. We believe Dr. Cole's qualifications to sit on our board of directors include his substantial experience as an investor in early stage biopharmaceutical and life sciences companies, as well as his experience of serving on the board of directors for several biopharmaceutical companies.

*Perry Karsen* has served as a member of our board of directors since November 2011. Mr. Karsen currently serves as the chief executive officer of the Celgene Cellular Therapeutics division of Celgene Corporation, a publicly-traded global biopharmaceutical company, and as executive vice president of Celgene Corporation. Mr. Karsen served as chief operations officer of Celgene from July 2010 to May 2013, and as senior vice president and head of worldwide business development of Celgene from 2004 to 2009. Between February 2009 and July 2010, Mr. Karsen was chief executive officer of Pearl Therapeutics, a privately held biotechnology company. Prior to his tenure with Celgene, Mr. Karsen held executive positions at Human Genome Sciences, Bristol-Myers Squibb, Genentech and Abbott Laboratories. In addition, Mr. Karsen served as a general partner at Pequot Ventures. Mr. Karsen serves as a member of the boards of directors of the Biotechnology Industry Organization (BIO), BayBio and the Life Sciences Foundation. Mr. Karsen has a Masters of Management degree from Northwestern University's Kellogg Graduate School of Management, a Masters in Teaching of Biology from Duke University, and a B.S. in Biological Sciences from the University of Illinois, Urbana-Champaign. Mr. Karsen brings to his service as a director his significant executive leadership experience, including his experience as an executive at some of the largest and most successful multi-national pharmaceutical companies, as well as his membership on boards of directors of various trade organizations.

*John M. Maraganore, Ph.D.* has served as a member of our board of directors since November 2011. Since December 2002, Dr. Maraganore has served as the chief executive officer and as a director of Alnylam Pharmaceuticals, Inc., a publicly-traded biopharmaceutical company. From December 2002 to December 2007, Dr. Maraganore served as president of Alnylam. From April 2000 to December 2002, Dr. Maraganore served as senior vice president, strategic product development with Millennium. Before Millennium, he served as director of molecular biology and director of market and business development at Biogen, Inc. (now Biogen Idec, Inc.), a publicly-traded company. Prior to Biogen, Dr. Maraganore was a scientist at ZymoGenetics, Inc. and The Upjohn Company. Dr. Maraganore is also chairman of Regulus Therapeutics, Inc., a publicly-traded company, and a director of bluebird bio, Inc. and Tempero Pharmaceuticals. In addition, he is a venture partner at Third Rock Ventures, L.P., where he participates in a limited capacity focusing on guiding strategy for Third Rock and its portfolio companies. He is also a member of the Immunology Advisory Council of Harvard Medical School and a member of the board of directors of the Biotechnology Industry Organization. Dr. Maraganore holds an M.S. and a Ph.D. in Biochemistry and Molecular Biology from the University of Chicago and a B.A. in Biological Sciences from the University of Chicago. Dr. Maraganore has over 25 years of experience in the biotechnology industry, bringing to our board critical scientific, research and development, and general management expertise.

*Robert T. Nelsen* has served as a member of our board of directors since December 2007. Mr. Nelsen was a co-founder of ARCH Venture Partners, a venture capital firm, and has served in various capacities for ARCH and affiliated entities since July 1986. He is currently a managing director of ARCH Venture Corporation. Mr. Nelsen has played a significant role in the early sourcing, financing and development of more than 30 companies. Mr. Nelsen is a director of Ikaria, Inc., Kythera Biopharmaceuticals, Inc., Sapphire Energy, Inc., Fate Therapeutics, Inc., Ensemble Therapeutics Corporation, NeurogesX, Inc., Syros Pharmaceuticals Inc., and serves as chairman of the board of Hua Medicine. Mr. Nelsen also serves as a Trustee of the Fred Hutchinson Cancer Research Institute, the Institute for Systems Biology, and is a director of the National Venture Capital

Association. Mr. Nelsen previously served on the boards of Illumina, Inc, Caliper Life Sciences, Inc, Adolor Corporation, Receptos, Inc., and entities affiliated with deCode Genetics, Inc, among others. Mr. Nelsen received a B.S. with majors in biology and economics from the University of Puget Sound and an M.B.A. from the University of Chicago. We believe Mr. Nelsen is qualified to sit on our board of directors due to his extensive experience as an investor in, and director of, early stage biopharmaceutical and life sciences companies.

*Kevin P. Starr* has served as a member of our board of directors since June 2008. Since April 2007, Mr. Starr has been a Partner of Third Rock Ventures, a venture capital firm. From January 2003 to March 2007, Mr. Starr was an entrepreneur. From December 2001 to December 2002, Mr. Starr served as chief operating officer of Millennium. He also served as Millennium's chief financial officer from December 1998 to December 2002. Mr. Starr currently serves on the board of directors of Alnylam. Mr. Starr also serves on the boards of Zafgen, Inc., PanOptica, Inc., MyoKardia, Inc., Global Blood Therapeutics, Inc., Afferent Pharmaceuticals, and SAGE Therapeutics. Mr. Starr received an M.S. in corporate finance from Boston College and a B.A. in mathematics and business from Colby College. Mr. Starr's qualifications to serve on our board of directors include executive management roles with responsibility over key financial and business planning functions, including extensive experience in the oversight of financial audits, the design and implementation of financial controls, and corporate governance best practices. In addition, as an entrepreneur and venture capitalist, Mr. Starr has focused on the formation, development and business strategy of multiple start-up companies.

*Marc Tessier-Lavigne, Ph.D.* has served as a member of our board of directors since September 2011. Dr. Tessier-Lavigne has served as president of the Rockefeller University, as well as professor and head of the Laboratory of Brain Development and Repair, since 2011. Previously, he was employed at Genentech Inc. from 2003 to 2011, where he became executive vice president for research and chief scientific officer, and directed 1,400 people in disease research and drug discovery in cancer, immune disorders, infectious diseases and neurodegenerative diseases. Prior to his tenure at Genentech, Dr. Tessier-Lavigne was an investigator with the Howard Hughes Medical Institute from 1994 to 2003 and a professor at Stanford University and the University of California, San Francisco from 1991 to 2003. He is a member of the Board of Directors of Pfizer Inc. and Regeneron Pharmaceuticals Inc. He is a member of the National Academy of Sciences and its Institute of Medicine, and a fellow of the Royal Society (UK), the Royal Society of Canada, the American Academy of Arts and Sciences, the American Association for the Advancement of Science, and the Academy of Medical Sciences (UK). Dr. Tessier-Lavigne earned undergraduate degrees from McGill University and from Oxford University, where he was a Rhodes Scholar. He received his Ph.D. from University College London, and conducted postdoctoral work at the MRC Developmental Neurobiology Unit in London and at Columbia University. Dr. Tessier-Lavigne's qualifications to sit on our board of directors include his pioneering research, his deep scientific knowledge and his reputation as an exceptional leader in the biotechnology industry.

**Board composition**

Our board of directors is currently authorized to have nine members. Upon the closing of this offering, our board of directors will consist of eight directors and one vacancy. In accordance with the terms of our certificate of incorporation and bylaws that will become effective upon the closing of this offering, our board of directors will be divided into three classes, class I, class II and class III, with members of each class serving staggered three-year terms. Upon the closing of this offering, the members of the classes will be divided as follows:

- the class I directors will be , and , and their term will expire at the annual meeting of stockholders to be held in 2014;
- the class II directors will be , and , and their term will expire at the annual meeting of stockholders to be held in 2015; and
- the class III directors will be , and , and their term will expire at the annual meeting of stockholders to be held in 2016.

Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires. In accordance

with the terms of our certificate of incorporation and bylaws that will become effective upon the closing of this offering, our directors may be removed only for cause by the affirmative vote of the holders of 75% or more of our voting stock.

We have no formal policy regarding board diversity. Our priority in selection of board members is identification of members who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business and understanding of the competitive landscape.

**Director independence**

Rule 5605 of the NASDAQ Listing Rules requires a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the NASDAQ Listing Rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Under Rule 5605(a)(2) of the NASDAQ Listing Rules, a director will only qualify as an "independent director" if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3 of the Exchange Act, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries.

In 2013, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors, with the exception of Dr. Schenkein and , is an "independent director" as defined under Rule 5605(a)(2) of the NASDAQ Listing Rules. Our board of directors also determined that , and , who will comprise our audit committee following this offering, , and , who will comprise our compensation committee following this offering, and , and , who will comprise our nominating and corporate governance committee following this offering, satisfy the independence standards for such committees established by the Securities and Exchange Commission and the NASDAQ Listing Rules, as applicable. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

There are no family relationships among any of our directors or executive officers.

**Board committees**

Our board has established three standing committees—audit, compensation, and nominating and corporate governance—each of which will, upon the closing of this offering, operate under a charter that has been approved by our board.

***Audit committee***

The members of our audit committee are , and . is the chair of the audit committee. Our board of directors has determined that qualifies as an audit committee financial expert within the meaning of SEC regulations and the NASDAQ Listing Rules. In making this determination, our board

has considered the formal education and nature and scope of his previous experience, coupled with past and present service on various audit committees. Our audit committee assists our board of directors in its oversight of our accounting and financial reporting process and the audits of our financial statements. Following this offering, our audit committee's responsibilities will include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our registered public accounting firm, including through the receipt and consideration of reports from such firm;
- reviewing and discussing with management and the registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function;
- discussing our risk management policies;
- establishing policies regarding hiring employees from the registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by SEC rules.

***Compensation committee***

The members of our compensation committee are , and . is the chair of the compensation committee. Our compensation committee assists our board of directors in the discharge of its responsibilities relating to the compensation of our executive officers. Following this offering, the compensation committee's responsibilities will include:

- reviewing and approving corporate goals and objectives relevant to CEO compensation;
- reviewing and approving, or making recommendations to our board with respect to, the compensation of our chief executive officer and our other executive officers;
- overseeing an evaluation of our senior executives;
- overseeing and administering our cash and equity incentive plans;
- reviewing and making recommendations to our board with respect to director compensation;
- reviewing and discussing with management our "Compensation Discussion and Analysis"; and
- preparing the compensation committee report required by SEC rules.

***Nominating and corporate governance committee***

The members of our nominating and corporate governance committee are , and . is the chair of the nominating and corporate governance committee. Following this offering, the nominating and corporate governance committee's responsibilities will include:

- identifying individuals qualified to become board members;
- recommending to our board the persons to be nominated for election as directors and to each committee of our board of directors;

- reviewing and making recommendations to the board with respect to management succession planning;
- developing and recommending corporate governance principles to the board; and
- overseeing periodic evaluations of the board.

**Compensation committee interlocks and insider participation**

During 2012, the members of our compensation committee were John M. Maraganore, Robert T. Nelsen, and Kevin P. Starr. Mr. Starr, who will cease to serve as a member of our compensation committee upon the closing of this offering, was formerly our interim chief executive officer. No other current or former member of our compensation committee is or has been a current or former officer or employee of Agios. None of our executive officers served as a director or a member of a compensation committee (or other committee serving an equivalent function) of any other entity, one of whose executive officers served as a director or member of our compensation committee during the fiscal year ended December 31, 2012.

**Code of ethics and code of conduct**

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We intend to post on our website, www.agios.com, a current copy of the code and all disclosures that are required by law or NASDAQ stock market listing standards concerning any amendments to, or waivers from, any provision of the code.

## Executive compensation

This section discusses the material elements of our executive compensation policies and decisions and the most important factors relevant to an analysis of these policies and decisions. It provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our executive officers named in the "Summary compensation table" below and is intended to place in perspective the data presented in the following tables and the corresponding narrative.

### Summary compensation table

The following table sets forth information regarding compensation earned by our chief executive officer and our other executive officers during the fiscal years ending December 31, 2011 and 2012. We sometimes refer to these executive officers as our named executive officers elsewhere in this prospectus.

| Name and principal position | Year | Salary ($) | Option awards ($)(1) | Non-equity incentive plan compensation ($)(2) | All other compensation ($)(3) | Total ($) |
|---|---|---|---|---|---|---|
| David P. Schenkein, M.D.(4) | 2012 | $ 425,000 | $ 134,513 | $ 136,000 | $ 2,764 | $ 698,277 |
| *Chief Executive Officer* | 2011 | $ 425,000 | $ 13,462 | $ 170,000 | $ 2,764 | $ 611,226 |
| Duncan Higgons | 2012 | $ 350,008 | $ 117,699 | $ 98,002 | $ 2,665 | $ 568,374 |
| *Chief Operating Officer* | 2011 | $ 350,008 | $ 5,387 | $ 122,503 | $ 2,665 | $ 480,563 |
| Scott Biller, Ph.D. | 2012 | $ 376,000 | $ 117,699 | $ 105,280 | $ 3,052 | $ 602,031 |
| *Chief Scientific Officer* | 2011 | $ 376,000 | — | $ 131,600 | $ 2,881 | $ 510,481 |
| Glenn Goddard | 2012 | $ 253,707 | $ 53,805 | $ 30,445 | $ 2,264 | $ 340,221 |
| *Vice President, Finance* | 2011 | $ 244,537 | $ 5,864 | $ 40,000 | $ 2,235 | $ 292,636 |

(1) Amounts listed represent the aggregate fair value amount computed as of the grant date of the option awards granted during 2011 and 2012 in accordance with FASB ASC Topic 718. Assumptions used in the calculation of these amounts are included in Note 9, Share-Based Payments, of the Notes to our Consolidated Financial Statements.

(2) Amounts represent awards to our named executive officers under our annual performance-based cash incentive program. See "—Annual performance-based cash incentives" for a description of that program. Annual cash incentive compensation for 2012 was earned in 2012 and paid in 2012. Annual cash incentive compensation for 2011 was earned in 2011 and paid in 2012.

(3) Amounts represent the dollar value of group life insurance premiums paid during the fiscal year with respect to life insurance for the named executive officer, as well as premiums paid by us for short- and long-term disability insurance policies consistent with those provided to all of our employees.

(4) Dr. Schenkein also serves as a member of our board of directors but does not receive any additional compensation for his service as a director.

#### *Base salary*

Base salaries are used to recognize the experience, skills, knowledge and responsibilities required of our executive officers. Base salaries for our executive officers typically are established through arm's length negotiation at the time the executive officer is hired, taking into account the position for which the executive officer is being considered and the executive officer's qualifications, prior experience and prior salary. None of our executive officers is currently party to an employment agreement that provides for automatic or scheduled increases in base salary. However, on an annual basis, our compensation committee reviews and evaluates, with input from our chief executive officer, the need for adjustment of the base salaries of our executive officers based on changes and expected changes in the scope of an executive officer's responsibilities, including promotions, the individual contributions made by and performance of the executive officer during the prior fiscal year, the executive officer's performance over a period of years, overall labor market conditions, the relative ease or

difficulty of replacing the executive with a well-qualified person, our overall growth and development as a company and general salary trends in our industry and among our peer group and where the executive officer's salary falls in the salary range presented by that data. In making decisions regarding salary increases, we may also draw upon the experience of members of our board of directors with other companies. No formulaic base salary increases are provided to our executive officers.

In each of 2012 and 2011, we paid base salaries to Dr. Schenkein, Mr. Higgons and Dr. Biller of $425,000, $350,008, and $376,000, respectively. We paid base salaries of $253,707 and $244,537 to Mr. Goddard in 2012 and 2011, respectively.

***Annual performance-based cash incentives***

We have designed our annual performance-based cash incentive program to emphasize pay-for-performance and to reward our executive officers for the achievement of the preceding year's performance guided by specified annual corporate and individual objectives. Historically, each executive officer has been eligible, at our board of directors' discretion, to receive an annual performance-based cash incentive, which we refer to as an annual cash incentive, in an amount corresponding to a percentage of his base salary. The amount of the annual cash incentive has been determined by our board of directors, based upon the recommendation of the compensation committee, by looking at the totality of anticipated and unanticipated achievements by us and the individual executive officer in the preceding year, including our performance against specific scientific, research, clinical, operational and financial corporate objectives. In recent years, these annual corporate objectives have primarily focused on the advancement of our lead programs.

Our compensation committee has historically targeted annual cash incentive levels for our executives below industry average for companies at the same life stage and approximate headcount. Our compensation committee has authority to adjust the incentive percentage each year in connection with its review of our and the executive officer's performance.

In 2012, we awarded cash incentives to Dr. Schenkein, Mr. Higgons, Dr. Biller and Mr. Goddard in the amounts of $136,000, $98,002, $105,280 and $30,445, respectively, in each case based on corporate and individual accomplishments with respect to research, preclinical and operational objectives. In 2011, we awarded cash incentives to Dr. Schenkein, Mr. Higgons, Dr. Biller and Mr. Goddard in the amounts of $170,000, $122,503, $131,600 and $40,000, respectively, in each case based on corporate and individual accomplishments with respect to research and operational objectives.

***Equity incentive awards***

Our equity award program is the primary vehicle for offering long-term incentives to our executives. While we do not currently have any equity ownership guidelines for our executives, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. Because our executives benefit from stock options only if our stock price increases relative to the stock option's exercise price through the creation of shareholder value, we believe stock options provide meaningful incentives to our executives to achieve increases in the value of our stock over time. In addition, the vesting feature of our equity grants contributes to executive retention by providing an incentive to our executives to remain employed by us during the vesting period. Prior to this offering, our executives were eligible to participate in the 2007 stock incentive plan, as amended, or the 2007 Plan. During 2012, all stock options were granted pursuant to the 2007 Plan. Following the closing of this offering, our employees and executive officers will be eligible to receive stock options and other stock-based awards pursuant to the 2013 stock incentive plan, or the 2013 Plan.

We use stock options to compensate our executive officers in the form of initial grants in connection with the commencement of employment, generally on an annual basis thereafter, and also at various times, often but not

necessarily annually, if we have performed as expected or better. Prior to this offering, the award of such stock options to our executive officers has been made upon the recommendation of the compensation committee and the approval of our board of directors. None of our executive officers is currently party to an employment agreement that provides for automatic award of stock options. We grant stock options to our executive officers with both time-based and performance-based vesting. The options that we grant to our executive officers with time-based vesting typically become exercisable as to 25% of the shares underlying the option on the first anniversary of the grant date, and as to an additional 1/48th of the shares underlying the option monthly thereafter. The options that we grant to our executive officers with performance-based vesting become exercisable upon the attainment of certain preclinical, clinical and regulatory milestone events recommended by the compensation committee and approved by our board of directors. Vesting and exercise rights cease shortly after termination of employment except in the case of death or disability; provided that, for certain of our executive officers, in the case of termination without cause or for good reason either before or after a change in control, a portion or all of the shares underlying unvested awards will accelerate and become exercisable. Prior to the exercise of an option, the holder has no rights as a stockholder with respect to the shares subject to such option, including no voting rights and no right to receive dividends or dividend equivalents.

In determining the size of the annual stock option grants to recommend for our executives, our compensation committee has historically considered industry data including information regarding comparative stock ownership and equity grants received by other executives in our industry. Our compensation committee has targeted equity ownership levels for our executive officers between the 50th and 75th percentile of the industry average for companies at the same life size, stage, approximate headcount and valuation. In addition, our compensation committee has considered our corporate performance, the potential for enhancing the creation of value for our stockholders, the amount of equity previously awarded to the executive officers and the vesting terms of such prior awards.

We have historically granted stock options with exercise prices that are equal to the fair market value of our common stock on the date of grant as determined by our board of directors, based on a number of objective and subjective factors. The exercise price of all stock options granted after the closing of this offering will be equal to the fair market value of shares of our common stock on the date of grant, which will be determined by reference to the closing market price of our common stock on the date of grant.

In 2012, we granted options to purchase 200,000, 175,000, 175,000 and 80,000 shares of our common stock to Dr. Schenkein, Mr. Higgons, Dr. Biller and Mr. Goddard, respectively. In 2011, we granted options to purchase 100,000, 40,000, and 30,000 shares of our common stock to Dr. Schenkein, Mr. Higgons and Mr. Goddard, respectively. In each case these grants were based on the executive officer's existing equity incentive holdings, level of responsibility within our company and our subjective assessment of the executive officer's individual performance and our overall corporate performance, in each case without reference to any specific metric.

In April 2013, our board of directors granted option awards to our named executive officers, pursuant to our 2007 Plan as follows:

| Name | Option award (#) | Grant date fair value(1) |
|---|---|---|
| David P. Schenkein, M.D. | 375,000 | $ 957,062 |
| Duncan Higgons | 187,500 | $ 478,531 |
| Scott Biller, Ph.D. | 187,500 | $ 478,531 |
| Glenn Goddard | 40,000 | $ 97,888 |

(1) See Note 9, Share-based Payments, of the Notes to our Consolidated Financial Statements regarding assumptions underlying the valuation of equity awards.

For more information on the terms of employment and compensation of our named executive officers, see "Employment, severance and change in control arrangements" below.

### 2012 Outstanding equity awards at fiscal year-end

The following table sets forth information concerning outstanding equity awards for each of our named executive officers at December 31, 2012:

| | Option awards | | | | | Stock awards | |
|---|---|---|---|---|---|---|---|
| Name | Number of securities underlying unexercised options exercisable (#) | Number of securities underlying unexercised options unexercisable (#) | Equity incentive plan awards: number of securities underlying unexercised unearned options (#) | Option exercise price ($) | Option expiration date | Number of shares or units of stock that have not vested (#) | Market value of shares or units of stock that have not vested ($)(1) |
| David P. Schenkein, M.D.(2) | | | | | | | |
| | | | | | | 250,000(3) | $ |
| | 623,637 | 56,696(4) | | $ 0.11 | 8/12/2019 | | |
| | 870,461 | 174,094(5) | | $ 0.11 | 8/12/2019 | | |
| | 25,000 | | 75,000(6) | $ 0.17 | 3/1/2021 | | |
| | | | 200,000(7) | $ 0.85 | 4/5/2022 | | |
| Duncan Higgons(2) | | | | | | | |
| | | | | | | 52,080(8) | $ |
| | 515,775 | 118,114(9) | | $ 0.11 | 8/12/2019 | | |
| | 114,583 | 10,417(4) | | $ 0.11 | 8/12/2019 | | |
| | 20,359 | 2,368(10) | | $ 0.11 | 8/12/2019 | | |
| | 91,666 | 8,334(4) | | $ 0.11 | 3/25/2020 | | |
| | 2,500 | | 7,500(6) | $ 0.17 | 3/1/2021 | | |
| | 14,375 | 15,625(11) | | $ 0.17 | 3/1/2021 | | |
| | | | 175,000(7) | $ 0.85 | 4/5/2022 | | |
| Scott Biller, Ph.D.(2) | | | | | | | |
| | | | 66,000(12) | $ 0.17 | 12/6/2020 | | |
| | | | 34,000(13) | $ 0.17 | 12/6/2020 | | |
| | 337,500 | 262,500(14) | | $ 0.17 | 12/6/2020 | | |
| | | | 175,000(7) | $ 0.85 | 4/5/2022 | | |
| Glenn Goddard | | | | | | | |
| | 75,520 | 49,480(15) | | $ 0.17 | 8/11/2020 | | |
| | 9,375 | 20,625(16) | | $ 0.25 | 9/14/2021 | | |
| | | | 80,000(7) | $ 0.85 | 4/5/2022 | | |

(1) There was no public market for our common stock at December 31, 2012. We have estimated the market value of the unvested stock awards based on an assumed initial public offering price of $ per share, the midpoint of the range listed on the cover of this prospectus.

(2) If the executive officer's employment is terminated by us without cause or by such named executive officer for good reason, as defined in his respective offer letter, prior to a change in control, the vesting of such named executive officer's option and restricted stock awards shall accelerate, such that (a) in the case of such a termination of the employment of Dr. Schenkein, all shares under any such awards held by him shall vest and (b) in the case of such a termination of the employment of Mr. Higgons or Dr. Biller, 25% of the original number of shares under any such awards held by him shall vest. The vesting of any option or restricted stock award held by such named executive officer shall be partially accelerated upon a change of control, such that 75% of the then unvested shares under any such award shall become vested. In addition, if such named executive officer's employment is terminated by us or our acquiror without cause or by such named executive officer for good reason within 18 months following a change of control, all of such named executive officer's option and restricted stock awards shall vest in full. See "Employment agreements, severance and change in control arrangements" below.

(3) The unvested shares are scheduled to vest and become free of the Company's repurchase rights in approximately equal monthly installments through August 1, 2013.

(4) The unvested shares are scheduled to vest in approximately equal monthly installments through June 3, 2013.

(5) The unvested shares are scheduled to vest in approximately equal monthly installments through August 1, 2013.

(6) The unvested shares are scheduled to vest as to 33% of the unvested shares upon the FDA's approval of our first IND application, with the remaining 67% vesting in approximately equal monthly installments over the following two years.
(7) The shares underlying this option vest as follows: 25% upon the identification of our second preclinical development candidate, as determined by our board of directors; 50% upon receipt of evidence of clinical efficacy or achievement of a pharmacodynamic endpoint, in each case, as defined within a clinical trial protocol with respect to any development candidate; and 25% on the first anniversary of the first date that both of the aforementioned milestones were achieved. On April 30, 2013, our board of directors determined that the first such milestone was achieved as of March 18, 2013, and 25% of the shares underlying the option vested.
(8) The unvested shares are scheduled to vest in approximately equal monthly installments through May 15, 2013.
(9) The unvested shares are scheduled to vest in approximately equal monthly installments through May 18, 2013.
(10) The unvested shares are scheduled to vest in approximately equal monthly installments through May 18, 2013.
(11) The unvested shares are scheduled to vest in approximately equal monthly installments through January 31, 2015.
(12) The unvested shares commence vesting upon the acceptance by Celgene of two development candidates under our collaboration agreement, at which point the shares will vest as follows: 25% immediately, with monthly vesting for the remaining unvested shares over the following three years. On April 30, 2013, our board of directors determined that this milestone was achieved as of March 18, 2013, and 25% of the shares underlying the option vested.
(13) The unvested shares commence vesting upon the closing of a significant new strategic collaboration, as determined by our board of directors, at which point the shares underlying this option will vest as follows: 25% immediately, with monthly vesting for the remaining unvested shares over the following three years.
(14) The unvested shares are scheduled to vest in approximately equal monthly installments through September 20, 2014.
(15) The unvested shares are scheduled to vest in approximately equal monthly installments through July 1, 2014.
(16) The unvested shares are scheduled to vest in approximately equal monthly installments through September 15, 2015.

For information on potential payments to our named executive officers in connection with their termination or a change in control, as provided in their respective offer letters, see "Employment agreements, severance and change in control arrangements" below.

**Employment, severance and change in control arrangements**

***Offer letters***

We have entered into employment offer letters with each of our executive officers pursuant to which such executive officer is employed "at will," meaning he or we may terminate the employment arrangement at any time. Such offer letters establish the executive officer's title, initial compensation arrangements, eligibility for benefits made available to employees generally, and, in the case of Drs. Schenkein and Biller and Mr. Higgons, also provide for certain benefits upon termination of employment under specified conditions. The following summarizes such termination benefits:

*Benefits provided upon termination without cause or for good reason*

Under the terms of the offer letters we have entered into with each of Drs. Schenkein and Biller and Mr. Higgons, subject to the execution and effectiveness of a release of claims against us, if such executive officer's employment is terminated by us without cause or by such executive officer for good reason, as defined in such offer letters, prior to a change of control, as defined in such offer letters, we will be obligated to (i) pay an amount equal to his then-current monthly base salary for a period of 12 months and his annual incentive cash incentive, (ii) continue to provide such executive officer with health and dental insurance consistent with the then-current benefit plans provided by us for a period of 12 months and (iii) accelerate the vesting of such

executive officer's option and restricted stock awards, such that (a) in the case of such a termination of the employment of Dr. Schenkein, all shares under any such awards held by him shall vest and (b) in the case of such a termination of the employment of Mr. Higgons or Dr. Biller, 25% of the original number of shares under any such awards held by him shall vest.

*Benefits provided upon a change in control*

Under the terms of the offer letters we have entered into with each of Drs. Schenkein and Biller and Mr. Higgons, the vesting of any option or restricted stock award held by such executive officers shall be partially accelerated upon a change of control, such that 75% of the then unvested shares under any such award shall become vested. In addition, if such executive officer's employment is terminated by us or our acquiror without cause or by such executive officer for good reason within 18 months following a change of control, all of such executive officer's option and restricted stock awards shall vest in full.

***Other agreements***

We have entered into non-competition, non-solicitation, confidentiality and assignment agreements with each of our executive officers. Under the non-competition, non-solicitation, confidentiality and assignment agreements, each executive officer has agreed (i) not to compete with us during his employment and for a period of one year after the termination of his employment, (ii) not to solicit our employees or customers during his employment and for a period of one year after the termination of his employment, (iii) to protect our confidential and proprietary information, and (iv) to assign to us related intellectual property that is developed during the course of his employment and for a period of six months after the termination of his employment, that results from tasks assigned by us or that results from the use of our property, premises, or confidential information.

**Equity and non-equity incentive plans**

***2013 Stock incentive plan***

In , 2013, our board of directors adopted and our stockholders approved the 2013 Plan, which will become effective immediately prior to the closing of this offering. The 2013 Plan provides for the grant of incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. Upon effectiveness of the 2013 Plan, the number of shares of our common stock that will be reserved for issuance under the 2013 Plan will be the sum of (1) shares plus (2) the number of shares (up to shares) equal to the sum of the number of shares of our common stock then available for issuance under the 2007 Plan, and the number of shares of our common stock subject to outstanding awards under the 2007 Plan, that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by us at their original issuance price pursuant to a contractual repurchase right plus (3) an annual increase, to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2014 and continuing until the expiration of the 2013 Plan, equal to the lesser of (i) shares of our common stock, (ii) % of the outstanding shares on such date or (iii) an amount determined by our board of directors.

Our employees, officers, directors, consultants and advisors are eligible to receive awards under the 2013 Plan. However, incentive stock options may only be granted to our employees. The maximum number of shares of our common stock with respect to which awards may be granted to any participant under the 2013 Plan is shares per calendar year. For purposes of this limit on the maximum number of shares that may be awarded to any participant, the combination of an option in tandem with a stock appreciation right will be treated as a single award.

Pursuant to the terms of the 2013 Plan, our board of directors administers the 2013 Plan and, subject to any limitations in the 2013 Plan, selects the recipients of awards and determines:

- the number of shares of our common stock covered by options and the dates upon which the options become exercisable;

- the type of options to be granted;
- the duration of options, which may not be in excess of ten years;
- the exercise price of options; and
- the number of shares of our common stock subject to any stock appreciation rights, restricted stock awards, restricted stock units or other stock-based awards and the terms and conditions of such awards, including conditions for repurchase, issue price and repurchase price.

If our board of directors delegates authority to an executive officer to grant awards under the 2013 Plan, the executive officer has the power to make awards to all of our employees, except executive officers. Our board of directors will fix the terms of the awards to be granted by such executive officer, including the exercise price of such awards, and the maximum number of shares subject to awards that such executive officer may make.

Upon a merger or other reorganization event, our board of directors may, in its sole discretion, take any one or more of the following actions pursuant to the 2013 Plan as to some or all outstanding awards other than restricted stock:

- provide that all outstanding awards shall be assumed, or substantially equivalent awards shall be substituted, by the acquiring or successor corporation (or an affiliate thereof);
- upon written notice to a participant, provide that all of the participant's unexercised awards will terminate immediately prior to the consummation of such reorganization event unless exercised by the participant;
- provide that outstanding awards shall become exercisable, realizable or deliverable, or restrictions applicable to an award shall lapse, in whole or in part, prior to or upon such reorganization event;
- in the event of a reorganization event pursuant to which holders of shares of our common stock will receive a cash payment for each share surrendered in the reorganization event, make or provide for a cash payment to the participants with respect to each award held by a participant equal to (i) the number of shares of common stock subject to the vested portion of the award (after giving effect to any acceleration of vesting that occurs upon or immediately prior to such reorganization event) multiplied by (ii) the excess, if any, of the cash payment for each share surrendered in the reorganization event over the exercise, measurement or purchase price of such award and any applicable tax withholdings, in exchange for the termination of such award;
- provide that, in connection with a liquidation or dissolution, awards shall convert into the right to receive liquidation proceeds; and/or
- any combination of the foregoing.

In the case of certain restricted stock units, no assumption or substitution is permitted, and the restricted stock units will instead be settled in accordance with the terms of the applicable restricted stock unit agreement.

Upon the occurrence of a reorganization event other than a liquidation or dissolution, the repurchase and other rights with respect to outstanding restricted stock will continue for the benefit of the successor company and will, unless the board of directors may otherwise determine, apply to the cash, securities or other property into which shares of our common stock are converted or exchanged pursuant to the reorganization event. Upon the occurrence of a reorganization event involving a liquidation or dissolution, all restrictions and conditions on each outstanding restricted stock award will automatically be deemed terminated or satisfied, unless otherwise provided in the agreement evidencing the restricted stock award.

At any time, our board of directors may, in its sole discretion, provide that any award under the 2013 Plan will become immediately exercisable in full or in part, free of some or all restrictions or conditions, or otherwise realizable in full or in part.

No award may be granted under the 2013 Plan on or after , 2023. Our board of directors may amend, suspend or terminate the 2013 Plan at any time, except that stockholder approval will be required to comply with applicable law or stock market requirements.

***2007 Stock incentive plan***

The 2007 Plan was first adopted by our board of directors and first approved by our stockholders in September 2007 and was amended in June 2008, August 2009, September 2010 and March 2012. The 2007 Plan provides for the grant of incentive stock options within the meaning of Section 422 of the Internal Revenue Code, non-statutory stock options, stock awards, restricted stock awards and stock appreciation rights. Our employees, officers, directors, consultants and advisors are eligible to receive awards and stock appreciation rights under the 2007 Plan. However, incentive stock options may only be granted to our employees. The terms of awards are set forth in the applicable award agreements. Pursuant to the terms of the 2007 Plan, our board of directors, or a committee appointed by our board, administers the 2007 Plan. Our board of directors may delegate authority to one or more of our officers to grant awards under the 2007 Plan, in which case such officer will have the power to make awards to all of our employees, except executive officers. Our board of directors will fix the terms of the awards to be granted by such officer, including the exercise price of such awards and the maximum number of shares subject to awards that such officer may make.

As of April 30, 2013, (i) there were 13,969,018 shares of our common stock reserved for issuance under the 2007 Plan, subject to adjustment as provided below; (ii) there were outstanding options to purchase an aggregate of 10,170,824 shares of common stock at a weighted average exercise price of $0.81 per share; and (iii) there were outstanding 256,812 shares of unvested restricted common stock. Upon the closing of this offering, we will grant no further stock options or other awards under the 2007 Plan. However, any shares of common stock reserved for issuance under the 2007 Plan that remain available for issuance and any shares of common stock subject to awards under the 2007 Plan that expire, terminate, or are otherwise surrendered, canceled, forfeited or repurchased without having been fully exercised or resulting in any common stock being issued will be available for issuance under the 2013 Plan up to a specified number of shares.

In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of our common stock other than an ordinary cash dividend:

- the number and class of securities available under the 2007 Plan;
- the number and class of securities and exercise price per share of each outstanding option under the 2007 Plan;
- the number of shares subject to and the repurchase price per share subject to each outstanding restricted stock award under the 2007 Plan; and/or
- the terms of each other outstanding award under the 2007 Plan

shall be equitably adjusted by the administrator (or substitute awards may be made, if applicable).

Upon a reorganization event, as defined in the 2007 Plan, the administrator may, in the case of awards under the 2007 Plan other than restricted stock awards, take one or more of the following actions as to all or any, or any portion of, outstanding awards, other than restricted stock awards:

- arrange for or provide that each outstanding award will be assumed or a substantially similar award will be substituted by the acquiring or succeeding corporation (or an affiliate thereof);
- provide, upon notice to the participant, that unexercised awards will terminate immediately prior to the consummation of such transaction unless exercised within a specified period of time following the date of such notice;

- provide that outstanding awards will become vested or exercisable, or restrictions applicable to such awards will lapse, in full or in part, at or immediately prior to such event;
- in the event of a reorganization event under the terms of which holders of our common stock will receive a cash payment per share surrendered in the transaction, make or provide for an equivalent cash payment in exchange for the termination of such equity awards;
- provide that in the event of a liquidation or dissolution, awards will convert into the right to receive liquidation proceeds; or
- any combination of the foregoing.

Upon a reorganization event, as defined in the 2007 Plan, other than a liquidation or dissolution, the repurchase and other rights we may have under each outstanding restricted stock award under the 2007 Plan shall inure to the benefit of our successor and shall, unless the administrator determines otherwise, apply to the cash, securities or other property which our common stock was converted into or exchanged for pursuant to such reorganization event in the same manner and to the same extent as they applied to the common stock subject to such restricted stock award. Upon a reorganization event involving a liquidation or dissolution, except to the extent specifically provided to the contrary in the instrument evidencing any restricted stock award under the 2007 Plan or any other agreement between a participant and us, all restrictions and conditions on all restricted stock awards then outstanding shall automatically be deemed terminated or satisfied.

The administrator may at any time provide that any award under the 2007 Plan shall become immediately exercisable in full or in part, free of some or all restrictions or conditions, or otherwise realizable in full or in part. The administrator may amend, modify or terminate any outstanding award under the 2007 Plan, including but not limited to, substituting another award of the same or a different type, changing the date of exercise or realization, and converting an incentive stock option to a nonstatutory stock option, subject in certain cases to the participant's consent.

***2013 Employee stock purchase plan***

On , 2013, our board of directors adopted and our stockholders approved the 2013 employee stock purchase plan, or the 2013 ESPP, which will become effective upon the closing of the offering. The 2013 ESPP will be administered by our board of directors or by a committee appointed by our board of directors. The 2013 ESPP initially provides participating employees with the opportunity to purchase up to an aggregate of shares of our common stock. The number of shares of our common stock reserved for issuance under the 2013 ESPP will automatically increase on the first day of each fiscal year, commencing on January 1, 2014 and ending on January 1, 2023, in an amount equal to the lowest of (i) shares of our common stock, (ii) of the total number of shares of our common stock outstanding on the first day of the applicable year, or (iii) an amount determined by our board of directors. The 2013 ESPP provides for six-month offering periods, commencing if and when approved by our board of directors, during which eligible employees may elect to have a specified percentage of their compensation withheld through payroll deductions for the purpose of purchasing shares at the end of the period. All of our employees or employees of any designated subsidiary, as defined in the 2013 ESPP, are eligible to participate in the 2013 ESPP, provided that:

- such person is customarily employed by us or a designated subsidiary for more than 20 hours a week and for more than five months in a calendar year;
- such person has been employed by us or by a designated subsidiary for at least six months prior to enrolling in the 2013 ESPP; and
- such person was our employee or an employee of a designated subsidiary on the first day of the applicable offering period under the 2013 ESPP.

No employee is eligible to purchase shares of our common stock that would result in the employee owning 5% or more of the total combined voting power or value of our stock immediately after such purchase. In addition under the 2013 ESPP, no employee may purchase common stock under the plan in excess of $25,000 for each calendar year, or such lesser amount as determined by our board of directors.

We expect to make one or more offerings to our employees to purchase stock under the 2013 ESPP. Offering periods under the 2013 ESPP will commence at such time or times as our board of directors may determine. Payroll deductions made during each offering period will be held for the purchase of our common stock at the end of the offering period.

On the commencement date of each offering period, each eligible employee may authorize up to a maximum of ten percent of his or her compensation to be deducted by us during the offering period. Each employee who continues to be a participant in the 2013 ESPP on the last business day of the offering period is deemed to have purchased shares, to the extent of accumulated payroll deductions within the 2013 ESPP ownership limits. Under the terms of the 2013 ESPP, the purchase price shall be determined by our board of directors for each offering period and will be at least 85% of the applicable closing price. If our board of directors does not make a determination of the purchase price, the purchase price will be 85% of the lesser of the closing price of our common stock on the first business day of the offering period or the last business day of the offering period. Our board of directors may, in its discretion, choose a different period of 12 months or less for each offering period.

An employee who is not a participant on the last day of the offering period is not entitled to purchase shares under the 2013 ESPP, and the employee's accumulated payroll deductions will be refunded. An employee's rights under the 2013 ESPP terminate upon voluntary withdrawal from an offering under the 2013 ESPP at any time, or when the employee ceases employment for any reason.

We will be required to make equitable adjustments in connection with the 2013 ESPP and any outstanding awards to reflect stock splits, reverse stock splits, stock dividends, recapitalizations, combination of shares, reclassification of shares, spin-offs and other similar changes in capitalization.

Our board of directors may at any time, and from time to time, amend or suspend the 2013 ESPP. We will obtain stockholder approval for any amendment if such approval is required by Section 423 of the Internal Revenue Code. Further, our board of directors may not make any amendment that would cause the 2013 ESPP to fail to comply with Section 423 of the Internal Revenue Code. Upon termination, we will refund all amounts in the accounts of participating employees that have not been used to purchase shares.

**401(k) retirement plan**

We maintain a 401(k) retirement plan that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code. In general, all of our employees are eligible to participate, beginning on the first day of the month following commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit, equal to $17,500 in 2013, and have the amount of the reduction contributed to the 401(k) plan. Participants that will turn age 50 in 2013 are also eligible to make "catch-up" contributions, which in 2013 may be up to an additional $5,500 above the statutory limit.

**2012 Director compensation**

The following table sets forth information concerning the compensation for our non-employee directors during the fiscal year ended December 31, 2012:

| Name | Fees earned or paid in cash ($) | Option awards ($) (1) | Total ($) |
|---|---|---|---|
| Lewis C. Cantley, Ph.D.(2) | — | — | — |
| Douglas G. Cole, M.D. | — | — | — |
| Perry Karsen | — | — | — |
| John M. Maraganore, Ph.D. | $ 35,000 | $ 42,135(3) | $ 77,135 |
| Robert T. Nelsen | — | — | — |
| Kevin P. Starr | — | — | — |
| Marc Tessier-Lavigne, Ph.D. | $ 20,000 | $ 21,067(4) | $ 41,067 |

(1) Amounts listed represent the aggregate fair value amount computed as of the grant date of the option awards granted during 2012 in accordance with FASB ASC Topic 718. Assumptions used in the calculation of these amounts are included in Note 9, Share-based Payments, of the Notes to our Consolidated Financial Statements.

(2) Excludes $175,000 in annual compensation paid to Dr. Cantley pursuant to a consulting agreement under which Dr. Cantley serves as a special scientific consultant to us, with a commitment of one day per week. As of December 31, 2012, Dr. Cantley held 999,999 shares of our common stock and options to purchase 400,000 shares of our common stock.

(3) Represents an option to purchase 24,000 shares granted to Dr. Maraganore during 2012 for service on our board of directors. The shares subject to this option vest in full on December 4, 2013. Pursuant to an early exercise provision in the option agreement, Dr. Maraganore exercised this option on December 21, 2012 and received 24,000 shares of restricted stock, which shares vest in full on December 4, 2013. As of December 31, 2012, Dr. Maraganore held 99,000 shares of our common stock.

(4) Represents an option to purchase 12,000 shares granted to Dr. Tessier-Lavigne during 2012 for service on our board of directors. The shares subject to this option vest in full on December 4, 2013. As of December 31, 2012, Dr. Tessier-Lavigne held 125,000 shares of our common stock and options to purchase 12,000 shares of our common stock.

Dr. Schenkein, one of our directors who also serves as our chief executive officer, does not receive any additional compensation for his service as a director.

Prior to December 4, 2012, the compensation of our non-employee directors was established through arm's length negotiation at the time the director was elected, taking into account the responsibilities of each director and the director's qualifications and prior experience and industry data for such positions. This compensation was reviewed and recommended by our compensation committee and approved by our board of directors.

Dr. Maraganore was appointed to our board of directors as a non-employee director and chairperson of our compensation committee in June 2010. His annual cash compensation was set at $35,000, and he was awarded an option to purchase 75,000 shares of common stock. On December 4, 2012, he was awarded an option to purchase an additional 24,000 shares of common stock.

Dr. Tessier-Lavigne was appointed to our board of directors in September 2011 as an independent director and chairperson of the scientific sub-committee. His cash compensation was set at $16,000, and he was awarded an option to purchase 125,000 shares of our common stock. On December 4, 2012, he was awarded an option to purchase an additional 12,000 shares of common stock.

On December 4, 2012, our board of directors, upon the recommendation of our compensation committee, established the following compensation guidelines for non-employee board members:

- each non-employee director receives an option to purchase 60,000 shares of common stock upon his or her election to the board;
- each non-employee director receives an option to purchase 10,000 shares of common stock on the anniversary of his or her election to the board;
- each non-employee director receives $8,750 per calendar quarter; and
- each non-employee director who serves as chairperson of a committee of the board receives additional equity compensation as follows:
  - the chairperson of the audit committee receives an annual grant of an option to purchase 4,000 shares of common stock; and
  - the chairperson of each of the nominating and corporate governance committee and compensation committee receives an annual grant of an option to purchase 2,000 shares of common stock.

The stock options granted to our non-employee directors have an exercise price equal to the fair market value of our common stock on the date of grant, expire ten years after the date of grant, and are subject to the director's continued service on our board.

To the extent that a non-employee director has other responsibilities, such director may receive additional compensation to the extent as deemed necessary by our board of directors.

Each member of our board of directors receives reimbursement for reasonable travel and other expenses incurred in connection with attending meetings of the board of directors, consistent with our employee travel expense reimbursement guidelines. Pursuant to a consulting agreement, Dr. Cantley serves as a special scientific consultant to us, with a commitment of one day per week, for which he is paid $175,000 annually. See "Certain relationships and related person transactions—Cantley consulting agreement."

**Limitation of liability and indemnification**

Our certificate of incorporation, which will become effective upon the closing of this offering, limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty or other duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director's duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- for voting or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the Delaware General Corporation Law is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the Delaware General Corporation Law.

In addition, our certificate of incorporation, which will become effective upon the closing of this offering, provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we have entered into indemnification agreements with certain of our directors, and we intend to enter into indemnification agreements with all of our directors. These indemnification agreements may require us, among other things, to indemnify each such director for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him in any action or proceeding arising out of his service as one of our directors.

Certain of our non-employee directors may, through their relationships with their employers, be insured and/or indemnified against certain liabilities incurred in their capacity as members of our board of directors.

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, or the Securities Act, may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

## Certain relationships and related person transactions

Since January 1, 2010, we have engaged in the following transactions with our directors and executive officers and holders of more than 5% of our voting securities, and affiliates of our directors, executive officers and 5% stockholders. We believe that all of the transactions described below were made on terms no less favorable to us than could have been obtained from unaffiliated third parties.

### Collaboration with Celgene and series B convertible preferred stock financing

In April 2010, we entered into a collaboration agreement with Celgene Corporation. In October 2011, we amended this collaboration agreement. See "Business—Collaboration with Celgene." Pursuant to the collaboration, we received an upfront payment of $121.2 million in April 2010 and a payment of $20.0 million in October 2011 in consideration of entering into an amendment to extend the discovery phase of the agreement.

Simultaneously with entering into the collaboration agreement, in April 2010, we issued and sold 5,190,551 shares of our series B convertible preferred stock to Celgene at a purchase price per share of $1.70 for an aggregate purchase price of $8.8 million. In connection with such sale of shares of our series B preferred stock to Celgene, we were granted the right to require Celgene to purchase, either in our initial public offering or, at our determination, in a concurrent private placement, at a per share purchase price equal to the public offering price, a number of shares of our common stock having an aggregate purchase price equal to the lesser of 10% of the total gross proceeds for the shares sold in the public offering or $10 million. If we do not exercise this option to issue and sell the shares to Celgene, then Celgene has the right to elect to purchase, at a per share purchase price equal to the public offering price, a number of shares of our common stock having an aggregate purchase price equal to 10% of the total gross proceeds for the shares sold in the public offering. Celgene has agreed to purchase $ million of our common stock in a private placement concurrent with this offering at a price per share equal to the initial public offering price. The sale of such shares of common stock are being issued pursuant to Section 4(2) under the Securities Act relating to transactions not involving any public offering, and will not be registered under the Securities Act. The closing of the offering to which this prospectus relates is not conditioned upon the closing of the concurrent private placement to Celgene.

After giving effect to the sale of (i) shares of series B preferred stock to an affiliate of Celgene as described herein, (ii) shares of series C-2 preferred stock to an affiliate of Celgene, as further described below, (iii) shares to Celgene in the concurrent private placement and (iv) shares to the public in this offering, Celgene will be the beneficial owner of % of our outstanding common stock.

Perry Karsen, a member of our board of directors, is the executive vice president of Celgene Corporation.

### Series C-1 convertible preferred stock and series C-2 convertible preferred stock financing

During November 2011, we issued and sold an aggregate of 7,395,829 shares of our series C-1 convertible preferred stock and 8,486,560 shares of our series C-2 convertible preferred stock, each at a purchase price per share of $4.9111, for an aggregate purchase price of approximately $78.0 million.

The following table sets forth the number of shares of series C-1 convertible preferred stock or series C-2 convertible preferred stock that were issued to holders of more than 5% of our voting securities and their affiliates in connection with the series C-1 convertible preferred stock and series C-2 convertible preferred stock financing and the aggregate cash purchase price paid by such entities.

| Purchaser(1) | Shares of series C-1 convertible preferred stock | Shares of series C-2 convertible preferred stock | Purchase price |
|---|---|---|---|
| ARCH Venture Fund VII, L.P.(2) | — | 617,031 | $ 3,030,301 |
| Flagship Ventures Fund 2007, L.P.(3) | — | 617,031 | $ 3,030,301 |
| Third Rock Ventures, L.P.(4) | — | 802,141 | $ 3,939,395 |
| Entities affiliated with Fidelity Management & Research Company(5) | 6,377,730 | — | $31,321,670 |
| Celgene European Investment Company LLC(6) | — | 5,839,496 | $28,678,349 |

(1) See “Principal stockholders” for more information about shares held by these entities.

(2) Robert T. Nelsen, a member of our board of directors, is a managing director of ARCH Venture Partners VII, LLC, the sole general partner of ARCH Venture Partners VII, L.P., the sole general partner of ARCH Venture Fund VII, L.P.

(3) Douglas Cole, a member of our board of directors, is a member of Flagship Ventures 2007 General Partner LLC, the sole general partner of Flagship Ventures Fund 2007 L.P. (the “Fund”). Dr. Cole does not have either voting or investment control over the Fund’s shares and he disclaims beneficial ownership of the Fund’s shares, except to the extent of his pecuniary interest therein. Dr. Cole does not own shares in his individual capacity.

(4) Kevin Starr, a member of our board of directors, is a partner of Third Rock Ventures. Mr. Starr may be deemed to have voting and investment power over the shares held by Third Rock Ventures, L.P. Mr. Starr disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.

(5) Consists of (a) 50,916 shares of series C-1 convertible preferred stock purchased by Fidelity Select Portfolios: Pharmaceuticals Portfolio, (b) 229,509 shares of series C-1 convertible preferred stock purchased by Fidelity Select Portfolios: Biotechnology Portfolio, (c) 13,990 shares of series C-1 convertible preferred stock purchased by Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund, (d) 2,036,659 shares of series C-1 convertible preferred stock purchased by Fidelity Mt. Vernon Street Trust: Fidelity Growth Company Fund, (e) 3,363,446 shares of series C-1 convertible preferred stock purchased by Fidelity Contrafund: Fidelity Advisor New Insights Fund, (f) 353,944 shares of series C-1 convertible preferred stock purchased by Fidelity Securities Fund: Fidelity Small Cap Opportunities Fund, and (g) 329,266 shares of series C-1 convertible preferred stock purchased by Fidelity Capital Trust: Fidelity Small Cap Independence Fund.

(6) Perry Karsen, a member of our board of directors, is the executive vice president of Celgene Corporation, the parent corporation of Celgene European Investment Company LLC.

**Registration rights**

We are a party to a second amended and restated investor rights agreement with holders of our series A convertible preferred stock, series B convertible preferred stock, series C-1 convertible preferred stock and series C-2 convertible preferred stock, including some of our directors, executive officers and 5% stockholders and their affiliates and entities affiliated with our directors. The investor rights agreement provides these holders the right, following the completion of this offering, to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing. Celgene will also be entitled to registration rights with respect to shares of our common stock purchased by them in the concurrent private placement. See “Description of capital stock—Registration rights” for additional information regarding these registration rights.

**Severance and change in control agreements**

See the "Executive compensation—Employment, severance and change in control arrangements" section of this prospectus for a further discussion of these arrangements.

**Schenkein loan**

In August 2009, we lent $500,000 to David Schenkein, M.D., our chief executive officer and a member of our board of directors, to assist with his relocation expenses in connection with the commencement of Dr. Schenkein's employment with us. The principal and interest under such loan was repaid in full in November 2010.

**Cantley consulting agreement**

In July 2010, we entered into a consulting agreement with Lewis C. Cantley, Ph.D., a member of our board of directors, under which Dr. Cantley is paid $175,000 annually to serve as a special scientific consultant to us, with a commitment of one day per week.

**Foundation Medicine**

In March 2013, we entered into a master services agreement with Foundation Medicine. Under that agreement, Foundation Medicine has agreed, on a non-exclusive basis, to provide mutation analysis for the clinical trials in our IDH1 and IDH2 programs. Nothing has been paid to date under this agreement, and we do not expect to incur meaningful costs under this agreement until 2014. Dr. Schenkein, our chief executive officer and a director, is a director of Foundation Medicine.

**Indemnification of officers and directors**

Our certificate of incorporation that will be effective as of the closing date of this offering provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we expect to enter into indemnification agreements with each of our directors that may be broader in scope than the specific indemnification provisions contained in the Delaware General Corporation Law. See the "Executive compensation—Limitation of liability and indemnification" section of this prospectus for a further discussion of these arrangements.

**Policies and procedures for related person transactions**

On , 2013, our board of directors adopted written policies and procedures for the review of any transaction, arrangement or relationship in which we are a participant, the amount involved exceeds $120,000, and one of our executive officers, directors, director nominees or 5% stockholders (or their immediate family members), each of whom we refer to as a "related person," has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a "related person transaction," the related person must report the proposed related person transaction to our principal financial officer. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by the audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the committee after full disclosure of the related person's interest in the transaction. As appropriate for the circumstances, the committee will review and consider:

- the related person's interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person's interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;
- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

The committee may approve or ratify the transaction only if the committee determines that, under all of the circumstances, the transaction is in or is not inconsistent with our best interests. The committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC's related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

- interests arising solely from the related person's position as an executive officer of another entity (whether or not the person is also a director of such entity), that is a participant in the transaction, where (a) the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, (b) the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction, (c) the amount involved in the transaction equals less than the greater of $1 million dollars or 2% of the annual consolidated gross revenues of the other entity that is a party to the transaction, and (d) the amount involved in the transaction equals less than 2% of our annual consolidated gross revenues; and
- a transaction that is specifically contemplated by provisions of our charter or bylaws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by the compensation committee in the manner specified in its charter.

## Principal stockholders

The following table sets forth information with respect to the beneficial ownership of our common stock, as of April 30, 2013 by:

- each person known by us to beneficially own more than 5% of our common stock;
- each of our directors;
- each of our named executive officers; and
- all of our executive officers and directors as a group.

The column entitled "Shares beneficially owned prior to offering—Percentage" is based on a total of 64,703,320 shares of our common stock outstanding as of April 30, 2013, assuming the automatic conversion of all outstanding shares of our preferred stock into an aggregate of 54,261,829 shares of our common stock upon the closing of this offering. The column entitled "Shares beneficially owned after offering—Percentage" is based on shares of our common stock to be outstanding after this offering, including the shares of our common stock that we are selling in this offering and the shares of our common stock that we are selling to Celgene in the concurrent private placement, but not including any additional shares issuable upon exercise of outstanding options.

The number of shares beneficially owned by each stockholder is determined under rules issued by the Securities and Exchange Commission and includes voting or investment power with respect to securities. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power. In computing the number of shares beneficially owned by an individual or entity and the percentage ownership of that person, shares of common stock subject to options or other rights held by such person that are currently exercisable or will become exercisable within 60 days as of April 30, 2013 are considered outstanding, although these shares are not considered outstanding for purposes of computing the percentage ownership of any other person. Unless otherwise indicated, the address of all listed stockholders is c/o Agios Pharmaceuticals, Inc., 38 Sidney Street, 2nd Floor, Cambridge, MA 02139. Each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

| | Shares beneficially owned prior to offering | | Shares beneficially owned after offering | |
|---|---|---|---|---|
| Name of beneficial owner | Number | Percentage | Number | Percentage |
| ***5% Stockholders*** | | | | |
| Third Rock Ventures, L.P.(1) | 15,302,141 | 23.65% | | % |
| Celgene European Investment Company LLC(2) | 11,030,047 | 17.05% | | % |
| ARCH Venture Fund VII, L.P.(3) | 10,617,031 | 16.41% | | % |
| Flagship Ventures Fund 2007, L.P.(4) | 10,617,031 | 16.41% | | % |
| Entities affiliated with Fidelity Management & Research Company(5) | 6,377,730 | 9.86% | | % |
| ***Named executive officers and directors*** | | | | |
| David P. Schenkein, M.D.(6) | 2,723,864 | 4.10% | | % |
| Duncan Higgons(7) | 1,245,366 | 1.90% | | % |
| Scott Biller, Ph.D.(8) | 476,875 | * | | % |
| Glenn Goddard(9) | 124,270 | * | | % |
| Lewis C. Cantley, Ph.D.(10) | 1,332,290 | 2.05% | | % |

| Name of beneficial owner | Shares beneficially owned prior to offering | | Shares beneficially owned after offering | |
|---|---|---|---|---|
| | Number | Percentage | Number | Percentage |
| Douglas G. Cole, M.D.(11) | — | — | | % |
| Perry Karsen(12) | 11,030,047 | 17.05% | | % |
| John M. Maraganore, Ph.D. | 99,000 | * | | % |
| Robert T. Nelsen(13) | 10,617,031 | 16.41% | | % |
| Kevin P. Starr(14) | 15,302,141 | 23.65% | | % |
| Marc Tessier-Lavigne, Ph.D. | 125,000 | * | | % |
| All executive officers and directors as a group (11 persons)(15) | 43,075,884 | 63.09% | | % |

* Less than 1%.

(1) Consists of (a) 13,000,000 shares of common stock issuable upon conversion of series A convertible preferred stock held by Third Rock Ventures, L.P. ("TRV LP"), (b) 802,141 shares of common stock issuable upon conversion of series C-2 convertible preferred stock held by TRV LP, and (c) 1,500,000 shares of common stock held by TRV LP. Each of Third Rock Ventures GP, LP ("TRV GP"), the general partner of TRV LP, and Third Rock Ventures GP, LLC ("TRV LLC"), the general partner of TRV GP, may be deemed to have voting and dispositive power over the shares held by TRV LP. Investment decisions with respect to the shares held by TRV LP are made by an investment committee at TRV GP comprised of Mark Levin, Kevin Starr, Bob Tepper, Neil Exter, Kevin Gillis, Lou Tartaglia, Craig Muir, Cary Pfeffer, Alexis Borisy and Craig Greaves. No stockholder, director, officer, manager, member or employee of TRV GP or TRV LLC has beneficial ownership (within the meaning of Rule 13d-3 promulgated under the Exchange Act) of any shares held by TRV LP. Mr. Starr, a member of our board of directors, is a partner of TRV LP and may be deemed to have voting and investment power over the shares held by TRV LP. Mr. Starr disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address of TRV LP is 29 Newbury Street, Suite 401, Boston, MA 02142.

(2) Consists of (a) 5,190,551 shares of common stock issuable upon conversion of series B convertible preferred stock held by Celgene European Investment Company LLC ("Celgene LLC"), and (b) 5,839,496 shares of common stock issuable upon conversion of series C-2 convertible preferred stock held by Celgene LLC. The number of shares beneficially owned after the offering includes shares issuable in the concurrent private placement of $ million of our common stock at the completion of this offering at the public offering price of $ per share. Perry Karsen, a member of our board of directors, is the executive vice president of Celgene. Celgene LLC is a wholly-owned subsidiary of Celgene, and Mr. Karsen may be deemed to share voting and dispositive power with respect to the shares held by Celgene LLC. Mr. Karsen disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address for Celgene LLC is 86 Morris Avenue, Summit, NJ 07901.

(3) Consists of (a) 10,000,000 shares of common stock issuable upon conversion of series A convertible preferred stock held by ARCH Venture Fund VII, L.P. ("ARCH VII"), and (b) 617,031 shares of common stock issuable upon conversion of series C-2 convertible preferred stock held by ARCH VII. ARCH Venture Partners VII, L.P. (the "GPLP"), as the sole general partner of ARCH VII and may be deemed to beneficially own certain of the shares held by ARCH VII. The GPLP disclaims beneficial ownership of all shares held by ARCH VII in which the GPLP does not have an actual pecuniary interest. ARCH Venture Partners VII, LLC (the "GPLLC"), as the sole general partner of the GPLP, may be deemed to beneficially own certain of the shares held by ARCH VII. The GPLLC disclaims beneficial ownership of all shares held by ARCH VII in which it does not have an actual pecuniary interest. The managing directors of the GPLLC, Robert T. Nelsen, Keith Crandell and Clinton Bybee (together, the "Managing Directors"), are deemed to have voting and dispositive power over the shares held by ARCH VII, and may be deemed to beneficially own certain of the shares held by ARCH VII. Mr. Nelsen, a member of our board of directors is one of the Managing Directors. The Managing Directors disclaim beneficial ownership of all shares held by ARCH VII in which they do not have an actual pecuniary interest. The address for ARCH VII is 8725 West Higgins Road, Suite 290, Chicago, IL 60631.

(4) Consists of (a) 10,000,000 shares of common stock issuable upon conversion of series A convertible preferred stock held by Flagship Ventures Fund 2007, L.P. ("Flagship 2007"), and (b) 617,031 shares of common stock issuable upon conversion of series C-2 convertible preferred stock held by Flagship 2007. Flagship Ventures 2007 General Partner, LLC ("Flagship 2007 LLC") is the general partner of Flagship 2007 and Noubar B. Afeyan Ph.D. and Edwin M. Kania, Jr. are the managers of Flagship 2007 LLC. Flagship 2007 LLC, Dr. Afeyan and Mr. Kania may be deemed to share voting and investment power with respect to all shares held by Flagship 2007. Flagship 2007 LLC, Dr. Afeyan and Mr. Kania expressly disclaim beneficial ownership of the securities listed above except to the extent of any pecuniary interest therein. Douglas G. Cole, M.D., a member of our board of directors, is a member of Flagship 2007 LLC, the sole general partner of Flagship 2007. Dr. Cole does not have either voting or investment control over Flagship 2007's shares and he disclaims beneficial ownership of Flagship 2007's shares, except to the extent of his pecuniary interest therein. The address for Flagship 2007 is One Memorial Drive, 7th Floor, Cambridge, MA 02142.

(5) Consists of (a) 50,916 shares of common stock issuable upon conversion of series C-1 convertible preferred stock held by Fidelity Select Portfolios: Pharmaceuticals Portfolio, (b) 229,509 shares of common stock issuable upon conversion of series C-1 convertible preferred stock held by Fidelity Select Portfolios: Biotechnology Portfolio, (c) 13,990 shares of common stock issuable upon conversion of series C-1 convertible preferred stock held by Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund, (d) 2,036,659 shares of common stock issuable upon conversion of series C-1 convertible preferred stock held by Fidelity Mt. Vernon Street Trust: Fidelity Growth Company Fund, (e) 3,363,446 shares of common stock issuable upon conversion of series C-1 convertible preferred stock held by Fidelity Contrafund: Fidelity Advisor New Insights Fund, (f) 353,944 shares of common stock issuable upon conversion of series C-1 convertible preferred stock held by Fidelity Securities Fund: Fidelity Series Small Cap Opportunities Fund, and (g) 329,266 shares of common stock issuable upon conversion of series C-1 convertible preferred stock held by Fidelity Capital Trust: Fidelity Stock Selector Small Cap Fund. Fidelity Management & Research Company ("Fidelity") a wholly-owned subsidiary of FMR LLC and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of 6,377,730 shares of series C-1 convertible preferred stock as a result of acting as investment adviser to various investment companies registered under Section 8 of the Investment Company Act of 1940. Edward C. Johnson 3d and FMR LLC, through its control of Fidelity and the funds, each has sole power to dispose of the 6,377,730 shares owned by the funds. Members of the family of Edward C. Johnson 3d, chairman of FMR LLC, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d, chairman of FMR LLC, has the sole power to vote or direct the voting of the shares owned directly by the Fidelity Funds, which power resides with the Funds' Boards of Trustees. Fidelity carries out the voting of the shares under written guidelines established by the Funds' Boards of Trustees. The address for Fidelity is 82 Devonshire Street, V13H, Boston, MA 02109.

(6) Consists of (a) 1,693,864 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 30, 2013, (b) 515,000 shares of common stock held by the David P. Schenkein 2004 Revocable Trust, and (c) 515,000 shares of common stock held by the Amy P. Schenkein 2004 Revocable Trust, of which Amy P. Schenkein, Dr. Schenkein's wife, is trustee.

(7) Consists of (a) 945,366 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 30, 2013 and (b) 300,000 shares of common stock.

(8) Consists of 476,875 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 30, 2013.

(9) Consists of 124,270 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 30, 2013.

(10) Includes 332,291 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 30, 2013.
(11) Dr. Cole does not own shares in his individual capacity. He is a member of Flagship 2007 LLC, the sole general partner of Flagship 2007. Dr. Cole does not have either voting or investment control over Flagship 2007's shares and he disclaims beneficial ownership of Flagship 2007's shares, except to the extent of his pecuniary interest therein.
(12) Consists of the shares described in note (2) above. Mr. Karsen is the executive vice president of Celgene. Celgene European Investment Company LLC is a wholly-owned subsidiary of Celgene, and Mr. Karsen may be deemed to share voting and dispositive power with respect to such shares. Mr. Karsen disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.
(13) Consists of the shares described in note (3) above. Mr. Nelsen is a managing director of ARCH Venture Partners VII, LLC, which is the sole general partner of ARCH Venture Partners VII, L.P., which is the sole general partner of ARCH Venture Fund VII, L.P., and as such may be deemed to beneficially own such shares. Mr. Nelsen disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.
(14) Consists of the shares described in note (1) above. Mr. Starr is a partner of Third Rock Ventures, L.P. and may be deemed to have voting and investment power over the shares held by Third Rock Ventures, L.P. Mr. Starr disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.
(15) Includes 3,572,666 shares of common stock issuable upon the exercise of options exercisable within 60 days after April 30, 2012.

## Description of capital stock

### General

Following the closing of this offering, our authorized capital stock will consist of 125,000,000 shares of common stock, par value $0.001 per share, and 25,000,000 shares of preferred stock, par value $0.001 per share.

The following description of our capital stock and provisions of our certificate of incorporation and by-laws are summaries and are qualified by reference to the certificate of incorporation and by-laws that will become effective upon the closing of this offering. Copies of these documents have been filed with the Securities and Exchange Commission as exhibits to our registration statement, of which this prospectus forms a part. The description of our common stock reflects changes to our capital structure that will occur upon the closing of this offering.

As of April 30, 2013, we had issued and outstanding:

- 10,441,491 shares of our common stock held of record by 68 stockholders;
- 33,188,889 shares of our series A convertible preferred stock that are convertible into 33,188,889 shares of our common stock;
- 5,190,551 shares of our series B convertible preferred stock that are convertible into 5,190,551 shares of our common stock; and
- 15,882,389 shares of our series C convertible preferred stock that are convertible into 15,882,389 shares of our common stock, consisting of 7,395,829 shares of our series C-1 convertible preferred stock and 8,486,560 shares of our series C-2 convertible preferred stock.

Upon the closing of this offering, all of the outstanding shares of our preferred stock will automatically convert into an aggregate of 54,261,829 shares of our common stock.

### Common stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are, and the shares offered by us in this offering will be, when issued and paid for, validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

### Preferred stock

Under the terms of our certificate of incorporation that will become effective upon the closing of this offering, our board of directors is authorized to direct us to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. Upon the closing of this offering, there will be no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

**Options**

As of April 30, 2013, options to purchase 10,170,824 shares of our common stock at a weighted average exercise price of $0.81 per share were outstanding.

**Registration rights**

We have entered into a second amended and restated investor rights agreement, dated November 16, 2011, which we refer to as the investor rights agreement, with certain holders of shares of our common stock and preferred stock. Upon the completion of this offering, holders of a total of 54,261,829 shares of our common stock as of April 30, 2013, consisting of shares issuable upon conversion of our preferred stock, will have the right to require us to register these shares under the Securities Act of 1933, as amended, or Securities Act, and to participate in future registrations of securities by us, under the circumstances described below. In addition, Celgene will also have these same registration rights with respect to shares acquired in the concurrent private placement. After registration pursuant to these rights, these shares will become freely tradable without restriction under the Securities Act. If not otherwise exercised, the rights described below will expire five years after the closing of this offering.

***Demand registration rights***

Beginning six months after the closing of this offering, subject to specified limitations set forth in the investor rights agreement, at any time, the holders of a majority of the then outstanding shares having rights under the investor rights agreement, which we refer to as registrable shares, may at any time demand in writing that we register all or a portion of the registrable shares under the Securities Act if the total amount of registrable shares registered have an aggregate offering price of at least $5 million (based on the then current market price). We are not obligated to file a registration statement pursuant to this provision on more than two occasions.

In addition, subject to specified limitations set forth in the investor rights agreement, at any time after we become eligible to file a registration statement on Form S-3, holders of at least 25% of the registrable shares then outstanding may request that we register their registrable securities on Form S-3 for purposes of a public offering if the total amount of registrable shares registered have an aggregate offering price of at least $5 million (based on the then current market price). We are not obligated to file a registration statement pursuant to this provision on more than two occasions in any 12-month period.

***Incidental registration rights***

If, at any time after the closing of this offering, we propose to file a registration statement to register any of our securities under the Securities Act, either for our own account or for the account of any of our stockholders, other than pursuant to the demand registration rights described above and other than pursuant to a Form S-4 or Form S-8, the holders of our registrable securities are entitled to notice of registration and, subject to specified exceptions, we will be required upon the holder’s request to use our best efforts to register their then held registrable securities.

In the event that any registration in which the holders of registrable shares participate pursuant to our investor rights agreement is an underwritten public offering, we agree to enter into an underwriting agreement containing customary representation and warranties and covenants, including without limitation customary provisions with respect to indemnification of the underwriters of such offering.

In the event that any registration in which the holders of registrable shares participate pursuant to our investor rights agreement is an underwritten public offering, we will use our best efforts to include the requested registrable shares to be included, but may be limited by market conditions.

***Expenses***

Pursuant to the investor rights agreement, we are required to pay all registration and filing fees, exchange listing fees, printing expenses, fees and expenses of one counsel to represent the selling stockholders, state Blue Sky fees and expenses, and the expense of any special audits incident to or required by any such registration, but excluding underwriting discounts, selling commissions and the fees and expenses of selling stockholders' own counsel (other than the counsel selected to represent all selling stockholders). We are not required to pay registration expenses if a demand registration request under the investor rights agreement is withdrawn at the request of holders who exercise their demand right to register the registrable securities, unless the withdrawal is due to discovery of a materially adverse change in our business.

The investor rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions in the registration statement attributable to them.

**Delaware anti-takeover law and certain charter and by-law provisions**

***Delaware law***

We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

***Staggered board; removal of directors***

Our certificate of incorporation and our bylaws that will be effective following this offering divide our board of directors into three classes with staggered three-year terms. In addition, such certificate of incorporation and bylaws provide that a director may be removed only for cause and only by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors. Under our certificate of incorporation and bylaws, any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Furthermore, our certificate of incorporation provides that the authorized number of directors may be changed only by the resolution of our board of directors.

The classification of our board of directors and the limitations on the removal of directors and filling of vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

***Super-majority voting***

The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless a corporation's certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Our by-laws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes which all our stockholders would be entitled to cast in an election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described in the prior two paragraphs.

***Stockholder action; special meeting of stockholders; advance notice requirements for stockholder proposals and director nominations***

Our certificate of incorporation and our bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our chairman of the board, our president or chief executive officer or our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock, because even if it acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

***Authorized but unissued shares***

The authorized but unissued shares of common stock and preferred stock are available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of The NASDAQ Global Market. These additional shares may be used for a variety of corporate finance transactions, acquisitions and employee benefit plans. The existence of authorized but unissued and unreserved common stock and preferred stock could make more difficult or discourage an attempt to obtain control of us by means of a proxy contest, tender offer, merger or otherwise.

**Transfer agent and registrar**

The transfer agent and registrar for our common stock will be .

**The NASDAQ Global Market**

We intend to apply to have our common stock listed on The NASDAQ Global Market under the symbol "AGIO."

## Shares eligible for future sale

Immediately prior to this offering, there was no public market for our common stock. Future sales of substantial amounts of common stock in the public market, or the perception that such sales may occur, could adversely affect the market price of our common stock. Although we intend to apply to have our common stock listed on The NASDAQ Global Market, we cannot assure you that there will be an active public market for our common stock.

Upon the closing of this offering and the concurrent private placement to Celgene, we will have outstanding an aggregate of shares of common stock, assuming the issuance of shares of common stock offered by us in this offering and the concurrent private placement and no exercise of options after , 2013. Of these shares, all shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act, whose sales would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

The remaining shares of common stock will be "restricted securities," as that term is defined in Rule 144 under the Securities Act and will further be subject to either restrictions on transfer under the lock-up agreements described below or restrictions on transfer for a period of 180 days from the effectiveness of the registration statement of which this prospectus forms a part under stock option and restricted stock agreements entered into between us and the holders of those shares. Following the expiration of these restrictions, these shares will become eligible for public sale if they are registered under the Securities Act or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act, which are summarized below. These restricted securities are eligible for public sale only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act, which are summarized below.

In addition, of the 10,170,824 shares of our common stock that were subject to stock options outstanding as of April 30, 2013, options to purchase 5,601,371 shares of common stock were vested as of April 30, 2013 and, upon exercise, these shares will be eligible for sale subject to the lock-up agreements described below and Rules 144 and 701 under the Securities Act.

### Lock-up agreements

We and each of our directors and executive officers and holders of substantially all of our outstanding capital stock, who collectively own shares of our common stock, based on shares outstanding as of April 30, 2013, have agreed that, without the prior written consent of J.P. Morgan Securities LLC and Goldman, Sachs & Co. on behalf of the underwriters, we and they will not, subject to limited exceptions, during the period ending 180 days after the date of this prospectus, subject to extension in specified circumstances:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock, or publicly disclose the intention to make any offer, sale, pledge or disposition; or
- enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities,

whether any transaction described above is to be settled by delivery of our common stock or such other securities, in cash or otherwise.

These agreements are subject to certain exceptions, and also subject to extensions for up to an additional 34 days, as described in the section of this prospectus entitled "Underwriting."

Upon the expiration of the applicable lock-up periods, substantially all of the shares subject to such lock-up restrictions will become eligible for sale, subject to the limitations discussed above.

**Rule 144**

***Affiliate resales of restricted securities***

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned shares of our common stock for at least six months would be entitled to sell in "broker's transactions" or certain "riskless principal transactions" or to market makers, a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately shares immediately after this offering and the concurrent private placement; or
- the average weekly trading volume in our common stock on The NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of $50,000, the seller must file a notice on Form 144 with the Securities and Exchange Commission and NASDAQ concurrently with either the placing of a sale order with the broker or the execution directly with a market maker.

***Non-affiliate resales of restricted securities***

In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the 90 days preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

**Rule 701**

In general, under Rule 701, any of an issuer's employees, directors, officers, consultants or advisors who purchases shares from the issuer in connection with a compensatory stock or option plan or other written agreement before the effective date of a registration statement under the Securities Act is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

The Securities and Exchange Commission has indicated that Rule 701 will apply to typical stock options granted by an issuer before it becomes subject to the reporting requirements of the Exchange Act, along with the shares acquired upon exercise of such options, including exercises after an issuer becomes subject to the reporting requirements of the Exchange Act.

**Equity plans**

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all shares of common stock subject to outstanding stock options and common stock issued or issuable under our stock plans. We expect to file the registration statement covering shares offered pursuant to our stock plans shortly

after the date of this prospectus, permitting the resale of such shares by nonaffiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market, subject to compliance with the resale provisions of Rule 144.

**Registration rights**

Upon the closing of this offering and the concurrent private placement, the holders of 54,261,829 shares of common stock or their transferees will be entitled to various rights with respect to the registration of these shares under the Securities Act. In addition, Celgene will also have the same registration rights with respect to shares acquired in the concurrent private placement. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, except for shares purchased by affiliates. See “Description of Capital Stock—Registration Rights” for additional information. Shares covered by a registration statement will be eligible for sale in the public market upon the expiration or release from the terms of the lock-up agreement.

**Material U.S. tax considerations for non-U.S. holders of common stock**

The following is a general discussion of material U.S. federal income and estate tax considerations relating to the ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term "non-U.S. holder" means a beneficial owner of our common stock that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or of any political subdivision of the United States;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or if the trust has a valid election to be treated as a U.S. person under applicable U.S. Treasury Regulations.

An individual may be treated as a resident instead of a nonresident of the United States in any calendar year for U.S. federal income tax purposes if the individual was present in the United States for at least 31 days in that calendar year and for an aggregate of at least 183 days during the three-year period ending with the current calendar year. For purposes of this calculation, all of the days present in the current year, one-third of the days present in the immediately preceding year and one-sixth of the days present in the second preceding year are counted. Residents are taxed for U.S. federal income tax purposes as if they were U.S. citizens.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. In addition, the Internal Revenue Service, or the IRS, could challenge one or more of the tax consequences described in this prospectus.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment). This discussion does not address all aspects of U.S. federal income and estate taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances nor does it address any aspects of U.S. state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as:

- insurance companies;
- tax-exempt organizations;
- financial institutions;
- brokers or dealers in securities;
- regulated investment companies;
- pension plans;
- controlled foreign corporations;
- passive foreign investment companies;
- owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment; and
- certain U.S. expatriates.

In addition, this discussion does not address the tax treatment of partnerships or persons who hold their common stock through partnerships or other entities that are pass-through entities for U.S. federal income tax purposes. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

**Prospective investors should consult their own tax advisors regarding the U.S. federal, state, local and non-U.S. income and other tax considerations of acquiring, holding and disposing of our common stock.**

**Dividends**

If we pay distributions on our common stock, those distributions generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading "Gain on Disposition of Common Stock." Any such distribution made after December 31, 2013 will also be subject to the discussion below under the heading "Withholding and Information Reporting Requirements—FATCA."

Dividends paid to a non-U.S. holder generally will be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence. If we determine, at a time reasonably close to the date of payment of a distribution on our common stock, that the distribution will not constitute a dividend because we do not anticipate having current or accumulated earnings and profits, we intend not to treat such distribution as subject to withholding of any U.S. federal income tax as permitted by U.S. Treasury Regulations.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States, and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States, are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same graduated U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN (or successor form) and satisfy applicable certification and other requirements. Non-U.S holders are urged to consult their own tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim with the IRS.

**Gain on disposition of common stock**

A non-U.S. holder generally will not be subject to U.S. federal income tax on gain recognized on a disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States, and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States; in these cases, the non-

U.S. holder will be taxed on a net income basis at the regular graduated rates and in the manner applicable to U.S. persons, and, if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a rate of 30%, or a lower rate as may be specified by an applicable income tax treaty, may also apply;

- the non-U.S. holder is an individual present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the net gain derived from the disposition, which may be offset by U.S.—source capital losses of the non-U.S. holder, if any; or
- we are or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation" unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, during the shorter of the 5-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. Generally, a corporation is a "U.S. real property holding corporation" if the fair market value of its "U.S. real property interests" equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we believe that we are not currently, and we do not anticipate becoming, a "U.S. real property holding corporation" for U.S. federal income tax purposes. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rule described above.

**Information reporting and backup withholding**

The gross amount of the distributions on our common stock paid to each non-U.S. holder and the tax withheld, if any, with respect to such distributions must be reported annually to the IRS. Non-U.S. holders may have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate, currently 28%, with respect to dividends on our common stock. Generally, a holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN (or other applicable Form W-8) or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under the heading "Dividends," will generally be exempt from backup withholding.

Information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker. Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

**Withholding and information reporting requirements—FATCA**

Recently enacted legislation (commonly referred to as "FATCA") will impose U.S. federal withholding tax of 30% on payments of dividends on, and gross proceeds from the sale or disposition of, our common stock if paid

to a foreign entity unless (i) in the case of a foreign entity that is a "foreign financial institution" (as defined under FATCA), the foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) in the case of a foreign entity that is not a foreign financial institution, the foreign entity identifies certain of its U.S. investors, or (iii) the foreign entity is otherwise exempt under FATCA. Although this legislation is effective with respect to amounts paid after December 31, 2012, under applicable U.S. Treasury Regulations, withholding under FATCA will only apply (1) to payments of dividends on our common stock made after December 31, 2013 and (2) to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2016. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of such taxes.

Prospective investors should consult their own tax advisors regarding the possible impact of the FATCA rules on their investment in our common stock and on the entities through which they hold our common stock including, without limitation, the process and deadlines for meeting the applicable requirements to prevent the imposition of the 30% withholding tax under FATCA.

**Federal estate tax**

Common stock owned or treated as owned by an individual (including by reason of holding interests in certain entities) who is a non-U.S. holder (as specially defined for U.S. federal estate tax purposes) at the time of death will be included in the individual's gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

**The preceding discussion of material U.S. federal tax considerations is for general information only. It is not tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.**

## Underwriting

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC and Goldman, Sachs & Co. are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

| Name | Number of shares |
|---|---|
| J.P. Morgan Securities LLC | |
| Goldman, Sachs & Co. | |
| Cowen and Company, LLC | |
| Leerink Swann LLC | |
| Total | |

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $ per share. After the initial public offering of the shares, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters. The representatives have advised us that the underwriters do not intend to confirm discretionary sales in excess of 5% of the common shares offered in this offering. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

The underwriters have an option to buy up to additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this over-allotment option. If any shares are purchased with this over-allotment option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is $ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

| | Without over-allotment exercise | With full over-allotment exercise |
|---|---|---|
| Per Share | $ | $ |
| Total | $ | $ |

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $ .

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of, directly or indirectly, or file with the Securities and Exchange Commission a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of our common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of our common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC and Goldman, Sachs & Co. for a period of 180 days after the date of this prospectus, other than (A) the shares of our common stock to be sold hereunder, (B) any shares of our common stock issued upon the exercise of options granted under company stock plans or warrants described as outstanding in this prospectus, (C) any options and other awards granted under company stock plans, (D) our filing of a registration statement on Form S-8 or a successor form thereto relating to the shares of our common stock granted pursuant to or reserved for issuance under company stock plans and (E) shares of our common stock or other securities issued in connection with a transaction that includes a commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or not less than a majority or controlling portion of the equity of another entity; provided that the aggregate number of shares of our common stock issued pursuant to clause (E) shall not exceed 5.0% of the total number of outstanding shares of our common stock immediately following the issuance and sale of the underwritten shares pursuant to the underwriting agreement; provided, further, the recipient of any such shares of our common stock and securities issued pursuant to clauses (B), (C) or (E) during the 180-day restricted period described above shall enter into an agreement substantially in the form described below. Notwithstanding the foregoing, if (1) during the last 17 days of the 180-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (2) prior to the expiration of the 180-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 180-day restricted period, the restrictions described above shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

Our directors and executive officers, and substantially all of our shareholders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, for a period of 180 days after the date of this prospectus, may not, without the prior written consent of J.P. Morgan Securities LLC and Goldman, Sachs & Co., (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, officers and shareholders in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), or publicly disclose the intention to make any offer, sale, pledge or disposition, (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of our common stock or such other securities, in cash or otherwise or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock, in each case subject to certain exceptions, including (A) transfers of shares of our common stock or other securities as

bona fide gifts, (B) transfers or dispositions of shares of our common stock or other securities to any trust for the direct or indirect benefit of the director, officer or shareholder or the immediate family of such person in a transaction not involving a disposition for value, (C) transfers or dispositions of shares of our common stock or other securities to any corporation, partnership, limited liability company or other entity all of the beneficial ownership interests of which are held by the director, officer or shareholder or the immediate family of such person in a transaction not involving a disposition for value, (D) transfers or dispositions of shares of our common stock or other securities by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the director, officer or shareholder, and (E) distributions of shares of our common stock or other securities to partners, members or stockholders of the shareholder. In the case of any transfer, disposition or distribution pursuant to clause (A), (B), (C), (D) or (E), each transferee, donee or distributee must execute and deliver to J.P. Morgan Securities LLC and Goldman, Sachs & Co. a lock-up agreement. In addition, in the case of any transfer, disposition or distribution pursuant to clause (A), (B), (C), (D) or (E), no filing by any party under the Exchange Act, or other public announcement may be required or voluntarily made in connection with such transfer, disposition or distribution, other than a filing on a Form 5 made after the expiration of the 180-day restricted period referred to above. In addition, notwithstanding the foregoing restrictions, the director, officer or shareholder may (i) transfer such person's shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock to us pursuant to any contractual arrangement in effect on the date of the lock-up agreement that provides for the repurchase of such person's common stock or such other securities by us or in connection with such person's termination of employment with us, provided that no filing by any party under the Exchange Act, or other public announcement may be required or voluntarily made in connection with such transfer, other than a filing on a Form 5 made after the expiration of the 180-day restricted period referred to above, (ii) establish a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of common stock, provided that such plan does not provide for any transfers of common stock, and no filing with the SEC or other public announcement shall be required or voluntarily made by the director, officer or shareholder or any other person in connection therewith, in each case during the 180-day restricted period or any extension thereof pursuant to the lock-up agreement, and (iii) transfer or dispose of shares of our common stock on the open market following the offering, provided that no filing by any party under the Exchange Act, or other public announcement reporting a reduction in the beneficial ownership of common stock held by the director, officer or shareholder may be required or voluntarily made in connection with such transfer, other than a filing on a Form 5 made after the expiration of the 180-day restricted period referred to above. Notwithstanding the foregoing, if (1) during the last 17 days of the 180-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (2) prior to the expiration of the 180-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 180-day restricted period, the restrictions described above shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

We intend to apply to have our common stock approved for listing on The NASDAQ Global Market under the symbol "AGIO."

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be "covered" shorts, which are short positions in an amount not greater than the underwriters' over-allotment option referred to above, or may be "naked" shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their over-allotment option, in whole or in part, or

by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the over-allotment option. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The NASDAQ Global Market, in the over-the-counter market or otherwise.

Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters expect to consider a number of factors including:

- the information set forth in this prospectus and otherwise available to the representatives;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our shares of common stock, or that the shares will trade in the public market at or above the initial public offering price.

The underwriters and their respective affiliates are full-service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, in the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to our assets, securities and/or instruments (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with us. The underwriters and their respective affiliates may also communicate independent investment recommendations,

market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

**Selling restrictions**

***General***

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

***United Kingdom***

Each underwriter has represented and agreed that:

(1) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) received by it in connection with the issue or sale of our common shares in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(2) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to our common shares in, from or otherwise involving the United Kingdom.

***European Economic Area***

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), an offer to the public of any shares which are the subject of the offering contemplated by this prospectus (the "Shares") may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any Shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(1) to any legal entity which is a qualified investor as defined in the Prospectus Directive;

(2) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or

(3) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of Shares shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any Shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the

terms of the offer and any Shares to be offered so as to enable an investor to decide to purchase any Shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

***Hong Kong***

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap.571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap.32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

***Singapore***

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

***Japan***

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

## Legal matters

The validity of the shares of common stock offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Davis Polk & Wardwell LLP, New York, New York, has acted as counsel for the underwriters in connection with certain legal matters related to this offering.

## Experts

Our consolidated financial statements as of December 31, 2011 and 2012, and for the years then ended, appearing in this prospectus and the related registration statement have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance on such report given on the authority of such firm as experts in accounting and auditing.

## Where you can find more information

We have filed with the Securities and Exchange Commission a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information about us and the common stock offered hereby, we refer you to the registration statement and the exhibits and schedules filed thereto. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. Upon completion of this offering, we will be required to file periodic reports, proxy statements, and other information with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934. You may read and copy this information at the Public Reference Room of the Securities and Exchange Commission, 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You may obtain information on the operation of the public reference rooms by calling the Securities and Exchange Commission at 1-800-SEC-0330. The Securities and Exchange Commission also maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the Securities and Exchange Commission. The address of that site is *www.sec.gov*.

Agios Pharmaceuticals, Inc.

Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
Agios Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Agios Pharmaceuticals, Inc. (the "Company") as of December 31, 2011 and 2012, and the related consolidated statements of operations, comprehensive loss, convertible preferred stock and stockholders' deficit, and cash flows for the years then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Agios Pharmaceuticals, Inc. at December 31, 2011 and 2012, and the consolidated results of its operations and its cash flows for the years then ended in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, Massachusetts
May 23, 2013

Agios Pharmaceuticals, Inc.

Consolidated Balance Sheets
(in thousands, except share and per share data)

| | December 31, 2011 | December 31, 2012 | March 31, 2013 | Pro forma March 31, 2013 |
|---|---|---|---|---|
| | | | (unaudited) | |
| **Assets** | | | | |
| Current assets: | | | | |
| Cash and cash equivalents | $117,661 | $ 91,297 | $ 83,377 | $ 83,377 |
| Marketable securities | 61,507 | 36,679 | 32,374 | 32,374 |
| Prepaid expenses and other current assets | 794 | 922 | 1,350 | 1,350 |
| Deferred tax assets | 10,623 | 1,246 | 1,246 | 1,246 |
| Total current assets | 190,585 | 130,144 | 118,347 | 118,347 |
| Property and equipment, net | 3,222 | 3,565 | 4,092 | 4,092 |
| Restricted cash | 571 | 571 | 571 | 571 |
| Deferred tax assets, net of current portion | 37 | 2,706 | 2,706 | 2,706 |
| Other assets | 55 | 22 | 137 | 137 |
| Total assets | $194,470 | $137,008 | $ 125,853 | $ 125,853 |
| **Liabilities, convertible preferred stock, and stockholders' (deficit) equity** | | | | |
| Current liabilities: | | | | |
| Accounts payable | $ 3,573 | $ 3,308 | $ 4,737 | $ 4,737 |
| Accrued expenses | 1,545 | 1,708 | 2,026 | 2,026 |
| Income taxes payable | 17,867 | 4,875 | 5,051 | 5,051 |
| Deferred revenue | 25,072 | 25,072 | 25,072 | 25,072 |
| Deferred rent | 46 | 85 | 94 | 94 |
| Restricted stock liability | 55 | 65 | 51 | 51 |
| Total current liabilities | 48,158 | 35,113 | 37,031 | 37,031 |
| Deferred revenue, net of current portion | 82,711 | 57,639 | 51,371 | 51,371 |
| Deferred rent, net of current portion | 428 | 343 | 318 | 318 |
| Restricted stock liability, net of current portion | 33 | 15 | 13 | 13 |
| Commitments and contingencies *(Note 6)* | | | | |
| Series A convertible preferred stock, $0.001 par value; 33,188,889 shares authorized, issued and outstanding at December 31, 2011 and 2012, and March 31, 2013 (unaudited) and no shares issued and outstanding pro forma (unaudited) *(Note 7); aggregate liquidation preference of $40,973 and $41,471 at December 31, 2012 and March 31, 2013 (unaudited), respectively* | 32,940 | 32,940 | 32,940 | — |
| Series B convertible preferred stock, $0.001 par value; 5,190,551 shares authorized, issued and outstanding at December 31, 2011 and 2012, and March 31, 2013 (unaudited) and no shares issued and outstanding pro forma (unaudited) (*Note 7); aggregate liquidation preference of $10,232 and $10,362 at December 31, 2012 and March 31, 2013 (unaudited), respectively* | 5,681 | 5,681 | 5,681 | — |
| Series C convertible preferred stock, $0.001 par value; 15,882,389 shares authorized, issued and outstanding at December 31, 2011 and 2012, and March 31, 2013 (unaudited) and no shares issued and outstanding pro forma (unaudited) *(Note 7); aggregate liquidation preference of $83,252 and $84,422 at December 31, 2012 and March 31, 2013 (unaudited), respectively* | 77,301 | 77,301 | 77,301 | — |
| Stockholders' (deficit) equity: | | | | |
| Common stock, $0.001 par value; 75,000,000, 78,300,000, and 78,300,000 shares authorized at December 31, 2011 and 2012, and March 31, 2013 (unaudited), respectively, and 8,792,906 , 9,944,278, and 10,124,595 shares issued and outstanding at December 31, 2011 and 2012, and March 31, 2013 (unaudited) respectively, and 64,386,424 shares issued and outstanding pro forma (unaudited) | 9 | 10 | 10 | 64 |
| Additional paid-in capital | 1,121 | 2,005 | 2,454 | 118,322 |
| Accumulated other comprehensive income (loss) | 23 | (2) | (1) | (1) |
| Accumulated deficit | (53,935) | (74,037) | (81,265) | (81,265) |
| Total stockholders' (deficit) equity | (52,782) | (72,024) | (78,802) | 37,120 |
| Total liabilities, convertible preferred stock, and stockholders' (deficit) equity | $194,470 | $137,008 | $ 125,853 | $ 125,853 |

*See accompanying notes.*

Agios Pharmaceuticals, Inc.

Consolidated Statements of Operations
(in thousands, except share and per share data)

| | Years Ended December 31, | | Three Months Ended March 31, | |
|---|---|---|---|---|
| | 2011 | 2012 | 2012 | 2013 |
| | | | (unaudited) | |
| Collaboration revenue | $ 21,803 | $ 25,072 | $ 6,268 | $ 6,268 |
| Grant revenue | 34 | 34 | — | — |
| Total revenue | 21,837 | 25,106 | 6,268 | 6,268 |
| Operating expenses: | | | | |
| Research and development | 31,253 | 41,037 | 9,551 | 11,462 |
| General and administrative | 7,215 | 7,064 | 1,981 | 1,852 |
| Total operating expenses | 38,468 | 48,101 | 11,532 | 13,314 |
| Loss from operations | (16,631) | (22,995) | (5,264) | (7,046) |
| Interest income | 132 | 69 | 26 | 8 |
| Loss before provision (benefit) for income taxes | (16,499) | (22,926) | (5,238) | (7,038) |
| Provision (benefit) for income taxes | 7,207 | (2,824) | (607) | 190 |
| Net loss | (23,706) | (20,102) | (4,631) | (7,228) |
| Cumulative preferred stock dividends | (3,100) | (7,190) | (1,798) | (1,798) |
| Net loss applicable to common stockholders | $ (26,806) | $ (27,292) | $ (6,429) | $ (9,026) |
| Net loss per share applicable to common stockholders – basic and diluted | $ (3.23) | $ (2.92) | $ (0.72) | $ (0.90) |
| Weighted-average number of common shares used in net loss per share applicable to common stockholders – basic and diluted | 8,286,757 | 9,354,729 | 8,928,822 | 10,059,545 |
| Pro forma net loss per share applicable to common stockholders – basic and diluted (unaudited) | | $ (0.43) | | $ (0.14) |
| Pro forma weighted average number of common shares used in net loss per share applicable to common stockholders – basic and diluted (unaudited) | | 63,616,558 | | 64,321,374 |

*See accompanying notes.*

Agios Pharmaceuticals, Inc.

Consolidated Statements of Comprehensive Loss
(in thousands)

| | Years Ended December 31, | | Three Months Ended March 31, | |
|---|---|---|---|---|
| | 2011 | 2012 | 2012 | 2013 |
| | | | (unaudited) | |
| Net loss | $(23,706) | $(20,102) | $(4,631) | $(7,228) |
| Other comprehensive income (loss): | | | | |
| Unrealized gain (loss) on available-for-sale securities | 31 | (25) | (2) | (1) |
| Comprehensive loss | $(23,675) | $(20,127) | $(4,633) | $(7,229) |

*See accompanying notes.*

Agios Pharmaceuticals, Inc.

Consolidated Statements of Convertible Preferred Stock and Stockholders' (Deficit) Equity
(in thousands, except share amounts)

| | Series A Convertible Preferred Stock | | Series B Convertible Preferred Stock | | Series C Convertible Preferred Stock | | Common Stock | | Additional Paid-In Capital | Accumulated Other Comprehensive (Loss) Income | Accumulated Deficit | Total Stockholders' (Deficit) Equity |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | Shares | Amount | Shares | Amount | | | | |
| Balance at December 31, 2010 | 33,188,889 | 32,940 | 5,190,551 | 5,681 | — | — | 7,804,411 | 8 | 638 | (8) | (30,229) | (29,591) |
| Unrealized gain on marketable securities | — | — | — | — | — | — | — | — | — | 31 | — | 31 |
| Net loss | — | — | — | — | — | — | — | — | — | — | (23,706) | (23,706) |
| Issuance of series C convertible preferred stock, net of issuance costs of $698.7 | — | — | — | — | 15,882,389 | 77,301 | — | — | — | — | — | — |
| Stock-based compensation expense | — | — | — | — | — | — | — | — | 371 | — | — | 371 |
| Vesting of restricted stock | — | — | — | — | — | — | 500,000 | 1 | 55 | — | — | 56 |
| Issuance of common stock upon exercise of stock options | — | — | — | — | — | — | 488,495 | — | 57 | — | — | 57 |
| Balance at December 31, 2011 | 33,188,889 | $ 32,940 | 5,190,551 | $ 5,681 | 15,882,389 | $ 77,301 | 8,792,906 | $ 9 | $ 1,121 | $ 23 | $ (53,935) | $ (52,782) |
| Unrealized loss on marketable securities | — | — | — | — | — | — | — | — | — | (25) | — | (25) |
| Net loss | — | — | — | — | — | — | — | — | — | — | (20,102) | (20,102) |
| Stock-based compensation expense | — | — | — | — | — | — | — | — | 742 | — | — | 742 |
| Vesting of restricted stock | — | — | — | — | — | — | 505,208 | — | 56 | — | — | 56 |
| Issuance of common stock upon exercise of stock options | — | — | — | — | — | — | 646,164 | 1 | 86 | — | — | 87 |
| Balance at December 31, 2012 | 33,188,889 | $ 32,940 | 5,190,551 | $ 5,681 | 15,882,389 | $ 77,301 | 9,944,278 | $ 10 | $ 2,005 | $ (2) | $ (74,037) | $ (72,024) |
| Unrealized gain on marketable securities (unaudited) | — | — | — | — | — | — | — | — | — | 1 | — | 1 |
| Net loss (unaudited) | — | — | — | — | — | — | — | — | — | — | (7,228) | (7,228) |
| Stock-based compensation expense (unaudited) | — | — | — | — | — | — | — | — | 424 | — | — | 424 |
| Vesting of restricted stock (unaudited) | — | — | — | — | — | — | 137,500 | — | 16 | — | — | 16 |
| Issuance of common stock upon exercise of stock options (unaudited) | — | — | — | — | — | — | 42,817 | — | 9 | — | — | 9 |
| Balance at March 31, 2013 (unaudited) | **33,188,889** | **$ 32,940** | **5,190,551** | **$ 5,681** | **15,882,389** | **$ 77,301** | **10,124,595** | **$ 10** | **$ 2,454** | **$ (1)** | **$ (81,265)** | **$ (78,802)** |
| Conversion of convertible preferred stock into common stock (unaudited) | (33,188,889) | $(32,940) | (5,191,551) | $ (5,681) | (15,882,389) | $(77,301) | 54,261,829 | $ 54 | $ 115,868 | | | $ 115,922 |
| Pro forma balance at March 31, 2013 (unaudited) | **—** | **$ —** | **—** | **$ —** | **—** | **$ —** | **64,386,424** | **$ 64** | **$ 118,322** | **$ (1)** | **$ (81,265)** | **$ 37,120** |

*See accompanying notes.*

Agios Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows
(in thousands)

| | Years Ended December 31, | | Three Months Ended March 31, | |
|---|---|---|---|---|
| | 2011 | 2012 | 2012 | 2013 |
| | | | (unaudited) | |
| **Operating activities** | | | | |
| Net loss | $ (23,706) | $ (20,102) | $ (4,631) | $ (7,228) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | | |
| Depreciation | 801 | 1,179 | 264 | 349 |
| Net loss on disposal of fixed assets | — | 10 | — | — |
| Stock-based compensation expense | 371 | 742 | 98 | 424 |
| Deferred rent | 243 | (46) | (5) | (15) |
| Deferred taxes | (10,660) | 6,707 | 1,505 | — |
| Amortization (accretion) of premium (discount) on investments | 391 | 287 | 88 | (5) |
| Changes in operating assets and liabilities: | | | | |
| Prepaid expenses and other assets | (63) | (94) | (172) | (544) |
| Accounts payable | 809 | (322) | (1,457) | 829 |
| Accrued expenses and other liabilities | 525 | 156 | 189 | 301 |
| Income taxes payable | 17,867 | (12,993) | (5,585) | 176 |
| Deferred revenue | (1,797) | (25,072) | (6,268) | (6,268) |
| Net cash used in operating activities | (15,219) | (49,548) | (15,974) | (11,981) |
| **Investing activities** | | | | |
| Purchases of marketable securities | (105,936) | (88,524) | (26,394) | (15,915) |
| Proceeds from maturities and sales of marketable securities | 85,482 | 113,041 | 36,804 | 20,226 |
| Purchases of property and equipment | (1,906) | (1,475) | (21) | (275) |
| Net cash (used in) provided by investing activities | (22,360) | 23,042 | 10,389 | 4,036 |
| **Financing activities** | | | | |
| Net proceeds from issuance of Series C convertible preferred stock | 77,301 | — | — | — |
| Net proceeds from stock option exercises and issuance of common and restricted common stock | 57 | 142 | 38 | 25 |
| Net cash provided by financing activities | 77,358 | 142 | 38 | 25 |
| Net increase (decrease) in cash and cash equivalents | 39,779 | (26,364) | (5,547) | (7,920) |
| Cash and cash equivalents at beginning of the period | 77,882 | 117,661 | 117,661 | 91,297 |
| Cash and cash equivalents at end of the period | $ 117,661 | $ 91,297 | $ 112,114 | $ 83,377 |
| **Supplemental cash flow information** | | | | |
| Cash paid for income taxes | $ — | $ 3,549 | $ 3,500 | $ — |

*See accompanying notes.*

Agios Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

*Information as of March 31, 2013 and for the three months ended March 31, 2012 and 2013 is unaudited.*

**1. Nature of Business**

Agios Pharmaceuticals, Inc. (“Agios” or “the Company”) is a biopharmaceutical company committed to the fundamental transformation of patients’ lives through scientific leadership in the field of cancer metabolism and inborn errors of metabolism. The Company has built a unique set of core capabilities in the field of cellular metabolism, with the goal of making transformative, first or best in class medicines. The Company’s therapeutic areas of focus are cancer and inborn errors of metabolism, which are a broad group of more than 600 rare genetic diseases caused by mutations, or defects, of single metabolic genes. In both of these areas, the Company is seeking to unlock the biology of cellular metabolism to create transformative therapies. The Company was incorporated in Delaware on August 7, 2007, and is located in Cambridge, Massachusetts.

***Liquidity***

The Company has an accumulated deficit as of December 31, 2012 of approximately $74.0 million and will require substantial additional capital for research and product development. The future success of the Company is dependent on its ability to develop its product candidates and ultimately upon its ability to attain profitable operations. The Company is subject to a number of risks similar to other life science companies, including, but not limited to, successful discovery and development of its drug candidates, raising additional capital, development by its competitors of new technological innovations, protection of proprietary technology and market acceptance of the Company’s products. At December 31, 2012, the Company believes its cash, cash equivalents and marketable securities, totaling approximately $128.0 million, are sufficient to fund operations for a period of at least 12 months from the balance sheet date.

**2. Summary of Significant Accounting Policies**

***Principles of Consolidation***

The Company’s consolidated financial statements include the Company’s accounts and the accounts of the Company’s wholly owned subsidiary, Agios Securities Corporation. All intercompany transactions have been eliminated in consolidation. The consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States (“GAAP”).

***Unaudited Interim Financial Statements***

The unaudited interim financial statements as of March 31, 2013 and for the three months ended March 31, 2012 and 2013 and the related interim information contained within the notes to the consolidated financial statements are unaudited. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to present fairly the Company’s consolidated financial position as of March 31, 2013 and its results of operations and cash flows for the three months ended March 31, 2012 and 2013. The consolidated results of operations and cash flows for the three months ended March 31, 2013 are not necessarily indicative of the results to be expected for the year ending December 31, 2013 or for any other future annual or interim period.

***Unaudited Pro Forma Financial Information***

On May 20, 2013, the Company's board of directors authorized the management of the Company to submit on a confidential basis a registration statement with the Securities and Exchange Commission ("SEC") for the Company to sell shares of its common stock (the "Common Stock") to the public. Upon the closing of a qualified initial public offering, all of the Company's outstanding convertible preferred stock will automatically convert into Common Stock. The unaudited pro forma consolidated balance sheet and statement of convertible preferred stock and stockholders' equity as of March 31, 2013 assumes the conversion of all outstanding convertible preferred stock into shares of Common Stock upon the completion of this proposed offering.

Unaudited pro forma net loss per share applicable to common stockholders is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all convertible preferred stock into shares of the Common Stock as if such conversion had occurred at the beginning of the period presented, or the date of original issuance, if later. Accordingly, the pro forma basic and diluted net loss per share attributable to common stockholders does not include the effects of the cumulative preferred stock dividends.

***Use of Estimates***

The preparation of financial statements in conformity with U.S. generally accepted accounting principles requires the Company's management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results could differ from those estimates.

The Company utilizes significant estimates and assumptions in determining the fair value of its Common Stock. The board of directors determined the estimated fair value of the Company's Common Stock based on a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector and the prices at which the Company sold shares of convertible preferred stock, the superior rights and preferences of securities senior to the Company's Common Stock at the time and the likelihood of achieving a liquidity event, such as an initial public offering or sale of the Company.

The Company utilized various valuation methodologies in accordance with the framework of the American Institute of Certified Public Accountants, or AICPA, *Audit and Accounting Practice Aid Series: Valuation of Privately Held Company Equity Securities Issued as Compensation*, or the AICPA Practice Aid, to estimate the fair value of its common stock and in performing retrospective valuation analyses for certain grant dates in 2012. The methodologies included the Option Pricing Method utilizing the Backsolve Method (a form of the market approach defined in the AICPA Practice Aid) and the Probability-Weighted Expected Return Method based upon the probability of occurrence of certain future liquidity events such as an initial public offering or sale of the Company. Each valuation methodology includes estimates and assumptions that require the Company's judgment. Significant changes to the key assumptions used in the valuations could result in different fair values of Common Stock at each valuation date.

***Revenue Recognition***

The Company recognizes revenue in accordance with Accounting Standards Codification ("ASC") 605, *Revenue Recognition*. Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- Persuasive evidence of an arrangement exists,
- Delivery has occurred or services have been rendered,
- The seller's price to the buyer is fixed or determinable, and
- Collectability is reasonably assured.

The Company's revenues have been generated from a Discovery and Development Collaboration and License Agreement with Celgene Corporation ("the Celgene Agreement") and from research grant agreements. Revenue related to research grant agreements is recognized as the underlying services are performed.

For multiple-element arrangements entered into prior to January 1, 2011 and not materially modified thereafter, the Company continues to apply its prior accounting policy with respect to such arrangements. Under this policy, when evaluating multiple element arrangements, the Company considers whether the components of the arrangement should be accounted for individually as separate units of accounting if (1) the elements have stand-alone value, and (2) the Company is able to estimate the fair value of all undelivered elements under the arrangement.

In January 2011, the Company adopted the Financial Accounting Standards Board's ("FASB") Accounting Standards Update ("ASU") No. 2009-13, *Multiple-Element Revenue Arrangements*, on a prospective basis for all revenue arrangements entered into or materially modified after the adoption date. The Celgene Agreement was entered into prior to the effective date of this ASU and has not been materially modified, and is therefore not subject to this ASU.

Pursuant to ASU 2009-13, revenue arrangements where multiple products or services are sold together are evaluated to determine if each deliverable represents a separate unit of accounting based on the following criteria:

- Delivered item or items have value to the customer on a standalone basis, and
- If the arrangement includes a general right of return relative to the delivered item or items, delivery or performance of the undelivered item or items is considered probable and substantially in the control of the vendor.

The arrangement consideration is then allocated to each separately identified unit of accounting based on the relative selling price of each deliverable. The provisions of ASC 605-25, *Multiple-Element Arrangements* are then applied to each unit of accounting to determine the appropriate revenue recognition. In the event that a deliverable of a multiple element arrangement does not represent a separate unit of accounting, the Company recognizes revenue from the combined unit of accounting over the term of the related contract or as undelivered items are delivered, as appropriate.

In January 2011, the Company adopted the FASB's ASU No. 2010-17, *Revenue Recognition – Milestone Method*, on a prospective basis. ASU 2010-17 provides guidance in applying the milestone method of revenue recognition to research or development arrangements. Under this guidance, management may recognize revenue contingent upon the achievement of a milestone in its entirety in the period in which the milestone is achieved, only if the milestone meets all the criteria within the guidance to be considered substantive. In accordance with ASU 2010-17, at the inception of each arrangement that includes milestone payments, the Company evaluates each contingent payment on an individual basis to determine whether they are considered substantive milestones, specifically reviewing factors such as the degree of certainty in achieving the milestone, the research and development risk and other risks that must be overcome to achieve the milestone, as well as the level of effort and investment required and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement.

Revenues from milestones, if they are nonrefundable and deemed substantive, are recognized upon achievement of the milestones. To the extent that non-substantive milestones are achieved and the Company has remaining performance obligations, milestones are deferred and recognized as revenue over the estimated remaining performance period. The Company recognizes revenue associated with the non-substantive milestones upon achievement of the milestone if there are no undelivered elements and the Company has no remaining performance obligations.

***Research and Development Costs***

Research and development costs are expensed as incurred. Research and development costs include salaries and personnel-related costs, consulting fees, fees paid for contract research services, the costs of laboratory equipment and facilities, and other external costs.

Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

***Stock-Based Compensation***

The Company accounts for its stock-based compensation awards in accordance with ASC Topic 718, *Compensation – Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees, including grants of employee stock options, to be recognized in the consolidated statements of operations based on their grant date fair values. For stock options granted to employees and to members of the board of directors for their services on the board of directors, the Company estimates the grant date fair value of each option award using the Black-Scholes option-pricing model. The use of the Black-Scholes option-pricing model requires management to make assumptions with respect to the expected term of the option, the expected volatility of the common stock consistent with the expected life of the option, risk-free interest rates and expected dividend yields of the common stock. For awards subject to service-based vesting conditions, the Company recognizes stock-based compensation expense, net of estimated forfeitures, equal to the grant date fair value of stock options on a straight-line basis over the requisite service period. For awards subject to both performance and service-based vesting conditions, the Company recognizes stock-based compensation expense using an accelerated recognition method.

Share-based payments issued to non-employees are recorded at their fair values, and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period in accordance with the provisions of ASC 718 and ASC Topic 505, *Equity*. For equity instruments granted to non-employees, the Company recognizes stock-based compensation expense using an accelerated recognition method.

During the years ended December 31, 2011 and 2012, and the three months ended March 31, 2012 and 2013, the Company recorded stock-based compensation expense for employee and non-employee stock options and restricted stock, which was allocated as follows in the consolidated statements of operations (in thousands):

| | Years Ended December 31, | | Three Months Ended March 31, | |
|---|---|---|---|---|
| | 2011 | 2012 | 2012 | 2013 |
| Research and development expense | $253 | $605 | $ 66 | $ 287 |
| General and administrative expense | 118 | 137 | 32 | 137 |
| | $371 | $742 | $ 98 | $ 424 |

No related tax benefits were recognized for the years ended December 31, 2011 and 2012 or for the three months ended March 31, 2012 and 2013.

***Income Taxes***

Income taxes are recorded in accordance with ASC 740, *Accounting for Income Taxes ("ASC 740")*, which provides for deferred taxes using an asset and liability approach. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. The Company determines its deferred tax assets and liabilities based on differences between financial reporting and tax bases of assets and liabilities, which are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. Valuation allowances are provided, if based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2011 and 2012 and March 31, 2013, the Company does not have any significant uncertain tax positions.

***Comprehensive Income (Loss)***

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions, and other events and circumstances from non-owner sources, and currently consists of net loss and changes in unrealized gains and losses on available-for-sale securities.

***Cash and Cash Equivalents***

The Company considers highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. Cash equivalents, which consist primarily of money market funds, are stated at fair value.

***Marketable Securities***

Marketable securities at December 31, 2012 and March 31, 2013 consisted primarily of investments in U.S. Treasuries. Marketable securities at December 31, 2011 consisted primarily of investments in U.S. Treasuries and corporate debt. Management determines the appropriate classification of the securities at the time they are acquired and evaluates the appropriateness of such classifications at each balance sheet date. The Company classifies its marketable securities as available-for-sale pursuant to ASC 320, *Investments – Debt and Equity Securities*. Marketable securities are recorded at fair value, with unrealized gains and losses included as a component of accumulated other comprehensive income (loss) in stockholders' (deficit) equity and a component of total comprehensive loss in the consolidated statements of comprehensive loss, until realized. The fair value of these securities is based on quoted prices for identical or similar assets. Realized gains and losses are included in investment income on a specific-identification basis. There were no realized gains or losses on marketable securities for the year ended December 31, 2012 and the three months ended March 31, 2013 and 2012. The Company sold five securities during 2011 for gross proceeds of $13.0 million and recognized a gain of $1,000 for the year ended December 31, 2011.

The Company reviews marketable securities for other-than-temporary impairment whenever the fair value of a marketable security is less than the amortized cost and evidence indicates that a marketable security's carrying amount is not recoverable within a reasonable period of time. Other-than-temporary impairments of investments are recognized in the consolidated statements of operations if the Company has experienced a credit loss, has the

intent to sell the marketable security, or if it is more likely than not that the Company will be required to sell the marketable security before recovery of the amortized cost basis. Evidence considered in this assessment includes reasons for the impairment, compliance with the Company's investment policy, the severity and the duration of the impairment and changes in value subsequent to the end of the period.

Marketable securities at December 31, 2011 consist of the following (in thousands):

| | Amortized Cost | Unrealized Gains | Unrealized Losses | Fair Value |
|---|---|---|---|---|
| Corporate debt securities | $ 20,819 | $ 12 | $ (1) | $20,830 |
| Certificates of deposit | 7,714 | — | (5) | 7,709 |
| U.S. Treasuries | 32,951 | 17 | — | 32,968 |
| | $ 61,484 | $ 29 | $ (6) | $61,507 |

Marketable securities at December 31, 2012 consist of the following (in thousands):

| | Amortized Cost | Unrealized Gains | Unrealized Losses | Fair Value |
|---|---|---|---|---|
| Certificates of deposit | $ 7,386 | $ — | $ (2) | $ 7,384 |
| U.S. Treasuries | 29,294 | 1 | — | 29,295 |
| | $ 36,680 | $ 1 | $ (2) | $36,679 |

Marketable securities at March 31, 2013 consist of the following (in thousands):

| | Amortized Cost | Unrealized Gains | Unrealized Losses | Fair Value |
|---|---|---|---|---|
| Certificates of deposit | $ 3,080 | $ — | $ (1) | $ 3,079 |
| U.S. Treasuries | 29,295 | 1 | (1) | 29,295 |
| | $ 32,375 | $ 1 | $ (2) | $32,374 |

All of the investments held at December 31, 2011 and 2012 and March 31, 2013 had maturities of less than one year.

At December 31, 2011, December 31, 2012 and March 31, 2013, the Company held 35, 30, and 14 debt securities that were in an unrealized loss position for less than one year, respectively. The aggregate fair value of debt securities in an unrealized loss position at December 31, 2011, December 31, 2012 and March 31, 2013 was $18.8 million, $13.7 million and $17.6 million, respectively. There were no individual securities that were in a significant unrealized loss position as of December 31, 2011 and 2012 and March 31, 2013. The Company evaluated its securities for other-than-temporary impairment and considered the decline in market value for the securities to be primarily attributable to current economic and market conditions. It is not more likely than not that the Company will be required to sell the securities, and the Company does not intend to do so prior to the recovery of the amortized cost basis. Based on this analysis, these marketable securities were not considered to be other-than-temporarily impaired as of December 31, 2011 and 2012 and March 31, 2013.

***Concentrations of Credit Risk***

Financial instruments which potentially subject the Company to credit risk consist primarily of cash, cash equivalents and marketable securities. The Company holds these investments in highly rated financial institutions, and, by policy, limits the amounts of credit exposure to any one financial institution. These amounts at times may exceed federally insured limits. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no significant off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

***Fair Value Measurements***

The Company records cash equivalents and marketable securities at fair value. ASC Topic 820, *Fair Value Measurements and Disclosures*, establishes a fair value hierarchy for those instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own assumptions (unobservable inputs). The hierarchy consists of three levels:

*Level 1* – Unadjusted quoted prices in active markets for identical assets or liabilities.

*Level 2* – Quoted prices for similar assets and liabilities in active markets, quoted prices in markets that are not active, or inputs which are observable, either directly or indirectly, for substantially the full term of the asset or liability.

*Level 3* – Unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability in which there is little, if any, market activity for the asset or liability at the measurement date.

The following table summarizes the cash equivalents and marketable securities measured at fair value on a recurring basis as of December 31, 2011 (in thousands):

| | Level 1 | Level 2 | Level 3 | Total |
|---|---|---|---|---|
| Cash equivalents | $116,150 | $ 480 | $ — | $116,630 |
| Marketable securities: | | | | |
| Corporate debt securities | — | 20,830 | — | 20,830 |
| Certificates of deposit | — | 7,709 | — | 7,709 |
| U.S. Treasuries | 32,968 | — | — | 32,968 |
| | $149,118 | $29,019 | $ — | $178,137 |

The following table summarizes the cash equivalents and marketable securities measured at fair value on a recurring basis as of December 31, 2012 (in thousands):

| | Level 1 | Level 2 | Level 3 | Total |
|---|---|---|---|---|
| Cash equivalents | $ 89,062 | $ — | $ — | $ 89,062 |
| Marketable securities: | | | | |
| Certificates of deposit | — | 7,384 | — | 7,384 |
| U.S. Treasuries | 29,295 | — | — | 29,295 |
| | $118,357 | $7,384 | $ — | $125,741 |

The following table summarizes the cash equivalents and marketable securities measured at fair value on a recurring basis as of March 31, 2013 (in thousands):

| | Level 1 | Level 2 | Level 3 | Total |
|---|---|---|---|---|
| Cash equivalents | $ 82,417 | $ 960 | $ — | $ 83,377 |
| Marketable securities: | | | | |
| Certificates of deposit | — | 3,079 | — | 3,079 |
| U.S. Treasuries | 29,295 | — | — | 29,295 |
| | $111,712 | $4,039 | $ — | $115,751 |

Cash equivalents and marketable securities have been initially valued at the transaction price and subsequently valued, at the end of each reporting period, utilizing third party pricing services or other market observable data. The pricing services utilize industry standard valuation models, including both income and market based approaches and observable market inputs to determine value. The Company validates the prices provided by our third party pricing services by reviewing their pricing methods and obtaining market values from other pricing sources. After completing its validation procedures, the Company did not adjust or override any fair value measurements provided by the pricing services as of December 31, 2011, December 31, 2012 or March 31, 2013.

The carrying amounts reflected in the consolidated balance sheets for cash, prepaid expenses and other current assets, other assets, accounts payable, and accrued expenses approximate their fair values at December 31, 2011 and 2012 and March 31, 2013, due to their short-term nature.

There have been no changes to the valuation methods during the years ended December 31, 2011 and 2012 or the three months ended March 31, 2012 and 2013. The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of assets or liabilities between Level 1 and Level 2 during the years ended December 31, 2011 and 2012 or the three months ended March 31, 2012 and 2013. The Company had no financial assets or liabilities that were classified as Level 3 at any point during the years ended December 31, 2011 or 2012 or the three months ended March 31, 2012 and 2013.

***Property and Equipment***

Property and equipment consist of laboratory equipment, computer equipment and software, leasehold improvements, furniture and fixtures, and office equipment. Property and equipment is stated at cost, and depreciated using the straight-line method over the estimated useful lives of the respective assets:

| | |
|---|---|
| Laboratory equipment | 5 years |
| Computer equipment and software | 3 years |
| Leasehold improvements | Shorter of asset’s useful life or remaining term of lease |
| Furniture and fixtures | 5 years |
| Office equipment | 5 years |

Costs of major additions and betterments are capitalized; maintenance and repairs, which do not improve or extend the life of the respective assets, are charged to expense as incurred. Upon retirement or sale, the cost of the disposed asset and the related accumulated depreciation are removed from the accounts and the resulting gain or loss is recognized.

***Impairment of Long-Lived Assets***

The Company periodically evaluates its long-lived assets for potential impairment in accordance with ASC Topic 360, *Property, Plant and Equipment*. Potential impairment is assessed when there is evidence that events or changes in circumstances indicate that the carrying amount of an asset may not be recovered. Recoverability of these assets is assessed based on undiscounted expected future cash flows from the assets, considering a number of factors, including past operating results, budgets and economic projections, market trends and product development cycles. If impairments are identified, assets are written down to their estimated fair value. The Company has not recognized any impairment charges through March 31, 2013.

***Segment and Geographic Information***

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, or decision making group, in making decisions on how to allocate resources and assess performance. The Company's chief operating decision maker is the chief executive officer. The Company and the chief decision maker view the Company's operations and manage its business as one operating segment. The Company operates in only one geographic segment.

***Subsequent Events***

The Company considered events or transactions occurring after the balance sheet date but prior to the date the consolidated financial statements are available to be issued for potential recognition or disclosure in its consolidated financial statements. Subsequent events have been evaluated through May 23, 2013, the date the consolidated financial statements were available to be issued.

***Net Loss per Share Applicable to Common Stockholders***

Basic net loss per share applicable to common stockholders is calculated by dividing net loss applicable to common stockholders by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Net loss applicable to common stockholders is calculated by adjusting the net loss of the Company for cumulative preferred stock dividends. Diluted net loss per share applicable to common stockholders is calculated by adjusting weighted average shares outstanding for the dilutive effect of common stock equivalents outstanding for the period, determined using the treasury-stock method. For purposes of the dilutive net loss per share applicable to common stockholders calculation, preferred stock, stock options, and unvested restricted stock are considered to be common stock equivalents but are excluded from the calculation of diluted net loss per share applicable to common stockholders, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share applicable to common stockholders were the same for all periods presented. The following common stock equivalents were excluded from the calculation of diluted net loss per share applicable to common stockholders for the periods indicated because including them would have had an anti-dilutive effect:

| | Years ended December 31, | | Three Months Ended March 31, | |
|---|---|---|---|---|
| | 2011 | 2012 | 2012 | 2013 |
| Convertible preferred stock | 54,261,829 | 54,261,829 | 54,261,829 | 54,261,829 |
| Stock options | 7,408,152 | 8,650,248 | 7,476,455 | 8,497,274 |
| Unvested restricted stock | 802,083 | 440,146 | 677,083 | 302,646 |
| | 62,472,064 | 63,352,223 | 62,415,367 | 63,061,749 |

**3. Collaboration Agreement**

In April 2010, the Company entered into a collaboration agreement with Celgene Corporation, or Celgene, focused on cancer metabolism. This agreement was amended in October 2011, as described below. The goal of the collaboration is to discover, develop and commercialize disease-altering therapies in oncology based on the Company's cancer metabolism research platform. The Company is leading discovery, preclinical and early clinical development for all cancer metabolism programs under the collaboration. The discovery phase of the amended collaboration expires in April 2014, subject to Celgene's option to extend the discovery phase for up to an additional two years with additional funding to the Company. Celgene has the option to obtain exclusive rights for the further development and commercialization of certain of the programs, and the Company will retain rights to the others. The Company may elect to participate in a portion of sales activities for the medicines from such programs in the United States. In addition, for certain of the programs that Celgene chooses to license, the Company may elect to retain full rights to develop and commercialize medicines from these programs in the United States.

Pursuant to the collaboration, the Company is responsible for nominating development candidates, of which two must be confirmed by the Joint Research Committee ("JRC") during the discovery phase. During the three months ended December 31, 2012, the Company nominated its first development candidate, and during the three months ended March 31, 2013, the Company nominated its second development candidate, both of which have been confirmed by the JRC, pursuant to the agreement. The JRC will be dissolved and its activities and authority terminated upon the end of the discovery phase. For each development candidate, Celgene may elect to progress into preclinical development. If Celgene makes such an election, the Company will be required to conduct studies to meet the requirements for filing an Investigational New Drug application, or IND, or IND-enabling studies, and, following the successful completion as confirmed by the JRC, the Company will file an IND to commence clinical studies of such development candidate. If the FDA accepts the IND, Celgene may request that the Company conduct an initial phase 1 study, for which the Company would be entitled to receive a milestone payment of $5.0 million upon enrollment of the last patient in the phase 1 study, unless such program becomes a split licensed program, as described below.

Celgene may elect to convert each discovery program for which the Company has nominated a development candidate into a co-commercialized licensed program, the attributes of which are described below. The Company has the right, exercisable during a specified period following FDA acceptance of the applicable IND, to convert one of every three co-commercialized licensed programs into a split licensed program, for which the Company will retain the United States rights, other attributes of which are further described below. The Company's IDH2 program will not be a split licensed program.

The Company will retain the rights to the development candidate and certain other compounds for which Celgene does not elect to progress into preclinical development or convert into a co-commercialized licensed program. In addition, if the JRC or Celgene elects not to continue collaboration activities with respect to a particular target, either the Company or Celgene would have the right to independently undertake a discovery program on such target and would have rights to specified compounds from such program, subject to certain "buy-in" rights granted to the other party.

The agreement provides for three types of licensed programs as discussed above:

*Co-Commercialized Licensed Programs*: Celgene will lead and, following either IND acceptance by the FDA or, if Celgene requests us to conduct a phase 1 study, upon completion of such phase 1 study, will fund global development and commercialization. The Company has the right to participate in a portion of sales activities in the United States for products from co-commercialized programs in accordance with the applicable commercialization plan. The Company will be eligible to receive milestone payments and royalties arising from the licensed program.

*Split Licensed Programs*: Celgene will lead development and commercialization outside the United States and the Company will lead development and commercialization in the United States. The Company and Celgene will equally fund the global development costs of each split licensed program that are not specific to any particular region or country, Celgene will be responsible for development and commercialization costs specific to countries outside the United States, and the Company will be responsible for development and commercialization costs specific to the United States. The Company will retain profits generated in the United States and will also be eligible to receive milestone payments and royalties arising from net sales outside the United States. The Company will be obligated to pay Celgene royalties arising from net sales in the United States.

*Buy-In Programs:* If a party elects to independently undertake a discovery program, with respect to a particular target under the agreement, the party that is conducting the independent program that becomes a buy-in program will lead the development and commercialization of such program. The party that elects to buy in to such program will be responsible for funding a portion of development costs incurred after acceptance of an IND for a buy-in program compound, and the lead party will be responsible for all other development costs and all commercialization costs for products from such buy-in program. The commercializing party will be obligated to pay the buy-in party specified royalties on worldwide net sales.

In addition, Celgene may license certain discovery programs for which the Company did not nominate or the JRC did not confirm as a development candidate and for which Celgene will lead and fund global development and commercialization.

The term of the agreement will continue, unless earlier terminated by either party, until the expiration of the last-to-expire of all royalty terms with respect to all royalty-bearing products or the expiration of the option term if Celgene fails to extend the term of the agreement, does not select any compounds pursuant to the agreement, and there are no existing programs covered by the agreement.

Celgene may terminate the agreement for convenience in its entirety or with respect to one or more programs upon ninety days written notice to the Company. Either the Company or Celgene may terminate the agreement in its entirety or with respect to one or more programs, if the other party is in material breach and fails to cure such breach within the specified cure period; however, if such breach relates solely to a specific program, the non-breaching party may only terminate the agreement with respect to such program. Either the Company or Celgene may terminate the agreement in the event of specified insolvency events involving the other party.

Under the terms of the agreement, the Company received an upfront payment of approximately $121.2 million. In addition, Celgene purchased 5,190,551 shares of Series B convertible preferred stock (Series B Preferred Stock) at a price of $1.70 per share, resulting in net proceeds of approximately $8.8 million. The Company determined the price paid by Celgene for the Series B Preferred Stock represented a premium over the fair value of the Company’s Series B Preferred Stock as determined by the implied value of the Series B Preferred Stock pursuant to a contemporaneous valuation analysis that allocated the equity value of the Company to the various classes of securities. The Company accounted for the $3.1 million premium as additional consideration under the agreement and the Series B Preferred Stock was recorded at its fair value of $5.7 million.

The Company identified several deliverables under the agreement, including the option to obtain a license or licenses and research and development services to be performed by the Company on behalf of Celgene, including manufacturing of clinical and preclinical supply through completion of phase 1 clinical trials. The Company concluded that the option to obtain a license does not have stand-alone value to Celgene apart from the related research and development services deliverables as there are no other vendors selling similar, competing products on a stand-alone basis, Celgene does not have the contractual right to resell the option to obtain a license, and Celgene is unable to use the license for its intended purpose without the Company’s performance of research and

development services. In addition, the Company was not able to estimate the fair value of the undelivered items in the agreement. Accordingly, the Company has accounted for the deliverables as one unit of accounting. As such, a total of $124.3 million of revenue is being recognized on a straight-line basis over the period over which the Company expects to fulfill its performance obligations (the performance period), which was determined to be 6 years. The Company evaluates the performance period at each reporting period.

In October 2011, the agreement was amended to extend the term of the initial discovery period from three to four years, to April 2014. The amendment was not deemed to be a material modification to the arrangement since there were no changes in the deliverables or the total arrangement consideration, as the provisions of the original agreement provided Celgene with the option to extend the research period for the same consideration. Celgene made a payment to Agios of $20.0 million pursuant to the amendment. The payment was combined with the unamortized upfront payment and premium and is being recognized as revenue on a straight-line basis over the performance period. The Company may also be eligible to receive up to $40.0 million in extension payments to extend the discovery phase until April 2016.

The Company recorded revenue of approximately $21.8 million, $25.1 million, $6.3 million, and $6.3 million for the years ended December 31, 2011 and 2012 and the three months ended March 31, 2012 and 2013, respectively.

The Company is eligible to receive up to $120.0 million in potential milestone payments payable for each program selected by Celgene. The potential milestone payments for each such program are comprised of: (i) a $25.0 million milestone payment upon achievement of a specified clinical development milestone event, (ii) up to $70.0 million in milestone payments upon achievement of specified regulatory milestone events, and (iii) a $25.0 million milestone payment upon achievement of a specified commercial milestone event.

The Company is also eligible to receive additional milestone payments specific to co-commercialized licensed programs and split licensed programs. Each co-commercialized licensed program is eligible to receive a minimum one-time payment of $5.0 million upon the enrollment of the last patient in a phase 1 multiple ascending dose study. In addition, we are eligible to receive a substantive milestone payment of $22.5 million upon achievement of an early clinical development milestone event for certain co-commercialized licensed programs. The first split licensed program under the collaboration is eligible to receive a one-time payment of $25.0 million upon the dosing of the last patient in a Company-sponsored phase 2 clinical trial. The Company may also receive royalties at tiered, low to mid-teen percentage rates on sales and has the option to participate in the development and commercialization of certain products in the United States. As of March 31, 2013 the Company has not received any milestone or royalty payments under the agreement. The next potential milestone that the Company might be entitled to receive under this agreement is $5.0 million upon enrollment of the last patient in a phase 1 multiple ascending dose study, unless such program becomes a split licensed program.

The Company has concluded that certain of the clinical development and regulatory milestones that may be received under the Celgene Agreement, if the Company is involved in future product development and commercialization, are substantive. Factors considered in the evaluation of the milestones included the degree of risk associated with performance of the milestone, the level of effort and investment required, whether the milestone consideration was reasonable relative to the deliverables and whether the milestone was earned at least in part based on the Company’s performance. Revenues from substantive milestones, if they are nonrefundable, are recognized as revenue upon successful accomplishment of the milestones. Clinical and regulatory milestones are deemed non-substantive if they are based solely on the collaborator’s performance. Non-substantive milestones will be recognized when achieved to the extent the Company has no remaining performance obligations under the arrangement. Milestone payments earned upon achievement of commercial milestone events will be recognized when earned.

**4. Property and Equipment**

Property and equipment consists of the following (in thousands):

| | December 31, | | March 31, |
|---|---|---|---|
| | 2011 | 2012 | 2013 |
| Laboratory equipment | $ 3,534 | $ 4,903 | $ 5,618 |
| Computer equipment and software | 820 | 902 | 982 |
| Leasehold improvements | 97 | 97 | 97 |
| Furniture and fixtures | 313 | 331 | 334 |
| Office equipment | 51 | 83 | 161 |
| Total property and equipment | 4,815 | 6,316 | 7,192 |
| Less accumulated depreciation | (1,593) | (2,751) | (3,100) |
| Total property and equipment, net | $ 3,222 | $ 3,565 | $ 4,092 |

Depreciation expense for the years ended December 31, 2011 and 2012 and for the three months ended March 31, 2012 and 2013 was $0.8 million, $1.2 million, $0.3 million, and $0.3 million, respectively.

**5. Accrued Expenses and Other Current Liabilities**

Accrued expenses and other current liabilities consist of the following (in thousands):

| | December 31, | | March 31, |
|---|---|---|---|
| | 2011 | 2012 | 2013 |
| Accrued compensation | $ 979 | $1,124 | $ 850 |
| Accrued contracted research costs | 226 | 410 | 708 |
| Accrued professional fees | 163 | 109 | 455 |
| Accrued other | 177 | 65 | 13 |
| Total | $1,545 | $1,708 | $2,026 |

**6. Commitments and Contingencies**

***Operating Lease***

On August 1, 2010, the Company entered into an operating lease for 38,536 square feet of office and laboratory space located at 38 Sidney Street, Cambridge, Massachusetts, which expires on April 14, 2016 (the “Lease”). At the end of the lease term, the Company has the option to extend the Lease for two additional consecutive terms of five years. The Lease agreement includes rent escalation clauses and a free rent period. The Company records rent expense on a straight-line basis over the effective term of the Lease, including any free rent periods. The Company was obligated to, and has provided, a standby letter of credit of $571,000 as security for the Lease. Accordingly, the Company classified $571,000 as restricted cash in the consolidated balance sheets as of December 31, 2011 and 2012, and March 31, 2013.

Rent expense for each of the years ended December 31, 2011 and 2012 was $2.2 million and rent expense for each of the three months ended March 31, 2012 and 2013 was $0.6 million. The operating lease requires the Company to share in prorated operating expenses and property taxes based upon actual amounts incurred; those amounts are not fixed for future periods and, therefore, are not included in the future commitments listed below.

Future annual minimum lease payments due under the operating lease at December 31, 2012 are as follows (in thousands):

| | |
|---|---|
| Year ending December 31: | |
| 2013 | $2,270 |
| 2014 | 2,309 |
| 2015 | 2,347 |
| 2016 | 787 |
| Total minimum lease payments | $7,713 |

***The Trustees of the University of Pennsylvania***

In August 2012, the Company entered into a license agreement with The Trustees of the University of Pennsylvania (Penn), pursuant to which Penn granted the Company a worldwide exclusive license to certain intellectual property rights for the development of diagnostic products to detect the metabolism of certain cancers. The Company is obligated to pay Penn up to $100,000 in milestone payments, contingent upon the issuance of certain patents. For each product developed under the agreement the Company has the right to elect to develop and commercialize the product or to grant Penn an exclusive license to develop and commercialize the product. Under the agreement, the applicable party will pay to the other party a royalty based on worldwide net sales of products. To date, there have been no milestones achieved or any sales of products licensed.

The term of the agreement will continue, unless earlier terminated by either party, until the expiration of the last-to-expire issued patent. Either party may terminate the agreement in the event of the failure of the other party to make required payments under the agreement or an uncured material breach by the other party. In addition, Penn may terminate the agreement if the Company becomes insolvent or challenges certain licensed patent rights.

***Other License Agreements***

The Company has entered into various cancelable license agreements for certain technology. None of the Company's lead product candidates utilize technology covered by these licenses. In consideration for the licensed rights the Company made up-front payments totaling $340,000 and issued a total of 447,000 shares of common stock to certain licensors. The Company is obligated to pay annual maintenance payments totaling $30,000 to certain of the licensors, which are recognized as research and development expense. The Company could be required to make patent-related, clinical development, regulatory and sales-based milestones of up to $0.2 million, $1.6 million, $5.3 million and $3.5 million, respectively, to the licensors. The license agreements also require the Company to remit royalties in amounts ranging from 0.5% to 2.5% based on net sales of products utilizing the licensed technology. The Company is also required to make payments in amounts ranging from 7.0% to 12.5% for non-royalty income received from any sublicense of the rights granted to the Company under the agreements. Total license expense incurred under the license agreements amounted to $30,000 during each of the years ended December 31, 2012 and 2011. The Company has not paid any milestones or royalties to date.

**Legal Contingencies**

The Company does not currently have any contingencies related to ongoing legal matters.

**7. Convertible Preferred Stock**

In 2008 and 2009, the Company sold a total of 33,188,889 shares of Series A convertible preferred stock to investors at $1.00 per share, resulting in aggregate proceeds of $33.1 million, including the conversion of the principal and interest on $2.0 million of convertible notes.

In April 2010, the Company executed a strategic collaboration agreement with Celgene Corporation (Note 3). In connection with the Celgene Agreement, the Company sold 5,190,551 shares of Series B convertible preferred stock (Series B Preferred Stock) to Celgene at $1.70 per share, resulting in aggregate proceeds of $8.8 million. The Company determined the fair value per share of the Series B Preferred Stock on the date of issuance to be $1.11 and has considered the premium paid over the fair value of the Series B Preferred Stock to be additional consideration under the Celgene Agreement. Refer to Note 3 for further discussion of the treatment of the implied premium on the Series B Preferred Stock.

In November 2011, the Company completed a Series C convertible preferred stock financing, pursuant to which the Company sold 15,882,389 shares of Series C convertible preferred stock to investors at $4.91 per share, resulting in aggregate proceeds of $78.0 million. The shares of Series C convertible preferred stock included 7,395,829 shares of Series C-1 convertible preferred stock (the C-1 Preferred Stock) and 8,486,560 shares of Series C-2 convertible preferred stock (the C-2 Preferred Stock) (collectively, the Series C Preferred Stock).

The Company assessed the Series A, B and C Preferred Stock (collectively, the “Preferred Stock”) for any embedded derivatives that would require bifurcation from the Preferred Stock and receive separate accounting treatment. No embedded derivatives were identified that would require bifurcation.

The holders of the Preferred Stock have the following rights:

***Conversion***

Each share of Preferred Stock is initially convertible into one share of common stock. The conversion ratio is subject to adjustment for certain dilutive events, such as, but not limited to, stock splits and dividends. Conversion is at the option of the holder; however, it is automatic upon:

(a) the closing of the sale of shares of common stock to the public in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, resulting in at least $30,000,000 of gross proceeds to the Company and with either (1) a price of at least $5.00 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Common Stock) or (2) a listing of the common stock on a nationally recognized securities exchange or trading system; or

(b) at a date agreed to in writing by (1) the holders of at least 60% of the outstanding shares of Series A Preferred Stock, (2) the holders of a majority of the outstanding shares of Series B Preferred Stock and (3) the majority of the holders of the Series C-1 Preferred Stock.

The Company evaluated each series of its preferred stock and determined that each individual series is considered an equity host under ASC 815, *Derivatives and Hedging*. In making this determination, the Company’s analysis followed the whole instrument approach which compares an individual feature against the entire preferred stock instrument which includes that feature. The Company’s analysis was based on a consideration of the economic characteristics and risks of each series of preferred stock. More specifically, the Company evaluated all of the stated and implied substantive terms and features, including: (i) whether the

preferred stock included redemption features, (ii) how and when any redemption features could be exercised, (iii) whether the holders of preferred stock were entitled to dividends, (iv) the voting rights of the preferred stock and (v) the existence and nature of any conversion rights. As a result of the Company's conclusion that the preferred stock represents an equity host, the conversion feature of all series of preferred stock is considered to be clearly and closely related to the associated preferred stock host instrument. Accordingly, the conversion feature of all series of preferred stock is not considered an embedded derivative that requires bifurcation.

The Company accounts for potentially beneficial conversion features under ASC 470-20, *Debt with Conversion and Other Options*. At the time of each of the issuances of convertible preferred stock, the Company's common stock into which each series of the Company's preferred stock is convertible had an estimated fair value less than the effective conversion prices of the convertible preferred stock. Therefore, there was no intrinsic value on the respective commitment dates.

***Dividends***

The holders of Series A, Series B, and Series C Preferred Stock are entitled to receive cumulative dividends at the rate of $0.06, $0.10, and $0.294666 per share per annum, respectively, in preference to any dividends on common stock, when, as, and if declared by the Board of Directors. These dividends are cumulative and accrue whether or not declared. As of December 31, 2012, dividends accrued but unpaid were $7.8 million for Series A Preferred Stock, $1.4 million for Series B Preferred Stock, and $5.3 million for Series C Preferred Stock. As of March 31, 2013, dividends accrued but unpaid were $8.3 million for Series A Preferred Stock, $1.5 million for Series B Preferred Stock, and $6.4 million for Series C Preferred Stock. No dividends have been declared through March 31, 2013.

***Voting***

The holders of Series A, Series B, and Series C Preferred Stock are entitled to the number of votes equal to the number of common shares into which the Series A, Series B, and Series C Preferred Stock are convertible.

***Liquidation***

The holders of the Series C Preferred Stock are entitled to receive, upon the liquidation of the Company, including certain transactions deemed to be a liquidation, proceeds in proportion to their liquidation preference. Such liquidation preference is equal to the greater of the original Series C issue price of $4.91 per share, plus all declared or accrued, but unpaid dividends or such amount per share as would have been payable had such share been converted into common stock. Subsequent to the payment of the Series C Preferred Stock liquidation preference, the holders of the Series A and B Preferred Stock would receive liquidation proceeds in proportion to their liquidation preference. Such liquidation preference is equal to the greater of the original Series A and Series B issue price of $1.00 per share and $1.70 per share, respectively, plus all declared or accrued, but unpaid dividends or such amount per share as would have been payable had such share been converted into common stock. Subsequent to the liquidation preference payments to the holders of Preferred Stock, the remaining assets of the Company would be distributed to the holders of common stock.

**8. Common Stock**

The voting, dividend and liquidation rights of holders of shares of Common Stock are subject to and qualified by the rights, powers and preferences of the holders of shares of Preferred Stock. The Company's Common Stock has the following characteristics:

***Voting***

The Holders of shares of Common Stock are entitled to one vote for each share of Common Stock held at all meetings of stockholders and written actions in lieu of meetings.

***Dividends***

The holders of shares of Common Stock are entitled to receive dividends, if and when declared by the Board of Directors. Cash dividends may not be declared or paid to holders of Common Stock until paid on each series of outstanding Preferred Stock in accordance with their respective terms. As of March 31, 2013, no dividends have been declared or paid since the Company's inception.

***Liquidation***

After payment to the holders of shares of Preferred Stock of their liquidation preferences, the holders of shares of Common Stock are entitled to share ratably in the Company's assets available for distribution to stockholders, in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or upon the occurrence of a Deemed Liquidation Event, as defined.

**Reserved for Future Issuance**

The Company has reserved for future issuance the following number of shares of Common Stock as of December 31, 2011, December 31, 2012 and March 31, 2013:

| | December 31, 2011 | December 31, 2012 | March 31, 2013 |
|---|---|---|---|
| Conversion of Series A Preferred Stock | 33,188,889 | 33,188,889 | 33,188,889 |
| Conversion of Series B Preferred Stock | 5,190,551 | 5,190,551 | 5,190,551 |
| Conversion of Series C Preferred Stock | 15,882,389 | 15,882,389 | 15,882,389 |
| Options to purchase Common Stock | 10,669,018 | 13,969,018 | 13,969,018 |
| | 64,930,847 | 68,230,847 | 68,230,847 |

**9. Share-Based Payments**

***2007 Stock Incentive Plan***

The Company maintains the 2007 Stock Incentive Plan (the "Plan") for employees, directors, consultants, and advisors to the Company. The Plan provides for the grant of incentive and non-qualified stock options and restricted stock grants as determined by the Board of Directors. The Company has reserved 13,969,018 shares of common stock under the Plan, and at December 31, 2012 and March 31, 2013, the Company had 1,881,341 and 1,991,498 shares available for future issuance under the Plan, respectively. Shares of common stock issued upon exercise of stock options are generally issued from new shares of the Company. The Plan provides that the exercise price of incentive stock options cannot be less than 100% of the fair market value of the common stock on the date of the award for participants who own less than 10% of the total combined voting power of stock of the Company, and not less than 110% for participants who own more than 10% of the Company's voting power. Stock options and restricted stock granted under the Plan vest over periods as determined by the Board of Directors, which is generally 25% on the first year anniversary of the grant date and then ratably monthly thereafter. Stock options generally expire ten years from the date of grant. Restricted stock issuances and early exercise of stock options are subject to the Company's right of repurchase at the original issuance price, which right lapses over the vesting period of the stock.

During the years ended December 31, 2011 and 2012, the Company granted 20,000 and 45,000 stock options to consultants and advisors of the Company, respectively. These awards are included within the following table which summarizes the activity of the Plan for the year ended December 31, 2012 and the three months ended March 31, 2013:

| | Number of Stock Options | Weighted-Average Exercise Price | Weighted-Average Remaining Contractual Term (in years) | Aggregate Intrinsic Value (in thousands) |
|---|---|---|---|---|
| Outstanding at December 31, 2011 | 7,408,152 | $ 0.14 | 8.17 | $ 5,249 |
| Granted | 2,290,850 | 0.85 | | |
| Exercised | (789,435) | 0.17 | | |
| Forfeited | (259,319) | 0.38 | | |
| Outstanding at December 31, 2012 | 8,650,248 | 0.32 | 7.72 | 15,402 |
| Exercised | (42,817) | 0.21 | | |
| Forfeited | (110,157) | 0.79 | | |
| Outstanding at March 31, 2013 | 8,497,274 | 0.31 | 7.45 | 25,288 |
| Exercisable at December 31, 2012 | 4,741,161 | 0.15 | 7.03 | 9,268 |
| Vested and expected to vest at December 31, 2012 | 6,898,369 | 0.24 | 7.43 | 12,862 |
| Exercisable at March 31, 2013 | 5,389,052 | 0.18 | 6.92 | 16,743 |
| Vested and expected to vest at March 31, 2013 | 7,154,683 | 0.25 | 7.24 | 21,743 |

The weighted-average grant date fair value of options granted was $0.16, $0.76 and $0.68, during the years ended December 31, 2011 and 2012 and the three months ended March 31, 2012, respectively. There were no options granted during the three months ended March 31, 2013. The total intrinsic value of options exercised was $65,000, $761,000, $169,000, and $132,000 during the years ended December 31, 2011 and 2012 and the three months ended March 31, 2012 and 2013, respectively.

At March 31, 2013, the total unrecognized compensation expense related to unvested stock option awards, including estimated forfeitures, was $0.8 million, which the Company expects to recognize over a weighted-average period of approximately 1.8 years. The Company also has unrecognized stock-based compensation expense of $0.5 million related to stock options with performance-based vesting criteria that are not considered probable of achievement as of March 31, 2013; therefore the Company has not yet begun to recognize the expense on these awards.

*Restricted Stock and Early Exercise of Stock Options*

From time to time, upon approval by the Company's Board, certain employee option holders have been granted restricted stock and certain directors have been permitted to early exercise their stock options in exchange for cash, at which time the awards became subject to restricted stock agreements. These shares of restricted stock granted upon early exercise of the options are subject to the same vesting provisions as the original stock option awards. Accordingly, the Company has recorded the exercise proceeds from early exercises as a restricted stock liability in the consolidated balance sheets. The restricted stock liability is reclassified into stockholders' (deficit) equity as the restricted stock and options vest.

At December 31, 2011 and 2012 and March 31, 2013, there were 802,083, 440,146 and 302,646 shares of unvested restricted stock which remain subject to the Company's right of repurchase, respectively.

Unvested restricted stock activity for the years ended December 31, 2011 and 2012 and the three months ended March 31, 2013 is summarized as follows:

| | Years Ended December 31, | | Three Months Ended March 31, 2013 |
|---|---|---|---|
| | 2011 | 2012 | |
| Unvested shares beginning of period | 1,302,083 | 802,083 | 440,146 |
| Granted | — | 143,271 | — |
| Vested | (500,000) | (505,208) | (137,500) |
| Forfeited | — | — | — |
| Unvested shares end of period | 802,083 | 440,146 | 302,646 |

The weighted-average exercise price of restricted stock granted was $0.33 during the year ended December 31, 2012.

*Performance-Based Stock Option Grants*

During the years ended December 31, 2011 and 2012, the Company granted options to purchase 250,000 and 1,033,000, respectively, shares of common stock to employees, including executive officers, which contain both performance-based and service-based vesting criteria. Milestone events are specific to the Company's corporate goals, including but not limited to certain preclinical and clinical development milestones related to the Company's product candidates. Stock-based compensation expense associated with these performance-based stock options is recognized if the performance condition is considered probable of achievement using management's best estimates. Management has concluded that the performance-based milestones, which were primarily related to preclinical and clinical development, were not probable of achievement at December 31, 2012. As such, no stock-based compensation expense was recorded as of December 31, 2012 related to these options. During the three months ended March 31, 2013 management assessed the probability of achieving the milestones and determined that certain performance-based milestones are probable of achievement as of March 31, 2013. The Company recorded stock-based compensation expense of $172,000 during the three months ended March 31, 2013, accordingly. The remaining milestones were not deemed to be probable of achievement as of March 31, 2013.

During 2010, the Company granted stock options to consultants of the Company which contained performance-based vesting criteria and no underlying service period. Stock-based compensation expense associated with these performance-based stock options is recognized if the performance condition is considered probable of achievement using management's best estimates. During the years ended December 31, 2011 and 2012 management concluded that the milestones associated with 150,000 and 75,000 performance-based stock options, respectively, were probable of achievement and the Company began to record stock-based compensation expense, accordingly. The Company recorded $24,000 and $150,000 of stock-based compensation expense for non-employee performance-based stock options in the years ended December 31, 2011 and 2012. There was no stock-based compensation expense for non-employee performance-based stock options recorded in the three months ended March 31, 2012 and 2013 as the remaining milestones were not considered probable of achievement as of March 31, 2012 and there were no remaining unvested performance-based stock options for non-employees subsequent to December 31, 2012.

***Stock-Based Compensation Expense***

The fair value of each stock option granted to employees is estimated on the date of grant and for non-employees on each vesting and reporting date using the Black-Scholes option-pricing model. The following table summarizes the weighted average assumptions used in calculating the fair value of the awards:

| | Years Ended December 31, | | Three Months Ended March 31, 2012 |
|---|---|---|---|
| | 2011 | 2012 | |
| Risk-free interest rate | 1.97% | 1.09% | 1.17% |
| Expected dividend yield | — | — | — |
| Expected term (in years) | 6.09 | 6.08 | 6.38 |
| Expected volatility | 98.60% | 97.75% | 99.51% |

Note: There were no stock options granted in the three months ended March 31, 2013.

***Volatility***

Since the Company is privately held as of the date of these consolidated financial statements, it does not have relevant historical data to support its expected volatility. As such, the Company has used a weighted-average of expected volatility based on the volatilities of a representative group of publicly-traded biopharmaceutical companies. For purposes of identifying representative companies, the Company considered characteristics such as number of product candidates in earlier stages of product development, area of therapeutic focus, length of trading history, similar vesting provisions and a similar percentage of stock options that are in-the-money. The expected volatility has been determined using a weighted-average of the historical volatilities of the representative group of companies for a period equal to the expected term of the option grant. The Company intends to continue to consistently apply this process using the same similar entities until a sufficient amount of historical information regarding the volatility of the Company's own share price becomes available or until circumstances change, such that the identified entities are no longer representative companies. In the latter case, more suitable, similar entities whose share prices are publicly available would be utilized in the calculation.

***Risk-Free Rate***

The risk-free rate is based on the yield curve of U.S. Treasury securities with periods commensurate with the expected term of the options being valued.

***Expected Term***

The Company uses the "simplified method" as prescribed by the Securities and Exchange Commission Staff Accounting Bulletin No. 107, *Share Based Payments*, to estimate the expected term of stock option grants. Under this approach, the weighted-average expected life is presumed to be the average of the contractual term (ten years) and the vesting term (generally four years) of the Company's stock options, taking into consideration multiple vesting tranches. The Company utilizes this method due to lack of historical exercise data and the plain-vanilla nature of the Company's share-based awards.

***Dividends***

The Company has never paid, and does not anticipate paying, any cash dividends in the foreseeable future, and therefore uses an expected dividend yield of zero in the option-pricing model.

***Forfeitures***

Forfeitures are required to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The Company based its estimate of forfeitures on data from a representative group of publicly-traded biopharmaceutical companies, as the Company does not currently have sufficient history, and records the stock-based compensation expense only on the awards that are expected to vest. To date forfeitures have been less than 5.0% of total grants.

**10. Income Taxes**

The provision (benefit) for income taxes is as follows for the years ended December 31, 2011 and 2012 and the three months ended March 31, 2012 and 2013 (in thousands):

| | December 31, | | March 31, | |
|---|---|---|---|---|
| | 2011 | 2012 | 2012 | 2013 |
| Current: | | | | |
| Federal | $ 14,406 | $(9,531) | $(2,139) | $190 |
| State | 3,461 | — | — | — |
| Total current | 17,867 | (9,531) | (2,139) | 190 |
| Deferred: | | | | |
| Federal | (10,660) | 6,707 | 1,532 | — |
| State | — | — | — | — |
| Total deferred | (10,660) | 6,707 | 1,532 | — |
| Total | $ 7,207 | $(2,824) | $ (607) | $190 |

A reconciliation of the expected income tax (benefit) expense computed using the federal statutory income tax rate to the Company's effective income tax rate is as follows for the years ended December 31, 2011 and 2012:

| | December 31, | |
|---|---|---|
| | 2011 | 2012 |
| Income tax benefit computed at federal statutory tax rate | 35.00% | 35.00% |
| State taxes, net of federal benefit | 3.95 | 7.07 |
| Change in valuation allowance | (74.29) | (28.08) |
| General business credits and other credits | (2.36) | 0.12 |
| Permanent differences | (0.60) | (0.63) |
| Interest and penalties | (1.72) | (1.95) |
| Other | (3.66) | 0.79 |
| Total | (43.68)% | 12.32% |

During the years ended December 31, 2011 and 2012 and the three months ended March 31, 2012 and 2013, the Company had $284,000, $583,000, $38,000 and $190,000 accrued for interest and penalties related to the non-payment of U.S. federal income taxes, respectively.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets and liabilities for the years ended December 31, 2011 and 2012 are as follows (in thousands):

| | 2011 | 2012 |
|---|---|---|
| Deferred tax assets (liabilities): | | |
| Net operating loss carryforwards | $ — | $ 1,666 |
| Deferred revenue | 35,727 | 33,250 |
| Tax credit carryforwards | — | 427 |
| Purchased intangible assets | 161 | 158 |
| Depreciation and amortization | (359) | (435) |
| Stock-based compensation | 102 | 269 |
| Deferred rent | 190 | 172 |
| Other | 187 | 232 |
| Total deferred tax asset | 36,008 | 35,739 |
| Valuation allowance | (25,349) | (31,786) |
| Net deferred tax asset | $ 10,659 | $ 3,953 |

As of December 31, 2012, the Company had net operating loss carryforwards available to reduce federal and state incomes taxes of approximately $0.5 million and $28.8 million, respectively. If not utilized, these carryforwards expire at various dates through 2032. At December 31, 2012, the Company also had available research and development tax credits for federal and state income tax purposes of approximately $27,000 and $616,000, respectively.

As of December 31, 2011, the Company had utilized its net operating loss carryforwards to reduce federal and state incomes taxes of approximately $27.2 million and $26.7 million, respectively. At December 31, 2011, the Company had also utilized research and development tax credits for federal and state income tax purposes of approximately $424,000 and $344,000, respectively. During 2011, the Company conducted a study of its research and development credit carryforwards. This study resulted in an adjustment to the Company's research and development credit carryforward, as the Company concluded that the credits were not more likely than not to be realized.

Utilization of the net operating loss carryforwards and credits may be subject to annual limitations as prescribed by federal and state statutory provisions. The annual limitation may result in the expiration of net operating loss carryforwards prior to its utilization. Utilization of the NOLs and tax credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future, as provided by Section 382 of the Internal Revenue Code of 1986 ("Section 382"), as well as similar state provisions. Ownership changes may limit the amount of NOLs and tax credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382, results from transactions that increase the ownership of 5% shareholders in the stock of a corporation by more than 50 percent in the aggregate over a three-year period. During 2011, the Company completed a study through December 31, 2011, to determine whether any ownership change has occurred since the Company's formation and has determined that transactions have resulted in two ownership changes, as defined by Section 382. The impact of the ownership changes have been reflected in the Company's deferred tax assets in the table above. There could be additional ownership changes in the future that could further limit the amount of NOLs and tax credit carryforwards that the Company can utilize.

As required by ASC 740, *Income Taxes* ("ASC 740"), management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of timing differences related to the recognition of revenue under the Celgene Agreement for book versus tax purposes. During the year ended December 31, 2011, management determined that it was more likely than not that it would realize a portion of its deferred tax assets because of the Company's ability to carryback future losses for U.S. federal income tax purposes. As a result, the Company reversed approximately $10.7 million of the valuation allowance on its deferred tax assets in the year ended December 31, 2011, representing the amount of deferred tax assets that will be realized in 2012 and 2013, the years available for carryback. The Company utilized certain of the deferred tax assets, including net operating losses, generated in the year ended December 31, 2012 to reduce its federal income taxes payable in the year ended December 31, 2012. For the remainder of the Company's deferred tax assets, management determined that it is more likely than not that the Company may not realize the benefit and has recorded a valuation allowance of approximately $25.3 million and $31.8 million at December 31, 2011 and 2012, respectively. The valuation allowance increased by $6.4 million in the year ended December 31, 2012.

The Company applies the accounting guidance in ASC 740 related to accounting for uncertainty in income taxes. The Company's reserves related to taxes are based on a determination of whether, and how much of, a tax benefit taken by the Company in its tax filings or positions is more likely than not to be realized following resolution of any potential contingencies present related to the tax benefit. As of December 31, 2011 and 2012, and as of March 31, 2013, the Company had no unrecognized tax benefits. The Company recognizes interest and penalties related to uncertain tax positions in income tax expense.

The statute of limitations for assessment by the Internal Revenue Service (IRS) and state tax authorities is open for tax years ending December 31, 2012, 2011, 2010, and 2009 although carryforward attributes that were generated for tax years prior to 2009 may still be adjusted upon examination by the IRS or state tax authorities if they either have been, or will be, used in a future period. There are currently no federal or state audits in progress.

**11. Defined Contribution Benefit Plan**

The Company sponsors a 401(k) retirement plan, in which substantially all of its full-time employees are eligible to participate. Participants may contribute a percentage of their annual compensation to this plan, subject to statutory limitations. The Company did not provide any contributions to this plan during the years ended December 31, 2011 and 2012 or the three months ended March 31, 2012 and 2013.

**12. Subsequent Events**

***Stock Option Awards***

On April 30, 2013, the Board of Directors of the Company granted stock option awards to employees of the Company to purchase an aggregate of 1,687,800 shares of common stock at an exercise price of $3.29 per share. The exercise price of the options was determined pursuant to a contemporaneous valuation using the Probability Weighted Expected Return Method.

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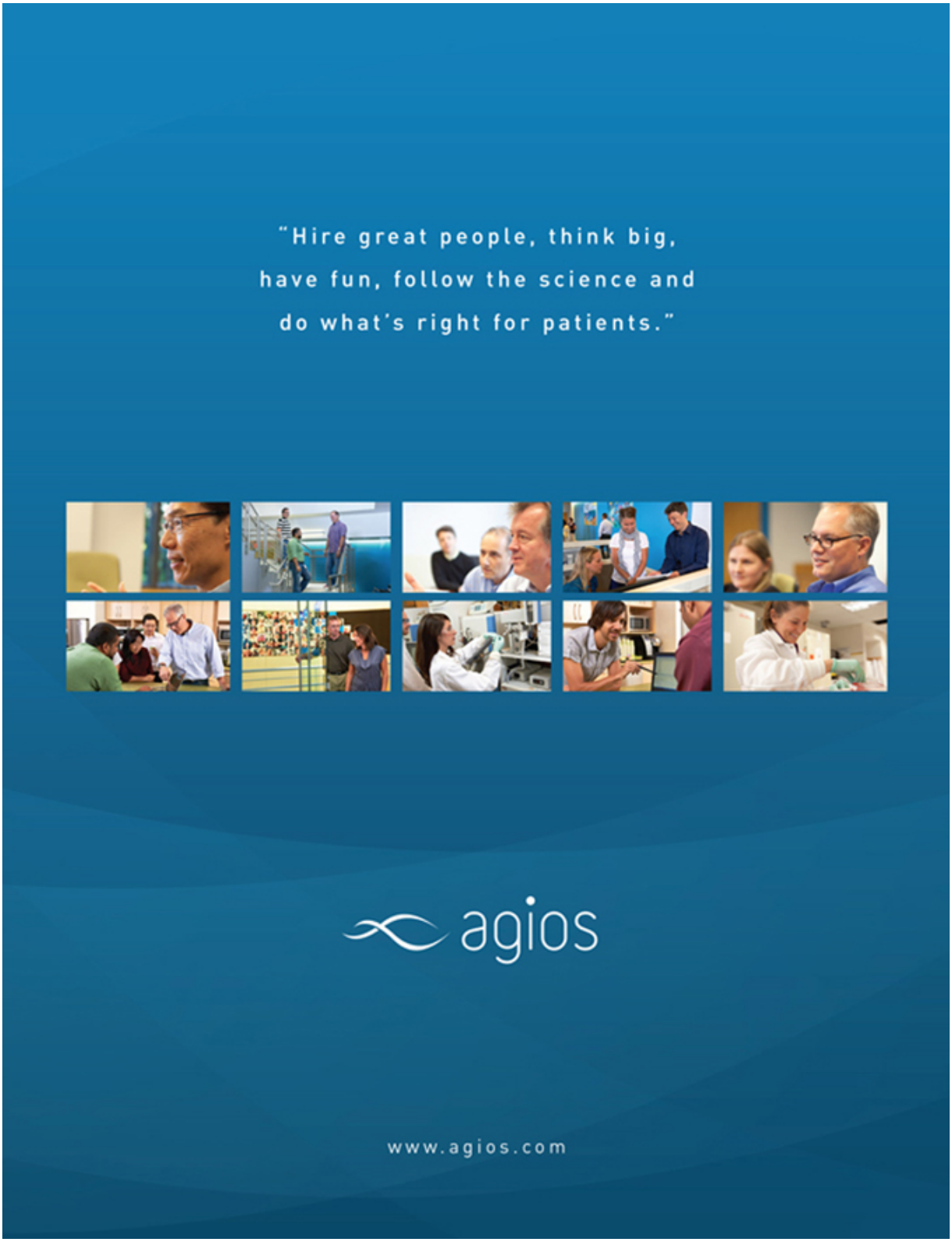

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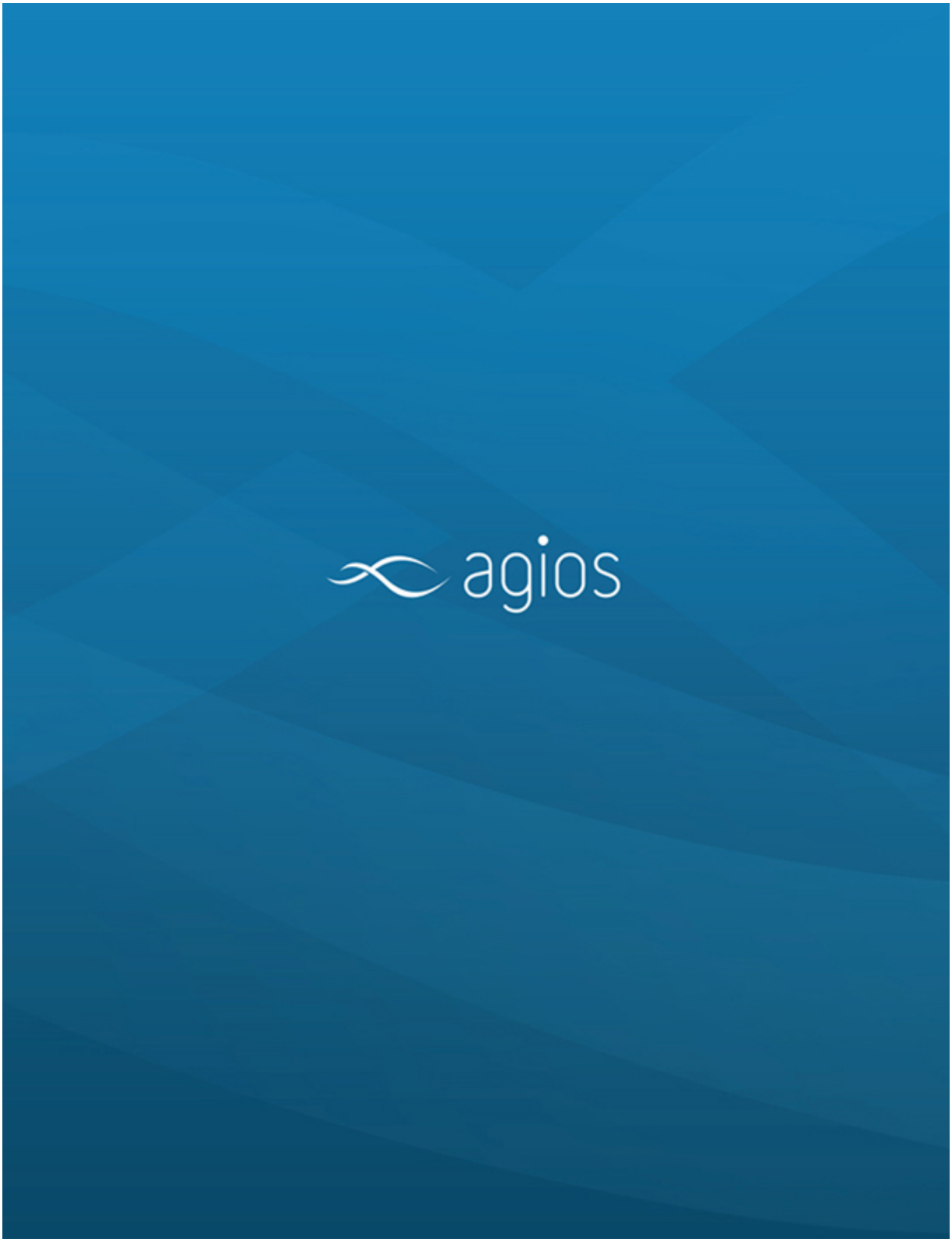

## Part II

## Information not required in prospectus

### Item 13. Other expenses of issuance and distribution.

The following table indicates the expenses to be incurred in connection with the offering described in this registration statement, other than underwriting discounts and commissions, all of which will be paid by us. All amounts are estimated except the Securities and Exchange Commission registration fee, the Financial Industry Regulatory Authority, Inc. ("FINRA") filing fee and The NASDAQ Global Market listing fee.

| | Amount |
|---|---|
| Securities and Exchange Commission registration fee | $ * |
| FINRA filing fee | * |
| NASDAQ Global Stock Market listing fee | * |
| Accountants' fees and expenses | * |
| Legal fees and expenses | * |
| Blue Sky fees and expenses | * |
| Transfer Agent's fees and expenses | * |
| Printing and engraving expenses | * |
| Miscellaneous | * |
| Total expenses | $ * |

* To be filed by amendment.

### Item 14. Indemnification of directors and officers.

Section 102 of the General Corporation Law of the State of Delaware permits a corporation to eliminate the personal liability of directors of a corporation to the corporation or its stockholders for monetary damages for a breach of fiduciary duty as a director, except where the director breached his duty of loyalty, failed to act in good faith, engaged in intentional misconduct or knowingly violated a law, authorized the payment of a dividend or approved a stock repurchase in violation of Delaware corporate law or obtained an improper personal benefit. Our certificate of incorporation provides that no director of the Registrant shall be personally liable to it or its stockholders for monetary damages for any breach of fiduciary duty as a director, notwithstanding any provision of law imposing such liability, except to the extent that the General Corporation Law of the State of Delaware prohibits the elimination or limitation of liability of directors for breaches of fiduciary duty.

Section 145 of the General Corporation Law of the State of Delaware provides that a corporation has the power to indemnify a director, officer, employee, or agent of the corporation, or a person serving at the request of the corporation for another corporation, partnership, joint venture, trust or other enterprise in related capacities against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by the person in connection with an action, suit or proceeding to which he was or is a party or is threatened to be made a party to any threatened, ending or completed action, suit or proceeding by reason of such position, if such person acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, in any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful, except that, in the case of actions brought by or in the right of the corporation, no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Court of Chancery or other adjudicating court determines that, despite the adjudication of liability but in view of all of the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Court of Chancery or such other court shall deem proper.

Our certificate of incorporation provides that we will indemnify each person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding (other than an action by or in the right of us) by reason of the fact that he or she is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise (all such persons being referred to as an "Indemnitee"), or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding and any appeal therefrom, if such Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, and, with respect to any criminal action or proceeding, he or she had no reasonable cause to believe his or her conduct was unlawful. Our certificate of incorporation provides that we will indemnify any Indemnitee who was or is a party to an action or suit by or in the right of us to procure a judgment in our favor by reason of the fact that the Indemnitee is or was, or has agreed to become, a director or officer, or is or was serving, or has agreed to serve, at our request as a director, officer, partner, employee or trustee of, or in a similar capacity with, another corporation, partnership, joint venture, trust or other enterprise, or by reason of any action alleged to have been taken or omitted in such capacity, against all expenses (including attorneys' fees) and, to the extent permitted by law, amounts paid in settlement actually and reasonably incurred in connection with such action, suit or proceeding, and any appeal therefrom, if the Indemnitee acted in good faith and in a manner he or she reasonably believed to be in, or not opposed to, our best interests, except that no indemnification shall be made with respect to any claim, issue or matter as to which such person shall have been adjudged to be liable to us, unless a court determines that, despite such adjudication but in view of all of the circumstances, he or she is entitled to indemnification of such expenses. Notwithstanding the foregoing, to the extent that any Indemnitee has been successful, on the merits or otherwise, he or she will be indemnified by us against all expenses (including attorneys' fees) actually and reasonably incurred in connection therewith. Expenses must be advanced to an Indemnitee under certain circumstances.

We have entered into indemnification agreements with each of our directors. These indemnification agreements may require us, among other things, to indemnify our directors and officers for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or officer in any action or proceeding arising out of his or her service as one of our directors or officers, or any of our subsidiaries or any other company or enterprise to which the person provides services at our request.

We maintain a general liability insurance policy that covers certain liabilities of directors and officers of our corporation arising out of claims based on acts or omissions in their capacities as directors or officers.

In any underwriting agreement we enter into in connection with the sale of common stock being registered hereby, the underwriters will agree to indemnify, under certain conditions, us, our directors, our officers and persons who control us within the meaning of the Securities Act of 1933, as amended (the "Securities Act"), against certain liabilities.

**Item 15. Recent sales of unregistered securities.**

Set forth below is information regarding securities issued by us within the past three years. Also included is the consideration received by us for such securities and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

***(a) Issuances of preferred stock***

In November 2011, we issued and sold an aggregate of 7,395,829 shares of our series C-1 preferred stock and 8,486,560 shares of our series C-2 preferred stock, each at a purchase price per share of $4.9111, for an aggregate purchase price of $78.0 million.

In April 2010, we issued and sold an aggregate of 5,190,551 shares of our Series B preferred stock at a price per share of $1.70 for an aggregate purchase price of $8.8 million.

No underwriters were involved in the foregoing sales of securities. The securities described in this section (a) of Item 15 were issued to investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(2) under the Securities Act and Regulation D promulgated thereunder relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All purchasers of shares of preferred stock described above represented to us in connection with their purchase that they were accredited investors and were acquiring the shares for their own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time. The purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration statement or an available exemption from such registration.

***(b) Issuances of common stock***

Since January 1, 2010, we have issued to certain employees an aggregate of 2,000,000 shares of restricted common stock at a purchase price of $0.11 per share. The issuances of common stock described in this section (b) of Item 15 were issued pursuant to written compensatory plans or arrangements with our employees in reliance on the exemption from the registration requirements of the Securities Act provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about us or had access, through employment relationships, to such information.

***(c) Stock option grants***

Since January 1, 2010, we have issued to certain employees, directors and consultants options to purchase an aggregate of 7,907,100 shares of common stock as of April 30, 2013, of which, 3,433,496 options to purchase shares of common stock had been exercised, options to purchase 717,159 shares had been forfeited or cancelled and options to purchase 10,170,824 shares of common stock remained outstanding at a weighted-average exercise price of $0.81 per share.

The issuance of stock options and the common stock issuable upon the exercise of such options as described in this section (c) of Item 15 were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption from the registration requirements of the Securities Act provided by either Section 4(2) of the Securities Act or Rule 701 promulgated under the Securities Act, or pursuant to Section 4(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

**Item 16. Exhibits and financial statement schedules.**

(a) Exhibits.

The exhibits to the registration statement are listed in the Exhibit Index attached hereto and incorporated by reference herein.

**Item 17. Undertakings.**

(a) The undersigned registrant hereby undertakes to provide to the underwriter, at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriter to permit prompt delivery to each purchaser.

(b) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

(c) The undersigned hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

**Signatures**

Pursuant to the requirements of the Securities Act, the registrant has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on this day of , 2013.

AGIOS PHARMACEUTICALS, INC.

By: _____

David P. Schenkein, M.D.
Chief Executive Officer

**Signatures and power of attorney**

We, the undersigned officers and directors of Agios Pharmaceuticals, Inc., hereby severally constitute and appoint David P. Schenkein, M.D., Duncan Higgons and Glenn Goddard, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him and in his name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement (or any other registration statement for the same offering that is to be effective upon filing pursuant to Rule 462(b) under the Securities Act of 1933), and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities held on the dates indicated.

| Signature | Title | Date |
|---|---|---|
| David P. Schenkein, M.D. | Chief Executive Officer and Director (principal executive officer) | , 2013 |
| Glenn Goddard | Vice President, Finance (principal financial and accounting officer) | , 2013 |
| Lewis C. Cantley, Ph.D. | Director | , 2013 |
| Douglas G. Cole, M.D. | Director | , 2013 |
| Perry Karsen | Director | , 2013 |
| John M. Maraganore, Ph.D. | Director | , 2013 |
| Robert T. Nelsen | Director | , 2013 |
| Kevin P. Starr | Director | , 2013 |
| Marc Tessier-Lavigne, Ph.D. | Director | , 2013 |

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## Exhibit index

| Exhibit number | Description of exhibit |
|---|---|
| | ***Underwriting agreement*** |
| 1.1* | Underwriting Agreement |
| | ***Articles of incorporation and bylaws*** |
| 3.1 | Third Amended and Restated Certificate of Incorporation of the Registrant, as amended |
| 3.2 | By-laws of the Registrant |
| 3.3* | Form of Certificate of Incorporation of the Registrant (to be effective upon the closing of this offering) |
| 3.4* | Form of By-laws of the Registrant (to be effective upon the closing of this offering) |
| | ***Instruments defining the rights of security holders, including indentures*** |
| 4.1* | Specimen Stock Certificate evidencing the shares of common stock |
| 4.2 | Second Amended and Restated Investor Rights Agreement dated as of November 16, 2011 |
| | ***Opinion re legality*** |
| 5.1* | Opinion of Wilmer Cutler Pickering Hale and Dorr LLP |
| | ***Material contracts—Management contracts and compensatory plans*** |
| 10.1 | 2007 Stock Incentive Plan |
| 10.2 | Form of Incentive Stock Option Agreement under 2007 Stock Incentive Plan |
| 10.3 | Form of Nonstatutory Stock Option Agreement under 2007 Stock Incentive Plan |
| 10.4* | 2013 Stock Incentive Plan |
| 10.5* | Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan |
| 10.6* | Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan |
| 10.7* | 2013 Employee Stock Purchase Plan |
| 10.8* | Letter Agreement, dated as of April 17, 2009, between the Registrant and Duncan Higgons, as amended |
| 10.9* | Letter Agreement, dated as of May 6, 2009, between the Registrant and David P. Schenkein, M.D., as amended |
| 10.10* | Letter Agreement, dated as of July 22, 2010, between the Registrant and Scott Biller, Ph.D., as amended |
| 10.11 | Letter Agreement, dated as of May 4, 2010, between the Registrant and Glenn Goddard |
| | ***Material contracts—Leases*** |
| 10.12 | Lease, dated as of August 2, 2010, between the Registrant and Thirty-Eight Sidney Street Limited Partnership |
| | ***Material contracts—License and strategic partnership agreements*** |
| 10.13† | Discovery and Development Collaboration and License Agreement, dated as of April 14, 2010, as amended on October 3, 2011, between the Registrant and Celgene Corporation |

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| Exhibit number | Description of exhibit |
|---|---|
| | ***Additional exhibits*** |
| 21.1 | Subsidiaries of the Registrant |
| 23.1 | Consent of Ernst & Young LLP |
| 23.2* | Consent of Wilmer Cutler Pickering Hale and Dorr LLP (included in Exhibit 5.1) |
| 24.1 | Power of Attorney (included on signature page) |

* To be filed by amendment.

† Confidential treatment requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

**Exhibit 3.1**

CERTIFICATE OF AMENDMENT

OF

THIRD AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

OF

AGIOS PHARMACEUTICALS, INC.

Agios Pharmaceuticals, Inc., a corporation organized and existing under the General Corporation Law of the State of Delaware (the "Corporation"), hereby certifies as follows:

1. The name of the Corporation is Agios Pharmaceuticals, Inc. The original Certificate of Incorporation of the Corporation was filed with the Secretary of State of the State of Delaware on August 7, 2007 under the name Cancer Metabolism Therapeutics, Inc. The original Certificate of Incorporation was amended on April 7, 2008; further amended and restated on June 20, 2008; further amended on August 21, 2009; and further amended and restated on April 14, 2010 and on November 15, 2011.

2. Pursuant to Section 242 of the General Corporation Law of the State of Delaware, this Certificate of Amendment of Third Amended and Restated Certificate of Incorporation amends the provisions of the Corporation's Third Amended and Restated Certificate of Incorporation.

3. The terms and provisions of this Certificate of Amendment of Third Amended and Restated Certificate of Incorporation have been duly approved by the Board of Directors of the Corporation and by written consent of the required number of shares of outstanding stock of the Corporation pursuant to Section 228 of the General Corporation Law of the State of Delaware.

4. The Third Amended and Restated Certificate of Incorporation of the Corporation is hereby amended by deleting the first sentence of Article FOURTH thereof in its entirety and by substituting the following in lieu thereof:

"The total number of shares of all classes of stock which the Corporation shall have authority to issue is (i) 78,300,000 shares of Common Stock, $0.001 par value per share ("**Common Stock**"), and (ii) 54,261,829 shares of Preferred Stock, $0.001 par value per share ("**Preferred Stock**"), of which 33,188,889 shares have been designated as "Series A Convertible Preferred Stock" ("**Series A Preferred Stock**"), 5,190,551 shares have been designated as "Series B Convertible Preferred Stock" ("**Series B Preferred Stock**"), 7,395,829 shares have been designated as "Series C-1 Convertible Preferred Stock" ("**Series C-1 Preferred Stock**") and 8,486,560 shares have been designated as "Series C-2 Convertible Preferred Stock" ("**Series C-2 Preferred Stock**")."

[The remainder of this page intentionally left blank]

IN WITNESS WHEREOF, this Certificate of Amendment of Third Amended and Restated Certificate of Incorporation has been signed this 28th day of March, 2012.

AGIOS PHARMACEUTICALS, INC.

By: /s/ David Schenkein
Name: David Schenkein
Title: Chief Executive Officer

THIRD AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
AGIOS PHARMACEUTICALS, INC.
**(**Pursuant to Sections 242 and 245 of the
General Corporation Law of the State of Delaware**)**

Agios Pharmaceuticals, Inc., a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the "**General Corporation Law**"),

**DOES HEREBY CERTIFY**:

**1.** The name of the Corporation is Agios Pharmaceuticals, Inc. The original Certificate of Incorporation was filed with the Secretary of State of the State of Delaware on August 7, 2007, under the name Cancer Metabolism Therapeutics, Inc. The original Certificate of Incorporation was amended on April 7, 2008; further amended and restated on June 20, 2008; further amended on August 21, 2009; and further amended and restated on April 14, 2010 (as so amended and restated, the "**Second Amended and Restated Certificate of Incorporation**").

**2.** That the Board of Directors duly adopted resolutions proposing to further amend and restate the Second Amended and Restated Certificate of Incorporation of this corporation, declaring said amendment and restatement to be advisable and in the best interests of this corporation and its stockholders, and authorizing the appropriate officers of this corporation to solicit the consent of the stockholders therefor, which resolution setting forth the proposed amendment and restatement is as follows:

**RESOLVED**, that the Second Amended and Restated Certificate of Incorporation of this corporation be amended and restated in its entirety to read as follows (as so amended and restated, the "**Certificate of Incorporation**"):

**FIRST**: The name of this corporation is Agios Pharmaceuticals, Inc. (the "**Corporation**").

**SECOND**: The address of the registered office of the Corporation in the State of Delaware is Corporation Trust Center, 1209 Orange Street, in the City of Wilmington, County of New Castle. The name of its registered agent at such address is The Corporation Trust Company.

**THIRD**: The nature of the business or purposes to be conducted or promoted is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law.

**FOURTH**: The total number of shares of all classes of stock which the Corporation shall have authority to issue is (i) 75,000,000 shares of Common Stock, $0.001 par value per share ("**Common Stock**"), and (ii) 54,261,829 shares of Preferred Stock, $0.001 par value per share ("**Preferred Stock**"), of which 33,188,889 shares have been designated as "Series A Convertible Preferred Stock" ("**Series A Preferred Stock**"), 5,190,551 shares have been designated as "Series B Convertible Preferred Stock" ("**Series B Preferred Stock**"), 7,395,829 shares have

been designated as “Series C-1 Convertible Preferred Stock” (“**Series C-1 Preferred Stock**”) and 8,486,560 shares have been designated as “Series C-2 Convertible Preferred Stock” (“**Series C-2 Preferred Stock**”). The Series C-1 Preferred Stock and Series C-2 Preferred Stock are referred to herein together as the “**Series C Preferred Stock**.”

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation.

A. COMMON STOCK

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights, powers and preferences of the holders of the Preferred Stock set forth herein.

2. Voting. The holders of the Common Stock are entitled to one vote for each share of Common Stock held at all meetings of stockholders (and written actions in lieu of meetings). There shall be no cumulative voting. The number of authorized shares of Common Stock may be increased or decreased (but not below the sum of (1) the number of shares thereof then outstanding plus (2) the number of shares issuable upon conversion of all Preferred Stock then outstanding) by (in addition to any vote of the holders of one or more series of Preferred Stock that may be required by the terms of the Certificate of Incorporation) the affirmative vote of the holders of shares of capital stock of the Corporation representing a majority of the votes represented by all outstanding shares of capital stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law.

B. PREFERRED STOCK

Unless otherwise indicated, references to “Sections” or “Subsections” in this Part B of this Article Fourth refer to sections and subsections of Part B of this Article Fourth.

1. Dividends.

From and after the date of the issuance of any shares of Series A Preferred Stock, dividends at the rate per annum of $0.06 per share shall accrue on such shares of Series A Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A Preferred Stock); from and after the date of the issuance of any shares of Series B Preferred Stock, dividends at the rate of $0.10 per share shall accrue on such shares of Series B Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B Preferred Stock); and from and after the date of the issuance of any shares of Series C Preferred Stock, dividends at the rate of $0.294666 per share shall accrue on such shares of Series C Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series C Preferred Stock). The dividends described in the preceding sentence are referred to herein as the “**Accruing Dividends**”. Accruing Dividends shall accrue from day to day, whether or not declared, and shall be cumulative; provided however, that except as set forth in the following sentence of this Section 1 or in Subsection 2.1, such Accruing Dividends shall

be payable only when, as, and if declared by the Board of Directors and the Corporation shall be under no obligation to pay such Accruing Dividends. The Corporation shall not declare, pay or set aside any dividends on shares of Common Stock (other than dividends on shares of Common Stock payable in shares of Common Stock) unless (in addition to the obtaining of any consents required elsewhere in the Certificate of Incorporation) (i) any Accruing Dividends accrued but unpaid on all shares of Preferred Stock, whether or not declared, are paid, and (ii) the holders of the Series A Preferred Stock, Series B Preferred Stock and Series C Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, in an amount equal to the product of (1) the dividend payable on each share of Common Stock and (2) the number of shares of Common Stock issuable upon conversion of a share of Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, in each case calculated on the record date for determination of holders entitled to receive such dividend.

2. Liquidation, Dissolution or Winding Up; Certain Mergers, Consolidations and Asset Sales.

2.1 Preferential Payments to Holders of Series C Preferred Stock. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event, the holders of shares of Series C Preferred Stock then outstanding shall be entitled to be paid out of the assets of the Corporation available for distribution to its stockholders before any payment shall be made to the holders of Series A Preferred Stock, Series B Preferred Stock or Common Stock by reason of their ownership thereof, an amount per share equal to the Original Issue Price (as defined below) for the Series C Preferred Stock, plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon (the amount payable pursuant to this sentence, or such greater amount as would be payable under Section 2.4, is hereinafter referred to as the "**Series C Liquidation Amount**"). If upon any such liquidation, dissolution or winding up of the Corporation, the assets of the Corporation available for distribution to its stockholders shall be insufficient to pay the holders of shares of Series C Preferred Stock the full amount to which they shall be entitled under this Subsection 2.1, the holders of shares of Series C Preferred Stock shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full. The "**Original Issue Price**" shall mean, in the case of shares of Series A Preferred Stock, $1.00 per share, in the case of shares of Series B Preferred Stock, $1.70 per share, and, in the case of shares of Series C Preferred Stock, $4.9111 per share, subject in each case to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to a series of Preferred Stock.

2.2 Preferential Payments to Holders of Series A Preferred Stock and Series B Preferred Stock. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event, after the payment of all preferential amounts required to be paid to the holders of shares of Series C Preferred Stock under Subsection 2.1, the holders of shares of Series A Preferred Stock and Series B Preferred Stock then outstanding shall be entitled to be paid out of the assets of the Corporation available for

distribution to its stockholders before any payment shall be made to the holders of Common Stock by reason of their ownership thereof, an amount per share equal to the applicable Original Issue Price, plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon (the amounts payable pursuant to this sentence, or such greater amounts as would be payable under Section 2.4, are hereinafter referred to as the "**Series A Liquidation Amount**" and the "**Series B Liquidation Amount**", as applicable). If upon any such liquidation, dissolution or winding up of the Corporation, the assets of the Corporation available for distribution to its stockholders shall be insufficient to pay the holders of shares of Series A Preferred Stock and Series B Preferred Stock the full amount to which they shall be entitled under this Subsection 2.2, the holders of shares of Series A Preferred Stock and Series B Preferred Stock shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

2.3 Distribution of Remaining Assets to Holders of Common Stock. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event, after the payment of all preferential amounts required to be paid to the holders of shares of Preferred Stock under Subsections 2.1 and 2.2, the remaining assets of the Corporation available for distribution to its stockholders shall be distributed among the holders of the shares of Common Stock, pro rata based on the number of shares held by each such holder.

2.4 As-Converted Payments to Holders of Preferred Stock. Notwithstanding the foregoing, for purposes of determining the amount each holder of shares of Preferred Stock is entitled to receive in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event, each such holder of shares of a series of Preferred Stock shall be deemed to have converted (regardless of whether such holder actually converted) such holder's shares of such series of Preferred Stock into shares of Common Stock pursuant to Section 4 immediately prior to such liquidation, dissolution or winding up of the Corporation or Deemed Liquidation Event if, as a result of an actual conversion, such holder would receive, in the aggregate, an amount greater than the amount that would be distributed to such holder if such holder did not convert such shares of such series of Preferred Stock into shares of Common Stock. If any such holder shall be deemed to have converted shares of Preferred Stock into Common Stock pursuant to this Subsection 2.4, then such holder shall not be entitled to receive any distribution in connection with such liquidation, dissolution or winding up or Deemed Liquidation Event that would otherwise be made to holders of Preferred Stock that have not converted (or have not been deemed to have converted) into shares of Common Stock.

2.5 Deemed Liquidation Events.

2.5.1 Definition. Each of the following events shall be considered a "**Deemed Liquidation Event**" unless (A) (1) the holders of at least 60% of the outstanding shares of Series A Preferred Stock, (2) the holders of a majority of the outstanding shares of Series B Preferred Stock and (3) the holders of a majority of the outstanding shares of Series C-1 Preferred Stock (the "**Requisite Series C-1 Vote**") elect otherwise by written notice sent to the Corporation prior to any such event or (B) (1) the holders of a majority of the outstanding shares

of Preferred Stock, voting together as a single class, which majority must include the holders of the Requisite Series C-1 Vote, elect otherwise by written notice sent to the Corporation prior to any such event and (2) all holders of Preferred Stock are treated in the same manner in connection with such event (except to the extent reflective of differences in liquidation preferences):

(a) a merger or consolidation in which

(i) the Corporation is a constituent party or

(ii) a subsidiary of the Corporation is a constituent party and the Corporation issues shares of its capital stock pursuant to such merger or consolidation,

except any such merger or consolidation involving the Corporation or a subsidiary in which the shares of capital stock of the Corporation outstanding immediately prior to such merger or consolidation continue to represent, or are converted into or exchanged for shares of capital stock that represent, immediately following such merger or consolidation, a majority, by voting power, of the capital stock of (1) the surviving or resulting corporation or (2) if the surviving or resulting corporation is a wholly owned subsidiary of another corporation immediately following such merger or consolidation, the parent corporation of such surviving or resulting corporation (provided that, for the purpose of this Subsection 2.5.1 all shares of Common Stock issuable upon exercise of Options (as defined below) outstanding immediately prior to such merger or consolidation or upon conversion of Convertible Securities (as defined below) outstanding immediately prior to such merger or consolidation shall be deemed to be outstanding immediately prior to such merger or consolidation and, if applicable, converted or exchanged in such merger or consolidation on the same terms as the actual outstanding shares of Common Stock are converted or exchanged); or

(b) the sale, lease, transfer or other disposition, in a single transaction or series of related transactions, by the Corporation or any subsidiary of the Corporation of all or substantially all the assets of the Corporation and its subsidiaries taken as a whole, or the sale or disposition (whether by merger or otherwise) of one or more subsidiaries of the Corporation if substantially all of the assets of the Corporation and its subsidiaries taken as a whole are held by such subsidiary or subsidiaries, except where such sale, lease, transfer or other disposition is to a wholly owned subsidiary of the Corporation; or

(c) the exclusive license, in a single transaction or series of related transactions, by the Corporation or any subsidiary of the Corporation of all or substantially all the rights to all or substantially all of the assets of the Corporation and its subsidiaries taken as a whole, except where such exclusive license is to a wholly owned subsidiary of the Corporation.

2.5.2 Effecting a Deemed Liquidation Event.

(a) The Corporation shall not have the power to effect a Deemed Liquidation Event referred to in Subsection 2.5.1(a)(i) unless the agreement or plan of merger or consolidation for such transaction (the "**Merger Agreement**") provides that the consideration payable to the stockholders of the Corporation shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1, 2.2, 2.3 and 2.4.

(b) In the event of a Deemed Liquidation Event referred to in Subsection 2.5.1(a)(ii) or Subsection 2.5.1(b), if the Corporation does not effect a dissolution of the Corporation under the General Corporation Law within 90 days after such Deemed Liquidation Event, then (i) the Corporation shall send a written notice to each holder of Preferred Stock no later than the 90th day after the Deemed Liquidation Event advising such holders of their right (and the requirements to be met to secure such right) pursuant to the terms of the following clause (ii) to require the redemption of such shares of Preferred Stock, and (ii) if the holders of a majority of the then outstanding shares of Preferred Stock so request in a written instrument delivered to the Corporation not later than 120 days after such Deemed Liquidation Event, the Corporation shall use the consideration received by the Corporation for such Deemed Liquidation Event (net of any retained liabilities associated with the assets sold or technology licensed, as determined in good faith by the Board of Directors of the Corporation), together with any other assets of the Corporation available for distribution to its stockholders, all to the extent permitted by Delaware law governing distributions to stockholders (the "**Available Proceeds**"), on the 150th day after such Deemed Liquidation Event (the "**Redemption Date**"), to redeem all outstanding shares of Preferred Stock at a price per share equal to (a) the Series A Liquidation Amount, in the case of Series A Preferred Stock, (b) the Series B Liquidation Amount, in the case of Series B Preferred Stock, or (c) the Series C Liquidation Amount, in the case of Series C Preferred Stock (the amount payable pursuant to this sentence is hereinafter referred to as the "**Redemption Price**"). Notwithstanding the foregoing, in the event of a redemption pursuant to the preceding sentence, if the Available Proceeds are not sufficient to redeem all outstanding shares of Preferred Stock, the Corporation shall first redeem all outstanding shares of Series C Preferred Stock (or, if the Available Proceeds are not sufficient to redeem all outstanding shares of Series C Preferred Stock, a pro rata portion of each holder's shares of Series C Preferred Stock), and then, to the extent Available Proceeds remain available for redemption, redeem a pro rata portion of each holder's shares of Series A Preferred Stock and Series B Preferred Stock, and then, redeem the remaining shares as soon as it may lawfully do so under Delaware law governing distributions to stockholders. The Corporation shall promptly send written notice of the mandatory redemption (the "**Redemption Notice**") to each holder of record of Preferred Stock setting forth (i) the Redemption Date and Redemption Price, (ii) the date upon which the holder's right to convert shares terminates (as determined in accordance with Subsection 4.1), and (iii) that the holder is to surrender to the Corporation, in the manner and at the place designated, his, her or its certificate or certificates representing the shares of Preferred Stock to be redeemed. On or before the Redemption Date, each holder of shares of Preferred Stock, unless such holder has exercised his, her or its right to convert such shares as provided in Section 4.1, shall surrender the certificate or certificates representing such shares (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation, in the manner and at the place designated in the Redemption Notice, and thereupon the Redemption Price shall be payable to the order of the person whose name appears on such certificate or certificates as the owner thereof. If the Redemption Notice shall have been duly given, and if on the Redemption Date the Redemption Price payable upon redemption of the shares of Preferred Stock is paid or tendered for payment

or deposited with an independent payment agent so as to be available therefor in a timely manner, then notwithstanding that the certificates evidencing any of the shares of Preferred Stock so called for redemption shall not have been surrendered, dividends with respect to such shares of Preferred Stock shall cease to accrue after such date and all rights with respect to such shares shall forthwith after the Redemption Date terminate, except only the right of the holders to receive the Redemption Price without interest upon surrender of their certificate or certificates therefor. Prior to the distribution or redemption provided for in this Subsection 2.5.2(b), the Corporation shall not expend or dissipate the consideration received for such Deemed Liquidation Event, except to discharge expenses incurred in connection with such Deemed Liquidation Event or in the ordinary course of business.

2.5.3 Amount Deemed Paid or Distributed. The amount deemed paid or distributed to the holders of capital stock of the Corporation upon any such merger, consolidation, sale, transfer, exclusive license, other disposition or redemption shall be the cash or the value of the property, rights or securities paid or distributed to such holders by the Corporation or the acquiring person, firm or other entity. The value of such property, rights or securities shall be determined in good faith by the Board of Directors of the Corporation.

2.5.4 Allocation of Escrow. In the event of a Deemed Liquidation Event pursuant to Subsection 2.5.1(a)(i), if any portion of the consideration payable to the stockholders of the Corporation is placed into escrow and/or is payable to the stockholders of the Corporation subject to contingencies, the merger agreement shall provide that (a) the portion of such consideration that is not placed in escrow and not subject to any contingencies (the "**Initial Consideration**") shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1, 2.2, 2.3 and 2.4 as if the Initial Consideration were the only consideration payable in connection with such Deemed Liquidation Event and (b) any additional consideration which becomes payable to the stockholders of the Corporation upon release from escrow or satisfaction of contingencies shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1, 2.2, 2.3 and 2.4 after taking into account the previous payment of the Initial Consideration as part of the same transaction.

3. Voting.

3.1 General. On any matter presented to the stockholders of the Corporation for their action or consideration at any meeting of stockholders of the Corporation (or by written consent of stockholders in lieu of meeting), each holder of outstanding shares of Preferred Stock shall be entitled to cast the number of votes equal to the number of whole shares of Common Stock into which the shares of Preferred Stock held by such holder are convertible as of the record date for determining stockholders entitled to vote on such matter. Except as provided by law or by the other provisions of the Certificate of Incorporation, holders of Preferred Stock shall vote together with the holders of Common Stock as a single class.

3.2 Election of Directors. The holders of record of the shares of Series A Preferred Stock, exclusively and as a separate class, shall be entitled to elect three (3) directors of the Corporation (the "**Series A Directors**"). The holders of record of the shares of Common Stock and of any other class or series of voting stock (including the Series A Preferred Stock, Series B Preferred Stock and Series C Preferred Stock), exclusively and voting together as a

single class, shall be entitled to elect the balance of the total number of directors of the Corporation. At any meeting held for the purpose of electing a director, the presence in person or by proxy of the holders of a majority of the outstanding shares of the class or series entitled to elect such director shall constitute a quorum for the purpose of electing such director. The rights of the holders of the Series A Preferred Stock under the first sentence of this Subsection 3.2 shall terminate on the first date following the Series C Original Issue Date (as defined below) on which there are issued and outstanding less than 1,000,000 shares of Series A Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A Preferred Stock).

3.3 Preferred Stock Protective Provisions. At any time when at least 1,000,000 shares of Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Preferred Stock) are outstanding, the Corporation shall not, either directly or indirectly, by amendment, merger, consolidation or otherwise, do any of the following without (in addition to any other vote required by law or the Certificate of Incorporation) (i) the written consent or affirmative vote of the holders of a majority of the then outstanding shares of Preferred Stock, voting together as a single class, given in writing or by vote at a meeting, consenting or voting (as the case may be) together as a class and (ii) the approval of the Corporation's Board of Directors (which approval must include all of the Independent Directors (as defined in the Second Amended and Restated Stockholders' Voting Agreement by and among the Corporation and certain stockholders, dated on or about the date of the filing of this Third Amended and Restated Certificate of Incorporation with the Secretary of State of the State of Delaware, as amended and/or restated from time to time) of which there must be at least two (2):

(a) liquidate, dissolve or wind-up the business and affairs of the Corporation, effect any Deemed Liquidation Event, or consent to any of the foregoing;

(b) amend, alter or repeal any provision of the Certificate of Incorporation or Bylaws of the Corporation;

(c) create, or authorize the creation of, or issue or obligate itself to issue shares of, any additional class or series of capital stock unless the same ranks junior to the Preferred Stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends and rights of redemption, or increase the authorized number of shares of Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock or increase the authorized number of shares of any additional class or series of capital stock unless the same ranks junior to the Preferred Stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends and rights of redemption;

(d) purchase or redeem (or permit any subsidiary to purchase or redeem) or pay or declare any dividend or make any distribution on, any shares of capital stock of the Corporation other than (i) redemptions of or dividends or distributions on the Preferred Stock as expressly authorized herein, (ii) dividends or other distributions payable on the Common Stock solely in the form of additional shares of Common Stock and (iii) repurchases of stock from former employees, officers, directors, consultants or other persons

who performed services for the Corporation or any subsidiary in connection with the cessation of such employment or service at the lower of the original purchase price or the then-current fair market value thereof; or

(e) create any subsidiary.

3.4 Series B Preferred Stock Protective Provisions. At any time when at least 1,000,000 shares of Series B Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B Preferred Stock) are outstanding, the Corporation shall not, and shall not permit any of its subsidiaries to, except for Excluded Transactions (as defined below), enter into or modify any agreement or enter into any transaction between the Corporation or one of its subsidiaries and a holder of Series A Preferred Stock or any of its Affiliated Parties (defined below) other than pursuant to an exercise by such holder of its rights hereunder or under any other agreement in effect on the Series C Original Issue Date without (in addition to any other vote required by law or the Certificate of Incorporation) the written consent or affirmative vote of the holders of a majority of the then outstanding shares of Series B Preferred Stock, given in writing or by vote at a meeting. "Excluded Transactions" means (a) equity financings in which holders of Series B Preferred Stock and Series C Preferred Stock are offered the opportunity to participate pursuant to Section 3 of the Second Amended and Restated Investor Rights Agreement, by and among the Corporation and certain stockholders of the Corporation, dated on or about the date of the filing of this Third Amended and Restated Certificate of Incorporation, and (b) transactions made on an arm's-length basis, pursuant to reasonable requirements of the Corporation's business and on reasonable and customary terms at least as favorable to the Corporation as would reasonably be expected to have been obtained from a third party. The Corporation shall provide any holder of more than 1,000,000 shares of Series B Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B Preferred Stock) prior notice of any Excluded Transaction that encumbers or disposes of the Corporation's interest in any material intellectual property outside the ordinary course of business, involves more than $500,000 per year or is otherwise material to the Corporation. "Affiliated Party" means, with respect to any Stockholder, any person or entity which, directly or indirectly, controls, is controlled by or is under common control with such Stockholder, including, without limitation, any general partner, officer or director of such Stockholder and any venture capital fund now or hereafter existing which is controlled by one or more general partners of, or shares the same management company as, such Stockholder.

3.5 Series C Preferred Stock Protective Provision. At any time when at least 500,000 shares of Series C Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series C Preferred Stock) are outstanding, the Corporation shall not change the preferences or rights of the Series C Preferred Stock in a manner that is adverse to the Series C Preferred Stock and not similarly adverse to the Series A Preferred Stock and Series B Preferred Stock without (in addition to any other vote required by law or the Certificate of Incorporation) the written consent or affirmative vote of the holders of a majority the outstanding shares of Series C Preferred Stock, given in writing or by vote at a meeting.

3.6 Series C-1 Preferred Stock Protective Provisions. At any time when at least 500,000 shares of Series C-1 Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series C-1 Preferred Stock) are outstanding, (a) the Corporation shall not, and shall not permit any of its subsidiaries to, except for Excluded Transactions, enter into or modify any agreement or enter into any transaction between the Corporation or one of its subsidiaries and a holder of Series A Preferred Stock or any of its Affiliated Parties other than pursuant to an exercise by such holder of its rights hereunder or under any other agreement in effect on the Series C Original Issue Date; and (b) and the Corporation shall not change the preferences or rights of the Series C-1 Preferred Stock in a manner that is adverse to the Series C-1 Preferred Stock without (in addition to any other vote required by law or the Certificate of Incorporation), in either case, the written consent or affirmative vote of the holders of the Requisite Series C-1 Vote, given in writing or by vote at a meeting. The Corporation shall provide any holder of more than 100,000 shares of Series C-1 Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series C-1 Preferred Stock) prior notice of any Excluded Transaction that encumbers or disposes of the Corporation's interest in any material intellectual property outside the ordinary course of business, involves more than $500,000 per year or is otherwise material to the Corporation.

3.7 Series C-2 Preferred Stock Protective Provision. At any time when at least 500,000 shares of Series C-2 Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series C-2 Preferred Stock) are outstanding, the Corporation shall not change the preferences or rights of the Series C-2 Preferred Stock in a manner that is adverse to the Series C-2 Preferred Stock and not similarly adverse to the Series C-1 Preferred Stock without (in addition to any other vote required by law or the Certificate of Incorporation) the written consent or affirmative vote of the holders of a majority the outstanding shares of Series C-2 Preferred Stock, given in writing or by vote at a meeting.

4. Optional Conversion.

The holders of Preferred Stock shall have conversion rights as follows (the "**Conversion Rights**"):

4.1 Right to Convert.

4.1.1 Conversion Ratio.

(a) Each share of Series A Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Series A Original Issue Price by the Series A Conversion Price (as defined below) in effect at the time of conversion. The "**Series A Conversion Price**" is currently equal to $1.00. Such Series A Conversion Price, and the rate at which shares of Series A Preferred Stock may be converted into shares of Common Stock, shall be subject to adjustment as provided below.

(b) Each share of Series B Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Series B Original Issue Price by the Series B Conversion Price (as defined below) in effect at the time of conversion. The "**Series B Conversion Price**" shall initially be equal to $1.70. Such initial Series B Conversion Price, and the rate at which shares of Series B Preferred Stock may be converted into shares of Common Stock, shall be subject to adjustment as provided below.

(c) Each share of Series C Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and nonassessable shares of Common Stock as is determined by dividing the Series C Original Issue Price by the Series C Conversion Price (as defined below) in effect at the time of conversion. The "**Series C Conversion Price**" shall initially be equal to $4.9111. Such initial Series C Conversion Price, and the rate at which shares of Series C Preferred Stock may be converted into shares of Common Stock, shall be subject to adjustment as provided below.

4.1.2 Termination of Conversion Rights. In the event of a liquidation, dissolution or winding up of the Corporation or a Deemed Liquidation Event, the Conversion Rights shall terminate at the close of business on the last full day preceding the date fixed for the payment of any such amounts distributable on such event to the holders of Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be.

4.2 Fractional Shares. No fractional shares of Common Stock shall be issued upon conversion of the Preferred Stock. In lieu of any fractional shares to which the holder would otherwise be entitled, the Corporation shall pay cash equal to such fraction multiplied by the fair market value of a share of Common Stock as determined in good faith by the Board of Directors of the Corporation. Whether or not fractional shares would be issuable upon such conversion shall be determined on the basis of the total number of shares of Preferred Stock the holder is at the time converting into Common Stock and the aggregate number of shares of Common Stock issuable upon such conversion.

4.3 Mechanics of Conversion.

4.3.1 Notice of Conversion. In order for a holder of Preferred Stock to voluntarily convert shares of Preferred Stock into shares of Common Stock, such holder shall surrender the certificate or certificates for such shares of Preferred Stock (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate), at the office of the transfer agent for the applicable series of Preferred Stock (or at the principal office of the Corporation if the Corporation serves as its own transfer agent), together with written notice that such holder elects to convert all or any number of the shares of the Preferred Stock represented by such certificate or certificates and, if applicable, any event on which such conversion is contingent. Such notice shall state such holder's name or the names of the nominees in which such holder wishes the certificate or

certificates for shares of Common Stock to be issued. If required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by a written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or his, her or its attorney duly authorized in writing. The close of business on the date of receipt by the transfer agent (or by the Corporation if the Corporation serves as its own transfer agent) of such certificates (or lost certificate affidavit and agreement) and notice shall be the time of conversion (the "**Conversion Time**"), and the shares of Common Stock issuable upon conversion of the shares represented by such certificate shall be deemed to be outstanding of record as of such date. The Corporation shall, as soon as practicable after the Conversion Time, (i) issue and deliver to such holder of Preferred Stock, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable upon such conversion in accordance with the provisions hereof and a certificate for the number (if any) of the shares of Preferred Stock, as the case may be, represented by the surrendered certificate that were not converted into Common Stock, (ii) pay in cash such amount as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and (iii) pay all declared but unpaid dividends on the shares of Preferred Stock converted.

4.3.2 Reservation of Shares. The Corporation shall at all times when any Preferred Stock shall be outstanding, reserve and keep available out of its authorized but unissued capital stock, for the purpose of effecting the conversion of the Preferred Stock, such number of its duly authorized shares of Common Stock as shall from time to time be sufficient to effect the conversion of all outstanding Preferred Stock; and if at any time the number of authorized but unissued shares of Common Stock shall not be sufficient to effect the conversion of all then outstanding shares of the Preferred Stock, the Corporation shall take such corporate action as may be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes, including, without limitation, engaging in best efforts to obtain the requisite stockholder approval of any necessary amendment to the Certificate of Incorporation. Before taking any action which would cause an adjustment reducing the Series A Conversion Price, Series B Conversion Price or Series C Conversion Price below the then par value of the shares of Common Stock issuable upon conversion of the applicable series of Preferred Stock, the Corporation will take any corporate action which may, in the opinion of its counsel, be necessary in order that the Corporation may validly and legally issue fully paid and nonassessable shares of Common Stock at such adjusted Series A Conversion Price, Series B Conversion Price or Series C Conversion Price, as the case may be.

4.3.3 Effect of Conversion. All shares of Preferred Stock which shall have been surrendered for conversion as herein provided shall no longer be deemed to be outstanding and all rights with respect to such shares shall immediately cease and terminate at the Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor, to receive payment in lieu of any fraction of a share otherwise issuable upon such conversion as provided in Subsection 4.2 and to receive payment of any dividends declared but unpaid thereon. Any shares of Preferred Stock so converted shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of such series of Preferred Stock accordingly.

4.3.4 No Further Adjustment. Upon any such conversion, no adjustment to the Series A Conversion Price, Series B Conversion Price or Series C Conversion Price shall be made for any declared but unpaid dividends on the Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, surrendered for conversion or on the Common Stock delivered upon conversion.

4.3.5 Taxes. The Corporation shall pay any and all issue and other similar taxes that may be payable in respect of any issuance or delivery of shares of Common Stock upon conversion of shares of Preferred Stock pursuant to this Section 4. The Corporation shall not, however, be required to pay any tax which may be payable in respect of any transfer involved in the issuance and delivery of shares of Common Stock in a name other than that in which the shares of Preferred Stock so converted were registered, and no such issuance or delivery shall be made unless and until the person or entity requesting such issuance has paid to the Corporation the amount of any such tax or has established, to the satisfaction of the Corporation, that such tax has been paid.

4.4 Adjustments to Conversion Price for Diluting Issues.

4.4.1 Special Definitions. For purposes of this Article Fourth, the following definitions shall apply:

(a) "**Option**" shall mean rights, options or warrants to subscribe for, purchase or otherwise acquire Common Stock or Convertible Securities.

(b) "**Series C Original Issue Date**" shall mean the date on which the first share of Series C Preferred Stock was issued.

(c) "**Convertible Securities**" shall mean any evidences of indebtedness, shares or other securities directly or indirectly convertible into or exchangeable for Common Stock, but excluding Options.

(d) "**Additional Shares of Common Stock**" shall mean all shares of Common Stock issued (or, pursuant to Subsection 4.4.3 below, deemed to be issued) by the Corporation on or after the Series C Original Issue Date, other than (1) the following shares of Common Stock and (2) shares of Common Stock deemed issued pursuant to the following Options and Convertible Securities (clauses (1) and (2), collectively, "**Exempted Securities**"):

(i) shares of Common Stock, Options or Convertible Securities issued as a dividend or distribution on Series A Preferred Stock, Series B Preferred Stock, and Series C Preferred Stock, provided (a) the number of shares of Common Stock, Options or Convertible Securities issued as a dividend or distribution on a share of Series A Preferred Stock multiplied by the number of shares of Common Stock into which a share of Series A Preferred Stock is then convertible is equal to both (b) the number of shares of Common Stock, Options or

Convertible Securities issued as a dividend or distribution on a share of Series B Preferred Stock multiplied by the number of shares of Common Stock into which a share of Series B Preferred Stock is then convertible and (c) the number of shares of Common Stock, Options or Convertible Securities issued as a dividend or distribution on a share of Series C Preferred Stock multiplied by the number of shares of Common Stock into which a share of Series C Preferred Stock is then convertible;

(ii) shares of Common Stock, Options or Convertible Securities issued by reason of a dividend, stock split, split-up or other distribution on shares of Common Stock that is covered by Subsection 4.5, 4.6, 4.7 or 4.8;

(iii) shares of Common Stock or Options issued to employees or directors of, or consultants or advisors to, the Corporation or any of its subsidiaries pursuant to the Corporation's 2007 Stock Incentive Plan or any other plan, agreement or arrangement approved by the Board of Directors of the Corporation, including a majority of the Series A Directors and all of the Independent Directors;

(iv) shares of Common Stock or Convertible Securities actually issued upon the exercise of Options or shares of Common Stock actually issued upon the conversion or exchange of Convertible Securities, in each case provided such issuance is pursuant to the terms of such Option or Convertible Security;

(v) shares of Common Stock, Options or Convertible Securities issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction approved by the Board of Directors of the Corporation, including a majority of the Series A Directors and all of the Independent Directors;

(vi) shares of Common Stock, Options or Convertible Securities issued pursuant to the acquisition of another corporation by the Corporation by merger, purchase of substantially all of the assets or other

reorganization or to a joint venture agreement, provided, that such issuances are approved by the Board of Directors of the Corporation, including a majority of the Series A Directors and all of the Independent Directors;

(vii) shares of Common Stock, Options or Convertible Securities issued in connection with sponsored research, collaboration, technology license, development, OEM, marketing or other similar agreements or strategic partnerships approved by the Board of Directors of the Corporation, including a majority of the Series A Directors and all of the Independent Directors; or

(viii) shares of Common Stock issued or deemed issued as a result of a decrease in the Conversion Price of any series of Preferred Stock.

(e) "**In-the-Money Options**" shall mean Options that have (i) an exercise price per share of Common Stock that is less than or equal to (ii) the consideration per share paid for the Additional Shares of Common Stock (in each case, measured on an as-converted to Common Stock basis).

4.4.2 No Adjustment of Conversion Prices. No adjustment in the Series A Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of at least 60% of the then outstanding shares of Series A Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock. No adjustment in the Series B Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of a majority of the then outstanding shares of Series B Preferred Stock agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock. No adjustment in the Series C Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of a majority of the outstanding shares of Series C Preferred Stock, including holders of the Requisite Series C-1 Vote, agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock. No adjustment in the Series A Conversion Price, Series B Conversion Price or Series C Conversion Price shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock at less than $0.75 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization) if the Corporation receives written notice from the holders of a majority of the then outstanding shares of Preferred Stock, voting together as a single class, which majority must include the holders of the Requisite Series C-1 Vote, agreeing that no such adjustment shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock.

4.4.3 Deemed Issue of Additional Shares of Common Stock.

(a) If the Corporation at any time or from time to time on or after the Series C Original Issue Date shall issue any Options or Convertible Securities (excluding Options or Convertible Securities which are themselves Exempted Securities) or shall fix a record date for the determination of holders of any class of securities entitled to receive any such Options or Convertible Securities, then the maximum number of shares of Common Stock (as set forth in the instrument relating thereto, assuming the satisfaction of any conditions to exercisability, convertibility or exchangeability but without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or, in the case of Convertible Securities and Options therefor, the conversion or exchange of such Convertible Securities, shall be deemed to be Additional Shares of Common Stock issued as of the time of such issue or, in case such a record date shall have been fixed, as of the close of business on such record date.

(b) If the terms of any Option or Convertible Security, the issuance of which resulted in an adjustment to the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price pursuant to the terms of Subsection 4.4.4 or 4.4.5, are revised as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase or decrease in the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any such Option or Convertible Security or (2) any increase or decrease in the consideration payable to the Corporation upon such exercise, conversion and/or exchange, then, effective upon such increase or decrease becoming effective, the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price, as applicable, computed upon the original issue of such Option or Convertible Security (or upon the occurrence of a record date with respect thereto) shall be readjusted to such Series A Conversion Price, Series B Conversion Price or the Series C Conversion Price, as applicable, as would have obtained had such revised terms been in effect upon the original date of issuance of such Option or Convertible Security. Notwithstanding the foregoing, no readjustment pursuant to this clause (b) shall have the effect of increasing the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price, as applicable, to an amount which exceeds the lower of (i) the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price, as applicable, in effect immediately prior to the original adjustment made as a result of the issuance of such Option or Convertible Security, or (ii) the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price, as applicable, that would have resulted from any issuances of Additional Shares of Common Stock (other than deemed issuances of Additional Shares of Common Stock as a result of the issuance of such Option or Convertible Security) between the original adjustment date and such readjustment date.

(c) If the terms of any Option or Convertible Security (excluding Options or Convertible Securities which are themselves Exempted Securities), the issuance of which did not result in an adjustment to the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price pursuant to the terms of Subsection 4.4.4 or 4.4.5 (either because the consideration per share (determined pursuant to Subsection 4.4.6) of the

Additional Shares of Common Stock subject thereto was equal to or greater than the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price, as applicable, then in effect, or because such Option or Convertible Security was issued before the Series C Original Issue Date), are revised on or after the Series C Original Issue Date as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase in the number of shares of Common Stock issuable upon the exercise, conversion or exchange of any such Option or Convertible Security or (2) any decrease in the consideration payable to the Corporation upon such exercise, conversion or exchange, then such Option or Convertible Security, as so amended or adjusted, and the Additional Shares of Common Stock subject thereto (determined in the manner provided in Subsection 4.4.3(a)) shall be deemed to have been issued effective upon such increase or decrease becoming effective.

(d) Upon the expiration or termination of any unexercised Option or unconverted or unexchanged Convertible Security (or portion thereof) which resulted (either upon its original issuance or upon a revision of its terms) in an adjustment to the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price pursuant to the terms of Subsections 4.4.4 or 4.4.5, the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price, as applicable, shall be readjusted to such Series A Conversion Price, Series B Conversion Price or Series C Conversion Price, as applicable, as would have obtained had such Option or Convertible Security (or portion thereof) never been issued.

(e) If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, is calculable at the time such Option or Convertible Security is issued or amended but is subject to adjustment based upon subsequent events, any adjustment to the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price provided for in this Subsection 4.4.3 shall be effected at the time of such issuance or amendment based on such number of shares or amount of consideration without regard to any provisions for subsequent adjustments (and any subsequent adjustments shall be treated as provided in clauses (b) and (c) of this Subsection 4.4.3). If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, cannot be calculated at all at the time such Option or Convertible Security is issued or amended, any adjustment to the Series A Conversion Price, Series B Conversion Price or the Series C Conversion Price that would result under the terms of this Subsection 4.4.3 at the time of such issuance or amendment shall instead be effected at the time such number of shares and/or amount of consideration is first calculable (even if subject to subsequent adjustments), assuming for purposes of calculating such adjustment to the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price that such issuance or amendment took place at the time such calculation can first be made.

4.4.4 Adjustment of Series A Conversion Price Upon Issuance of Additional Shares of Common Stock. In the event the Corporation shall at any time on or after the Series C Original Issue Date issue Additional Shares of Common Stock (including

Additional Shares of Common Stock deemed to be issued pursuant to Subsection 4.4.3), without consideration or for a consideration per share less than the Series A Conversion Price in effect immediately prior to such issue, then the Series A Conversion Price shall be reduced, concurrently with such issue, to a price (calculated to the nearest one-hundredth of a cent) determined in accordance with the following formula:

$$CP_2 = CP_1 * (A + B) \div (A + C).$$

For purposes of the foregoing formula, the following definitions shall apply:

(a) "$CP_2$" shall mean the Series A Conversion Price in effect immediately after such issue of Additional Shares of Common Stock

(b) "$CP_1$" shall mean the Series A Conversion Price in effect immediately prior to such issue of Additional Shares of Common Stock;

(c) "A" shall mean the number of shares of Common Stock outstanding immediately prior to such issue of Additional Shares of Common Stock (treating for this purpose as outstanding all shares of Common Stock issuable upon exercise of In-the-Money Options outstanding immediately prior to such issue or upon conversion or exchange of Convertible Securities (including the Preferred Stock) outstanding (assuming exercise of any outstanding In-the Money Options therefor) immediately prior to such issue);

(d) "B" shall mean the number of shares of Common Stock that would have been issued if such Additional Shares of Common Stock had been issued at a price per share equal to $CP_1$ (determined by dividing the aggregate consideration received by the Corporation in respect of such issue by $CP_1$); and

(e) "C" shall mean the number of such Additional Shares of Common Stock issued in such transaction.

4.4.5 Adjustment of Series B Conversion Price Upon Issuance of Additional Shares of Common Stock. In the event the Corporation shall at any time on or after the Series C Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Subsection 4.4.3), without consideration or for a consideration per share less than the Series B Conversion Price in effect immediately prior to such issue, then the Series B Conversion Price shall be reduced, concurrently with such issue, to a price (calculated to the nearest one-hundredth of a cent) determined in accordance with the following formula:

$$CP_2 = CP_1 * (A + B) \div (A + C).$$

For purposes of the foregoing formula, the following definitions shall apply:

(a) "$CP_2$" shall mean the Series B Conversion Price in effect immediately after such issue of Additional Shares of Common Stock

(b) "$CP_1$" shall mean the Series B Conversion Price in effect immediately prior to such issue of Additional Shares of Common Stock;

(c) "A" shall mean the number of shares of Common Stock outstanding immediately prior to such issue of Additional Shares of Common Stock (treating for this purpose as outstanding all shares of Common Stock issuable upon exercise of In-the-Money Options outstanding immediately prior to such issue or upon conversion or exchange of Convertible Securities (including the Preferred Stock) outstanding (assuming exercise of any outstanding In-the-Money Options therefor) immediately prior to such issue);

(d) "B" shall mean the number of shares of Common Stock that would have been issued if such Additional Shares of Common Stock had been issued at a price per share equal to $CP_1$ (determined by dividing the aggregate consideration received by the Corporation in respect of such issue by $CP_1$); and

(e) "C" shall mean the number of such Additional Shares of Common Stock issued in such transaction.

4.4.6 Adjustment of Series C Conversion Price Upon Issuance of Additional Shares of Common Stock. In the event the Corporation shall at any time on or after the Series C Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Subsection 4.4.3), without consideration or for a consideration per share less than the Series C Conversion Price in effect immediately prior to such issue, then the Series C Conversion Price shall be reduced, concurrently with such issue, to a price (calculated to the nearest one-hundredth of a cent) determined in accordance with the following formula:

$$CP_2 = CP_1 * (A + B) \div (A + C).$$

For purposes of the foregoing formula, the following definitions shall apply:

(a) "$CP_2$" shall mean the Series C Conversion Price in effect immediately after such issue of Additional Shares of Common Stock

(b) "$CP_1$" shall mean the Series C Conversion Price in effect immediately prior to such issue of Additional Shares of Common Stock;

(c) "A" shall mean the number of shares of Common Stock outstanding immediately prior to such issue of Additional Shares of Common Stock (treating for this purpose as outstanding all shares of Common Stock issuable upon exercise of In-the-Money Options outstanding immediately prior to such issue or upon conversion or exchange of Convertible Securities (including the Preferred Stock) outstanding (assuming exercise of any outstanding In-the-Money Options therefor) immediately prior to such issue);

(d) "B" shall mean the number of shares of Common Stock that would have been issued if such Additional Shares of Common Stock had been issued at a price per share equal to $CP_1$ (determined by dividing the aggregate consideration received by the Corporation in respect of such issue by $CP_1$); and

(e) “C” shall mean the number of such Additional Shares of Common Stock issued in such transaction.

4.4.7 Determination of Consideration. For purposes of this Subsection 4.4, the consideration received by the Corporation for the issue of any Additional Shares of Common Stock shall be computed as follows:

(a) Cash and Property: Such consideration shall:

(i) insofar as it consists of cash, be computed at the aggregate amount of cash received by the Corporation, excluding amounts paid or payable for accrued interest;

(ii) insofar as it consists of property other than cash, be computed at the fair market value thereof at the time of such issue, as determined in good faith by the Board of Directors of the Corporation (including a majority of the Series A Directors); and

(iii) in the event Additional Shares of Common Stock are issued together with other shares or securities or other assets of the Corporation for consideration which covers both, be the proportion of such consideration so received, computed as provided in clauses (i) and (ii) above, as determined in good faith by the Board of Directors of the Corporation (including a majority of the Series A Directors).

(b) Options and Convertible Securities. The consideration per share received by the Corporation for Additional Shares of Common Stock deemed to have been issued pursuant to Subsection 4.4.3, relating to Options and Convertible Securities, shall be determined by dividing

(i) the total amount, if any, received or receivable by the Corporation as consideration for the issue of such Options or Convertible Securities, plus the minimum aggregate amount of additional consideration (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such consideration) payable to the Corporation upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities, by

(ii) the maximum number of shares of Common Stock (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities.

4.4.8 Multiple Closing Dates. In the event the Corporation shall issue on more than one date Additional Shares of Common Stock that are a part of one transaction or a series of related transactions and that would result in an adjustment to the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price pursuant to the terms of Subsections 4.4.4, 4.4.5 or 4.4.6, and such issuance dates occur within a period of no more than 90 days from the first such issuance to the final such issuance, then, upon the final such issuance, the Series A Conversion Price, the Series B Conversion Price or the Series C Conversion Price, as applicable, shall be readjusted to give effect to all such issuances as if they occurred on the date of the first such issuance (and without giving effect to any additional adjustments as a result of any such subsequent issuances within such period).

4.5 Adjustment for Stock Splits and Combinations. If the Corporation shall at any time or from time to time on or after the Series C Original Issue Date effect a subdivision of the outstanding Common Stock, the Series A Conversion Price, Series B Conversion Price and Series C Conversion Price in effect immediately before that subdivision shall be proportionately decreased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be increased in proportion to such increase in the aggregate number of shares of Common Stock outstanding. If the Corporation shall at any time or from time to time on or after the Series B Original Issue Date combine the outstanding shares of Common Stock, the Series A Conversion Price, Series B Conversion Price and Series C Conversion Price in effect immediately before the combination shall be proportionately increased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be decreased in proportion to such decrease in the aggregate number of shares of Common Stock outstanding. Any adjustment under this subsection shall become effective at the close of business on the date the subdivision or combination becomes effective.

4.6 Adjustment for Certain Dividends and Distributions. In the event the Corporation at any time or from time to time on or after the Series C Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable on the Common Stock in additional shares of Common Stock, then and in each such event the Series A Conversion Price, Series B Conversion Price and Series C Conversion Price in effect immediately before such event shall be decreased as of the time of such issuance or, in the event such a record date shall have been fixed, as of the close of business on such record date, by multiplying the Series A Conversion Price, Series B Conversion Price or Series C Conversion Price, as the case may be, then in effect by a fraction:

(1) the numerator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date, and

(2) the denominator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date plus the number of shares of Common Stock issuable in payment of such dividend or distribution.

Notwithstanding the foregoing, (a) if such record date shall have been fixed and such dividend is not fully paid or if such distribution is not fully made on the date fixed therefor, the Series A Conversion Price, Series B Conversion Price and Series C Conversion Price shall be recomputed accordingly as of the close of business on such record date and thereafter the Series A Conversion Price, Series B Conversion Price and Series C Conversion Price shall be adjusted pursuant to this subsection as of the time of actual payment of such dividends or distributions; and (b) no such adjustment shall be made with respect to the Series A Conversion Price, Series B Conversion Price or Series C Conversion Price if the holders of Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, simultaneously receive a dividend or other distribution of shares of Common Stock in a number equal to the number of shares of Common Stock as they would have received if all outstanding shares of Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, had been converted into Common Stock on the date of such event.

4.7 Adjustments for Other Dividends and Distributions. In the event the Corporation at any time or from time to time on or after the Series C Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable in securities of the Corporation (other than a distribution of shares of Common Stock in respect of outstanding shares of Common Stock) or in other property and the provisions of Section 1 do not apply to such dividend or distribution, then and in each such event the holders of Series A Preferred Stock, Series B Preferred Stock and Series C Preferred Stock shall receive, simultaneously with the distribution to the holders of Common Stock, a dividend or other distribution of such securities or other property in an amount equal to the amount of such securities or other property as they would have received if all outstanding shares of Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, had been converted into Common Stock on the date of such event.

4.8 Adjustment for Merger or Reorganization, etc. Subject to the provisions of Subsection 2.3, if there shall occur any reorganization, recapitalization, reclassification, consolidation or merger involving the Corporation in which the Common Stock (but not either the Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock) is converted into or exchanged for securities, cash or other property (other than a transaction covered by

Subsections 4.4, 4.5, 4.7 or 4.8), then, following any such reorganization, recapitalization, reclassification, consolidation or merger, each share of Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, shall thereafter be convertible in lieu of the Common Stock into which it was convertible prior to such event into the kind and amount of securities, cash or other property which a holder of the number of shares of Common Stock of the Corporation issuable upon conversion of one share of Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, immediately prior to such reorganization, recapitalization, reclassification, consolidation or merger would have been entitled to receive pursuant to such transaction; and, in such case, appropriate adjustment (as determined in good faith by the Board of Directors of the Corporation) shall be made in the application of the provisions in this Section 4 with respect to the rights and interests thereafter of the holders of the Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, to the end that the provisions set forth in this Section 4 (including provisions with respect to changes in and other adjustments of the Series A Conversion Price, Series B Conversion Price or Series C Conversion Price, as the case may be) shall thereafter be applicable, as nearly as reasonably may be, in relation to any securities or other property thereafter deliverable upon the conversion of the Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be.

4.9 Certificate as to Adjustments. Upon the occurrence of each adjustment or readjustment of the Series A Conversion Price, Series B Conversion Price or Series C Conversion Price pursuant to this Section 4, the Corporation at its expense shall, as promptly as reasonably practicable but in any event not later than 10 days thereafter, compute such adjustment or readjustment in accordance with the terms hereof and furnish to each holder of Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, a certificate setting forth such adjustment or readjustment (including the kind and amount of securities, cash or other property into which the Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, is convertible) and showing in detail the facts upon which such adjustment or readjustment is based. The Corporation shall, as promptly as reasonably practicable after the written request at any time of any holder of Preferred Stock (but in any event not later than 10 days thereafter), furnish or cause to be furnished to such holder a certificate setting forth (i) the Series A Conversion Price, Series B Conversion Price and Series C Conversion Price then in effect, and (ii) the number of shares of Common Stock and the amount, if any, of other securities, cash or property which then would be received upon the conversion of Series A Preferred Stock, Series B Preferred Stock and Series C Preferred Stock.

4.10 Notice of Record Date. In the event:

(a) the Corporation shall take a record of the holders of its Common Stock (or other capital stock or securities at the time issuable upon conversion of the Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock) for the purpose of entitling or enabling them to receive any dividend or other distribution, or to receive any right to subscribe for or purchase any shares of capital stock of any class or any other securities, or to receive any other security; or

(b) of any capital reorganization of the Corporation, any reclassification of the Common Stock of the Corporation, or any Deemed Liquidation Event; or

(c) of the voluntary or involuntary dissolution, liquidation or winding-up of the Corporation,

then, and in each such case, the Corporation will send or cause to be sent to the holders of Preferred Stock a notice specifying, as the case may be, (i) the record date for such dividend, distribution or right, and the amount and character of such dividend, distribution or right, or (ii) the effective date on which such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up is proposed to take place, and the time, if any is to be fixed, as of which the holders of record of Common Stock (or such other capital stock or securities at the time issuable upon the conversion of the Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock) shall be entitled to exchange their shares of Common Stock (or such other capital stock or securities) for securities or other property deliverable upon such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up, and the amount per share and character of such exchange applicable to the Series A Preferred Stock, Series B Preferred Stock, Series C Preferred Stock and the Common Stock. Such notice shall be sent at least 10 days prior to the record date or effective date for the event specified in such notice.

5. Mandatory Conversion.

5.1 Trigger Events. Upon either (a) the closing of the sale of shares of Common Stock to the public in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended (the "**Securities Act**"), resulting in at least $30,000,000 of gross proceeds to the Corporation and with either (1) a price of at least $5.00 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Common Stock) or (2) a listing of the Common Stock on a nationally recognized securities exchange or trading system, (b) with the vote or written consent of a majority of the then outstanding shares of Preferred Stock, voting together as a single class, which majority shall include the holders of the Requisite Series C-1 Vote, the closing of the sale of shares of Common Stock to the public in any other firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act or (c) the date and time, or the occurrence of an event, specified by vote or written consent of (1) the holders of at least 60% of the then outstanding shares of Series A Preferred Stock, (2) the holders of a majority of the outstanding shares of Series B Preferred Stock and (3) the holders of the Requisite Series C-1 Vote (the time of such closing or the date and time specified or the time of the event specified in such votes or written consents is referred to herein as the "**Mandatory Conversion Time**"), (i) all outstanding shares of Preferred Stock shall automatically be converted into shares of Common Stock, at the then effective conversion rate, and (ii) such shares may not be reissued by the Corporation.

5.2 Procedural Requirements. All holders of record of shares of Preferred Stock shall be sent written notice of the Mandatory Conversion Time and the place designated for mandatory conversion of all such shares of Preferred Stock pursuant to this Section 5. Such notice need not be sent in advance of the occurrence of the Mandatory Conversion Time. Upon receipt of such notice, each holder of shares of Preferred Stock shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to

the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Preferred Stock converted pursuant to Section 5.1, including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate at the Mandatory Conversion Time (notwithstanding the failure of the holder or holders thereof to surrender the certificates at or prior to such time), except only the rights of the holders thereof, upon surrender of their certificate or certificates (or lost certificate affidavit and agreement) therefor, to receive the items provided for in the next sentence of this Subsection 5.2. As soon as practicable after the Mandatory Conversion Time and the surrender of the certificate or certificates (or lost certificate affidavit and agreement) for Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, the Corporation shall issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof, together with cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and the payment of any declared but unpaid dividends on the shares of Series A Preferred Stock, Series B Preferred Stock or Series C Preferred Stock, as the case may be, converted. Such converted Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Series A Preferred Stock, Series B Preferred Stock and Series C Preferred Stock accordingly.

6. Redeemed or Otherwise Acquired Shares. Any shares of Preferred Stock that are redeemed or otherwise acquired by the Corporation or any of its subsidiaries shall be automatically and immediately cancelled and retired and shall not be reissued, sold or transferred. Neither the Corporation nor any of its subsidiaries may exercise any voting or other rights granted to the holders of Preferred Stock following redemption.

7. Waiver. Except as otherwise expressly set forth in the Certificate of Incorporation, (i) any of the rights, powers, preferences and other terms of the Preferred Stock set forth herein may be waived on behalf of all holders of Preferred Stock by the affirmative consent or vote of the holders of a majority of the shares of Preferred Stock then outstanding, voting together as a single class, provided such waiver by its terms is equally applicable to the Series A Preferred Stock, the Series B Preferred Stock and the Series C Preferred Stock and to the holders of Series A Preferred Stock, Series B Preferred Stock and Series C Preferred Stock; (ii) any of the rights, powers, preferences and other terms of the Series A Preferred Stock set forth herein may be waived (in a manner that does not apply equally to the Series B Preferred Stock and Series C Preferred Stock or the respective holders thereof) on behalf of all holders of Series A Preferred Stock by the affirmative written consent or vote of the holders of at least 60% of the shares of Series A Preferred Stock then outstanding; (iii) any of the rights, powers, preferences and other terms of the Series B Preferred Stock set forth herein may be waived (in a manner that does not apply equally to the Series A Preferred Stock and Series C Preferred Stock or the respective holders thereof) on behalf of all holders of Series B Preferred Stock by the

affirmative written consent or vote of the holders of a majority of the shares of Series B Preferred Stock then outstanding; and (iv) any of the rights, powers, preferences and other terms of the Series C Preferred Stock set forth herein may be waived (in a manner that does not equally apply to the Series A Preferred Stock and Series B Preferred Stock or the respective holders thereof) on behalf of all holders of Series C Preferred Stock by the affirmative written consent or vote of the holders of a majority of the shares of Series C Preferred Stock then outstanding, which majority must include the holders of the Requisite Series C-1 Vote.

8. Notices. Any notice required or permitted by the provisions of this Article Fourth to be given to a holder of shares of Preferred Stock shall be mailed, postage prepaid, to the post office address last shown on the records of the Corporation, or given by electronic communication in compliance with the provisions of the General Corporation Law, and shall be deemed sent upon such mailing or electronic transmission.

**FIFTH**: Subject to any additional vote required by the Certificate of Incorporation or Bylaws, in furtherance and not in limitation of the powers conferred by statute, the Board of Directors is expressly authorized to make, repeal, alter, amend and rescind any or all of the Bylaws of the Corporation.

**SIXTH**: Subject to any additional vote required by the Certificate of Incorporation, the number of directors of the Corporation shall be determined in the manner set forth in the Bylaws of the Corporation.

**SEVENTH**: Elections of directors need not be by written ballot unless the Bylaws of the Corporation shall so provide.

**EIGHTH**: Meetings of stockholders may be held within or without the State of Delaware, as the Bylaws of the Corporation may provide. The books of the Corporation may be kept outside the State of Delaware at such place or places as may be designated from time to time by the Board of Directors or in the Bylaws of the Corporation.

**NINTH**: To the fullest extent permitted by law, a director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director. If the General Corporation Law or any other law of the State of Delaware is amended after approval by the stockholders of this Article Ninth to authorize

corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law as so amended.

Any repeal or modification of the foregoing provisions of this Article Ninth by the stockholders of the Corporation shall not adversely affect any right or protection of a director of the Corporation existing at the time of, or increase the liability of any director of the Corporation with respect to any acts or omissions of such director occurring prior to, such repeal or modification.

**TENTH**: The following indemnification provisions shall apply to the persons enumerated below.

1. Right to Indemnification of Directors and Officers. The Corporation shall indemnify and hold harmless, to the fullest extent permitted by applicable law as it presently exists or may hereafter be amended, any person (an "**Indemnified Person**") who was or is made or is threatened to be made a party or is otherwise involved in any action, suit or proceeding, whether civil, criminal, administrative or investigative (a "**Proceeding**"), by reason of the fact that such person, or a person for whom such person is the legal representative, is or was a director or officer of the Corporation or, while a director or officer of the Corporation, is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation or of a partnership, joint venture, limited liability company, trust, enterprise or nonprofit entity, including service with respect to employee benefit plans, against all liability and loss suffered and expenses (including attorneys' fees) reasonably incurred by such Indemnified Person in such Proceeding. Notwithstanding the preceding sentence, except as otherwise provided in Section 3 of this Article Tenth, the Corporation shall be required to indemnify an Indemnified Person in connection with a Proceeding (or part thereof) commenced by such Indemnified Person only if the commencement of such Proceeding (or part thereof) by the Indemnified Person was authorized in advance by the Board of Directors.

2. Prepayment of Expenses of Directors and Officers. The Corporation shall pay the expenses (including attorneys' fees) incurred by an Indemnified Person in defending any Proceeding in advance of its final disposition, provided, however, that, to the extent required by law, such payment of expenses in advance of the final disposition of the Proceeding shall be made only upon receipt of an undertaking by the Indemnified Person to repay all amounts advanced if it should be ultimately determined that the Indemnified Person is not entitled to be indemnified under this Article Tenth or otherwise.

3. Claims by Directors and Officers. If a claim for indemnification or advancement of expenses under this Article Tenth is not paid in full within 30 days after a written claim therefor by the Indemnified Person has been received by the Corporation, the Indemnified Person

may file suit to recover the unpaid amount of such claim and, if successful in whole or in part, shall be entitled to be paid the expense of prosecuting such claim. In any such action the Corporation shall have the burden of proving that the Indemnified Person is not entitled to the requested indemnification or advancement of expenses under applicable law.

4. Indemnification of Employees and Agents. The Corporation may indemnify and advance expenses to any person who was or is made or is threatened to be made or is otherwise involved in any Proceeding by reason of the fact that such person, or a person for whom such person is the legal representative, is or was an employee or agent of the Corporation or, while an employee or agent of the Corporation, is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation or of a partnership, joint venture, limited liability company, trust, enterprise or nonprofit entity, including service with respect to employee benefit plans, against all liability and loss suffered and expenses (including attorney's fees) reasonably incurred by such person in connection with such Proceeding. The ultimate determination of entitlement to indemnification of persons who are non-director or officer employees or agents shall be made in such manner as is determined by the Board of Directors in its sole discretion. Notwithstanding the foregoing sentence, the Corporation shall not be required to indemnify a person in connection with a Proceeding initiated by such person if the Proceeding was not authorized in advance by the Board of Directors.

5. Advancement of Expenses of Employees and Agents. The Corporation may pay the expenses (including attorney's fees) incurred by an employee or agent in defending any Proceeding in advance of its final disposition on such terms and conditions as may be determined by the Board of Directors.

6. Non-Exclusivity of Rights. The rights conferred on any person by this Article Tenth shall not be exclusive of any other rights which such person may have or hereafter acquire under any statute, provision of the certificate of incorporation, these by-laws, agreement, vote of stockholders or disinterested directors or otherwise.

7. Other Indemnification. The Corporation's obligation, if any, to indemnify any person who was or is serving at its request as a director, officer or employee of another Corporation, partnership, limited liability company, joint venture, trust, organization or other enterprise shall be reduced by any amount such person may collect as indemnification from such other Corporation, partnership, limited liability company, joint venture, trust, organization or other enterprise.

8. Insurance. The Board of Directors may, to the full extent permitted by applicable law as it presently exists, or may hereafter be amended from time to time, authorize an appropriate officer or officers to purchase and maintain at the Corporation's expense insurance: (a) to indemnify the Corporation for any obligation which it incurs as a result of the indemnification of directors, officers and employees under the provisions of this Article Tenth; and (b) to indemnify or insure directors, officers and employees against liability in instances in which they may not otherwise be indemnified by the Corporation under the provisions of this Article Tenth.

9. Amendment or Repeal. Any repeal or modification of the foregoing provisions of this Article Tenth shall not adversely affect any right or protection hereunder of any person in respect of any act or omission occurring prior to the time of such repeal or modification. The rights provided hereunder shall inure to the benefit of any Indemnified Person and such person's heirs, executors and administrators.

**ELEVENTH**: The Corporation renounces any interest or expectancy of the Corporation in, or in being offered an opportunity to participate in, any Excluded Opportunity. An "**Excluded Opportunity**" is any matter, transaction or interest that is presented to, or acquired, created or developed by, or which otherwise comes into the possession of, (i) any director of the Corporation who is not an employee of the Corporation or any of its subsidiaries, or (ii) any holder of Preferred Stock or any Affiliated Party, partner, member, director, stockholder, employee or agent of any such holder, other than someone who is an employee of the Corporation or any of its subsidiaries (collectively, "**Covered Persons**"), unless such matter, transaction or interest is presented to, or acquired, created or developed by, or otherwise comes into the possession of, a Covered Person expressly and solely in such Covered Person's capacity as a director of the Corporation.

* * * *

**3.** That the foregoing amendment and restatement was approved by the holders of the requisite number of shares of this corporation in accordance with Section 228 of the General Corporation Law.

**4.** That this Third Amended and Restated Certificate of Incorporation, which restates and integrates and further amends the provisions of this corporation's Certificate of Incorporation, has been duly adopted in accordance with Sections 242 and 245 of the General Corporation Law.

**IN WITNESS WHEREOF**, this Third Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of this corporation on this 15th day of November, 2011.

By: /s/ David Schenkein
David Schenkein, President

**Exhibit 3.2**

# BY-LAWS

# OF

# CANCER METABOLISM THERAPEUTICS, INC.

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**ARTICLE I**

**STOCKHOLDERS**

1.1 Place of Meetings. All meetings of stockholders shall be held at such place as may be designated from time to time by the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President or, if not so designated, at the principal office of the corporation. The Board of Directors may, in its sole discretion, determine that a meeting shall not be held at any place, but may instead be held solely by means of remote communication in a manner consistent with the General Corporation Law of the State of Delaware.

1.2 Annual Meeting. The annual meeting of stockholders for the election of directors and for the transaction of such other business as may properly be brought before the meeting shall be held on a date and at a time designated by the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President (which date shall not be a legal holiday in the place where the meeting is to be held).

1.3 Special Meetings. Special meetings of stockholders for any purpose or purposes may be called at any time by only the Board of Directors, the Chairman of the Board, the Chief Executive Officer or the President, and may not be called by any other person or persons. The Board of Directors may postpone or reschedule any previously scheduled special meeting of stockholders. Business transacted at any special meeting of stockholders shall be limited to matters relating to the purpose or purposes stated in the notice of meeting.

1.4 Notice of Meetings. Except as otherwise provided by law, notice of each meeting of stockholders, whether annual or special, shall be given not less than 10 nor more than 60 days before the date of the meeting to each stockholder entitled to vote at such meeting. Without limiting the manner by which notice otherwise may be given to stockholders, any notice shall be effective if given by a form of electronic transmission consented to (in a manner consistent with the General Corporation Law of the State of Delaware) by the stockholder to whom the notice is given. The notices of all meetings shall state the place, if any, date and time of the meeting and the means of remote communications, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such meeting. The notice of a special meeting shall state, in addition, the purpose or purposes for which the meeting is called. If notice is given by mail, such notice shall be deemed given when deposited in the United States mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the records of the corporation. If notice is given by electronic transmission, such notice shall be deemed given at the time specified in Section 232 of the General Corporation Law of the State of Delaware.

1.5 Voting List. The Secretary shall prepare, at least 10 days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting, for a period of at least 10 days prior to the meeting: (a) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or (b) during

ordinary business hours, at the principal place of business of the corporation. If the meeting is to be held at a physical location (and not solely by means of remote communication), then the list shall be produced and kept at the time and place of the meeting during the whole time thereof, and may be inspected by any stockholder who is present. If the meeting is to be held solely by means of remote communication, then the list shall also be open to the examination of any stockholder during the whole time of the meeting on a reasonably accessible electronic network, and the information required to access such list shall be provided with the notice of the meeting. The list shall presumptively determine the identity of the stockholders entitled to vote at the meeting and the number of shares held by each of them.

1.6 Quorum. Except as otherwise provided by law, the Certificate of Incorporation or these By-laws, the holders of a majority in voting power of the shares of the capital stock of the corporation issued and outstanding and entitled to vote at the meeting, present in person, present by means of remote communication in a manner, if any, authorized by the Board of Directors in its sole discretion, or represented by proxy, shall constitute a quorum for the transaction of business; provided, however, that where a separate vote by a class or classes or series of capital stock is required by law or the Certificate of Incorporation, the holders of a majority in voting power of the shares of such class or classes or series of the capital stock of the corporation issued and outstanding and entitled to vote on such matter, present in person, present by means of remote communication in a manner, if any, authorized by the Board of Directors in its sole discretion, or represented by proxy, shall constitute a quorum entitled to take action with respect to the vote on such matter. A quorum, once established at a meeting, shall not be broken by the withdrawal of enough votes to leave less than a quorum.

1.7 Adjournments. Any meeting of stockholders may be adjourned from time to time to any other time and to any other place at which a meeting of stockholders may be held under these By-laws by the chairman of the meeting or by the stockholders present or represented at the meeting and entitled to vote, although less than a quorum. It shall not be necessary to notify any stockholder of any adjournment of less than 30 days if the time and place, if any, of the adjourned meeting, and the means of remote communication, if any, by which stockholders and proxyholders may be deemed to be present in person and vote at such adjourned meeting, are announced at the meeting at which adjournment is taken, unless after the adjournment a new record date is fixed for the adjourned meeting. At the adjourned meeting, the corporation may transact any business which might have been transacted at the original meeting.

1.8 Voting and Proxies. Each stockholder shall have one vote for each share of stock entitled to vote held of record by such stockholder and a proportionate vote for each fractional share so held, unless otherwise provided by law or the Certificate of Incorporation. Each stockholder of record entitled to vote at a meeting of stockholders, or to express consent or dissent to corporate action without a meeting, may vote or express such consent or dissent in person (including by means of remote communications, if any, by which stockholders may be deemed to be present in person and vote at such meeting) or may authorize another person or persons to vote or act for such stockholder by a proxy executed or transmitted in a manner permitted by the General Corporation Law of the State of Delaware by the stockholder or such stockholder’s authorized agent and delivered (including by electronic transmission) to the Secretary of the corporation. No such proxy shall be voted or acted upon after three years from the date of its execution, unless the proxy expressly provides for a longer period.

1.9 Action at Meeting. When a quorum is present at any meeting, any matter other than the election of directors to be voted upon by the stockholders at such meeting shall be decided by the vote of the holders of shares of stock having a majority in voting power of the votes cast by the holders of all of the shares of stock present or represented at the meeting and voting affirmatively or negatively on such matter (or if there are two or more classes or series of stock entitled to vote as separate classes, then in the case of each such class or series, the holders of a majority in voting power of the shares of stock of that class or series present or represented at the meeting and voting affirmatively or negatively on such matter), except when a different vote is required by law, the Certificate of Incorporation or these By-laws. When a quorum is present at any meeting, any election by stockholders of directors shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election.

1.10 Conduct of Meetings.

(a) Chairman of Meeting. Meetings of stockholders shall be presided over by the Chairman of the Board, if any, or in the Chairman's absence by the Vice Chairman of the Board, if any, or in the Vice Chairman's absence by the Chief Executive Officer, or in the Chief Executive Officer's absence, by the President, or in the President's absence by a Vice President, or in the absence of all of the foregoing persons by a chairman designated by the Board of Directors, or in the absence of such designation by a chairman chosen by vote of the stockholders at the meeting. The Secretary shall act as secretary of the meeting, but in the Secretary's absence the chairman of the meeting may appoint any person to act as secretary of the meeting.

(b) Rules, Regulations and Procedures. The Board of Directors may adopt by resolution such rules, regulations and procedures for the conduct of any meeting of stockholders of the corporation as it shall deem appropriate including, without limitation, such guidelines and procedures as it may deem appropriate regarding the participation by means of remote communication of stockholders and proxyholders not physically present at a meeting. Except to the extent inconsistent with such rules, regulations and procedures as adopted by the Board of Directors, the chairman of any meeting of stockholders shall have the right and authority to prescribe such rules, regulations and procedures and to do all such acts as, in the judgment of such chairman, are appropriate for the proper conduct of the meeting. Such rules, regulations or procedures, whether adopted by the Board of Directors or prescribed by the chairman of the meeting, may include, without limitation, the following: (i) the establishment of an agenda or order of business for the meeting; (ii) rules and procedures for maintaining order at the meeting and the safety of those present; (iii) limitations on attendance at or participation in the meeting to stockholders of record of the corporation, their duly authorized and constituted proxies or such other persons as shall be determined; (iv) restrictions on entry to the meeting after the time fixed for the commencement thereof; and (v) limitations on the time allotted to questions or comments by participants. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of stockholders shall not be required to be held in accordance with the rules of parliamentary procedure.

1.11 Action without Meeting.

(a) Taking of Action by Consent. Any action required or permitted to be taken at any annual or special meeting of stockholders of the corporation may be taken without a meeting, without prior notice and without a vote, if a consent in writing, setting forth the action so taken, is signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote on such action were present and voted. Except as otherwise provided by the Certificate of Incorporation, stockholders may act by written consent to elect directors; provided, however, that, if such consent is less than unanimous, such action by written consent may be in lieu of holding an annual meeting only if all of the directorships to which directors could be elected at an annual meeting held at the effective time of such action are vacant and are filled by such action.

(b) Electronic Transmission of Consents. A telegram, cablegram or other electronic transmission consenting to an action to be taken and transmitted by a stockholder or proxyholder, or by a person or persons authorized to act for a stockholder or proxyholder, shall be deemed to be written, signed and dated for the purposes of this section, provided that any such telegram, cablegram or other electronic transmission sets forth or is delivered with information from which the corporation can determine (i) that the telegram, cablegram or other electronic transmission was transmitted by the stockholder or proxyholder or by a person or persons authorized to act for the stockholder or proxyholder and (ii) the date on which such stockholder or proxyholder or authorized person or persons transmitted such telegram, cablegram or electronic transmission. The date on which such telegram, cablegram or electronic transmission is transmitted shall be deemed to be the date on which such consent was signed. No consent given by telegram, cablegram or other electronic transmission shall be deemed to have been delivered until such consent is reproduced in paper form and until such paper form shall be delivered to the corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to a corporation's registered office shall be made by hand or by certified or registered mail, return receipt requested. Notwithstanding the foregoing limitations on delivery, consents given by telegram, cablegram or other electronic transmission may be otherwise delivered to the principal place of business of the corporation or to an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded if, to the extent and in the manner provided by resolution of the Board of Directors. Any copy, facsimile or other reliable reproduction of a consent in writing may be substituted or used in lieu of the original writing for any and all purposes for which the original writing could be used, provided that such copy, facsimile or other reproduction shall be a complete reproduction of the entire original writing.

(c) Notice of Taking of Corporate Action. Prompt notice of the taking of corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented in writing and who, if the action had been taken at a meeting, would have been entitled to notice of the meeting if the record date for such meeting had been the date that written consents signed by a sufficient number of holders to take the action were delivered to the corporation.

## ARTICLE II

## DIRECTORS

2.1 General Powers. The business and affairs of the corporation shall be managed by or under the direction of a Board of Directors, who may exercise all of the powers of the corporation except as otherwise provided by law or the Certificate of Incorporation.

2.2 Number, Election and Qualification. Subject to the rights of holders of any series of Preferred Stock to elect directors, the number of directors of the corporation shall be established from time to time by the stockholders or the Board of Directors. The directors shall be elected at the annual meeting of stockholders by such stockholders as have the right to vote on such election. Election of directors need not be by written ballot. Directors need not be stockholders of the corporation.

2.3 Chairman of the Board; Vice Chairman of the Board. The Board of Directors may appoint from its members a Chairman of the Board and a Vice Chairman of the Board, neither of whom need be an employee or officer of the corporation. If the Board of Directors appoints a Chairman of the Board, such Chairman shall perform such duties and possess such powers as are assigned by the Board of Directors and, if the Chairman of the Board is also designated as the corporation's Chief Executive Officer, shall have the powers and duties of the Chief Executive Officer prescribed in Section 3.7 of these By-laws. If the Board of Directors appoints a Vice Chairman of the Board, such Vice Chairman shall perform such duties and possess such powers as are assigned by the Board of Directors. Unless otherwise provided by the Board of Directors, the Chairman of the Board or, in the Chairman's absence, the Vice Chairman of the Board, if any, shall preside at all meetings of the Board of Directors.

2.4 Tenure. Each director shall hold office until the next annual meeting of stockholders and until a successor is elected and qualified, or until such director's earlier death, resignation or removal.

2.5 Quorum. The greater of (a) a majority of the directors at any time in office and (b) one-third of the number of directors fixed pursuant to Section 2.2 of these By-laws shall constitute a quorum of the Board of Directors. If at any meeting of the Board of Directors there shall be less than such a quorum, a majority of the directors present may adjourn the meeting from time to time without further notice other than announcement at the meeting, until a quorum shall be present.

2.6 Action at Meeting. Every act or decision done or made by a majority of the directors present at a meeting of the Board of Directors duly held at which a quorum is present shall be regarded as the act of the Board of Directors, unless a greater number is required by law or by the Certificate of Incorporation.

2.7 Removal. Except as otherwise provided by the General Corporation Law of the State of Delaware, any one or more or all of the directors of the corporation may be removed, with or without cause, by the holders of a majority of the shares then entitled to vote at an election of directors, except that the directors elected by the holders of a particular class or series of stock may be removed without cause only by vote of the holders of a majority of the outstanding shares of such class or series.

2.8 Vacancies. Subject to the rights of holders of any series of Preferred Stock to elect directors, unless and until filled by the stockholders, any vacancy or newly-created directorship on the Board of Directors, however occurring, may be filled by vote of a majority of the directors then in office, although less than a quorum, or by a sole remaining director. A director elected to fill a vacancy shall be elected for the unexpired term of such director's predecessor in office, and a director chosen to fill a position resulting from a newly-created directorship shall hold office until the next annual meeting of stockholders and until a successor is elected and qualified, or until such director's earlier death, resignation or removal.

2.9 Resignation. Any director may resign by delivering a resignation in writing or by electronic transmission to the corporation at its principal office or to the Chairman of the Board, the Chief Executive Officer, the President or the Secretary. Such resignation shall be effective upon delivery unless it is specified to be effective at some later time or upon the happening of some later event.

2.10 Regular Meetings. Regular meetings of the Board of Directors may be held without notice at such time and place as shall be determined from time to time by the Board of Directors; provided that any director who is absent when such a determination is made shall be given notice of the determination. A regular meeting of the Board of Directors may be held without notice immediately after and at the same place as the annual meeting of stockholders.

2.11 Special Meetings. Special meetings of the Board of Directors may be held at any time and place designated in a call by the Chairman of the Board, the Chief Executive Officer, the President, two or more directors, or by one director in the event that there is only a single director in office.

2.12 Notice of Special Meetings. Notice of the date, place, if any, and time of any special meeting of directors shall be given to each director by the Secretary or by the officer or one of the directors calling the meeting. Notice shall be duly given to each director (a) in person or by telephone at least 24 hours in advance of the meeting, (b) by sending written notice by reputable overnight courier, telecopy, facsimile or electronic transmission, or delivering written notice by hand, to such director's last known business, home or electronic transmission address at least 48 hours in advance of the meeting, or (c) by sending written notice by first-class mail to such director's last known business or home address at least 72 hours in advance of the meeting. A notice or waiver of notice of a meeting of the Board of Directors need not specify the purposes of the meeting.

2.13 Meetings by Conference Communications Equipment. Directors may participate in meetings of the Board of Directors or any committee thereof by means of conference telephone or other communications equipment by means of which all persons participating in the meeting can hear each other, and participation by such means shall constitute presence in person at such meeting.

2.14 Action by Consent. Any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof may be taken without a meeting, if all members of the Board of Directors or committee, as the case may be, consent to the action in writing or by electronic transmission, and the written consents or electronic transmissions are filed with the minutes of proceedings of the Board of Directors or committee. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

2.15 Committees. The Board of Directors may designate one or more committees, each committee to consist of one or more of the directors of the corporation with such lawfully delegable powers and duties as the Board of Directors thereby confers, to serve at the pleasure of the Board of Directors. The Board of Directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee. In the absence or disqualification of a member of a committee, the member or members of the committee present at any meeting and not disqualified from voting, whether or not such member or members constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of any such absent or disqualified member. Any such committee, to the extent provided in the resolution of the Board of Directors and subject to the provisions of law, shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation and may authorize the seal of the corporation to be affixed to all papers which may require it. Each such committee shall keep minutes and make such reports as the Board of Directors may from time to time request. Except as the Board of Directors may otherwise determine, any committee may make rules for the conduct of its business, but unless otherwise provided by the directors or in such rules, its business shall be conducted as nearly as possible in the same manner as is provided in these By-laws for the Board of Directors. Except as otherwise provided in the Certificate of Incorporation, these By-laws, or the resolution of the Board of Directors designating the committee, a committee may create one or more subcommittees, each subcommittee to consist of one or more members of the committee, and delegate to a subcommittee any or all of the powers and authority of the committee.

2.16 Compensation of Directors. Directors may be paid such compensation for their services and such reimbursement for expenses of attendance at meetings as the Board of Directors may from time to time determine. No such payment shall preclude any director from serving the corporation or any of its parent or subsidiary entities in any other capacity and receiving compensation for such service.

## ARTICLE III

## OFFICERS

3.1 Titles. The officers of the corporation shall consist of a Chief Executive Officer, a President, a Secretary, a Treasurer and such other officers with such other titles as the Board of Directors shall determine, including one or more Vice Presidents, Assistant Treasurers and Assistant Secretaries. The Board of Directors may appoint such other officers as it may deem appropriate.

3.2 Election. The Chief Executive Officer, President, Treasurer and Secretary shall be elected annually by the Board of Directors at its first meeting following the annual meeting of stockholders. Other officers may be appointed by the Board of Directors at such meeting or at any other meeting.

3.3 Qualification. No officer need be a stockholder. Any two or more offices may be held by the same person.

3.4 Tenure. Except as otherwise provided by law, by the Certificate of Incorporation or by these By-laws, each officer shall hold office until such officer's successor is elected and qualified, unless a different term is specified in the resolution electing or appointing such officer, or until such officer's earlier death, resignation or removal.

3.5 Resignation and Removal. Any officer may resign by delivering a written resignation to the corporation at its principal office or to the Chief Executive Officer, the President or the Secretary. Such resignation shall be effective upon receipt unless it is specified to be effective at some later time or upon the happening of some later event. Any officer may be removed at any time, with or without cause, by vote of a majority of the directors then in office. Except as the Board of Directors may otherwise determine, no officer who resigns or is removed shall have any right to any compensation as an officer for any period following such officer's resignation or removal, or any right to damages on account of such removal, whether such officer's compensation be by the month or by the year or otherwise, unless such compensation is expressly provided for in a duly authorized written agreement with the corporation.

3.6 Vacancies. The Board of Directors may fill any vacancy occurring in any office for any reason and may, in its discretion, leave unfilled for such period as it may determine any offices other than those of Chief Executive Officer, President, Treasurer and Secretary. Each such successor shall hold office for the unexpired term of such officer's predecessor and until a successor is elected and qualified, or until such officer's earlier death, resignation or removal.

3.7 President; Chief Executive Officer. Unless the Board of Directors has designated another person as the corporation's Chief Executive Officer, the President shall be the Chief Executive Officer of the corporation. The Chief Executive Officer shall have general charge and supervision of the business of the corporation subject to the direction of the Board of Directors, and shall perform all duties and have all powers that are commonly incident to the office of chief executive or that are delegated to such officer by the Board of Directors. The President shall perform such other duties and shall have such other powers as the Board of Directors or the Chief Executive Officer (if the President is not the Chief Executive Officer) may from time to time prescribe. In the event of the absence, inability or refusal to act of the Chief Executive Officer or the President (if the President is not the Chief Executive Officer), the Vice President (or if there shall be more than one, the Vice Presidents in the order determined by the Board of Directors) shall perform the duties of the Chief Executive Officer and when so performing such duties shall have all the powers of and be subject to all the restrictions upon the Chief Executive Officer.

3.8 Vice Presidents. Each Vice President shall perform such duties and possess such powers as the Board of Directors or the Chief Executive Officer may from time to time prescribe. The Board of Directors may assign to any Vice President the title of Executive Vice President, Senior Vice President or any other title selected by the Board of Directors.

3.9 Secretary and Assistant Secretaries. The Secretary shall perform such duties and shall have such powers as the Board of Directors or the Chief Executive Officer may from time to time prescribe. In addition, the Secretary shall perform such duties and have such powers as are incident to the office of the secretary, including without limitation the duty and power to give notices of all meetings of stockholders and special meetings of the Board of Directors, to attend all meetings of stockholders and the Board of Directors and keep a record of the proceedings, to maintain a stock ledger and prepare lists of stockholders and their addresses as required, to be custodian of corporate records and the corporate seal and to affix and attest to the same on documents.

Any Assistant Secretary shall perform such duties and possess such powers as the Board of Directors, the Chief Executive Officer or the Secretary may from time to time prescribe. In the event of the absence, inability or refusal to act of the Secretary, the Assistant Secretary (or if there shall be more than one, the Assistant Secretaries in the order determined by the Board of Directors) shall perform the duties and exercise the powers of the Secretary.

In the absence of the Secretary or any Assistant Secretary at any meeting of stockholders or directors, the chairman of the meeting shall designate a temporary secretary to keep a record of the meeting.

3.10 Treasurer and Assistant Treasurers. The Treasurer shall perform such duties and shall have such powers as may from time to time be assigned by the Board of Directors or the Chief Executive Officer. In addition, the Treasurer shall perform such duties and have such powers as are incident to the office of treasurer, including without limitation the duty and power to keep and be responsible for all funds and securities of the corporation, to deposit funds of the corporation in depositories selected in accordance with these By-laws, to disburse such funds as ordered by the Board of Directors, to make proper accounts of such funds, and to render as required by the Board of Directors statements of all such transactions and of the financial condition of the corporation.

The Assistant Treasurers shall perform such duties and possess such powers as the Board of Directors, the Chief Executive Officer or the Treasurer may from time to time prescribe. In the event of the absence, inability or refusal to act of the Treasurer, the Assistant Treasurer (or if there shall be more than one, the Assistant Treasurers in the order determined by the Board of Directors) shall perform the duties and exercise the powers of the Treasurer.

3.11 Salaries. Officers of the corporation shall be entitled to such salaries, compensation or reimbursement as shall be fixed or allowed from time to time by the Board of Directors.

3.12 Delegation of Authority. The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

## ARTICLE IV

## CAPITAL STOCK

4.1 Issuance of Stock. Subject to the provisions of the Certificate of Incorporation, the whole or any part of any unissued balance of the authorized capital stock of the corporation or the whole or any part of any shares of the authorized capital stock of the corporation held in the corporation's treasury may be issued, sold, transferred or otherwise disposed of by vote of the Board of Directors in such manner, for such lawful consideration and on such terms as the Board of Directors may determine.

4.2 Stock Certificates; Uncertificated Shares. The shares of the corporation shall be represented by certificates, provided that the Board of Directors may provide by resolution or resolutions that some or all of any or all classes or series of its stock shall be uncertificated shares. Every holder of stock of the corporation represented by certificates shall be entitled to have a certificate, in such form as may be prescribed by law and by the Board of Directors, representing the number of shares held by such holder registered in certificate form. Each such certificate shall be signed in a manner that complies with Section 158 of the General Corporation Law of the State of Delaware.

Each certificate for shares of stock which are subject to any restriction on transfer pursuant to the Certificate of Incorporation, these By-laws, applicable securities laws or any agreement among any number of stockholders or among such holders and the corporation shall have conspicuously noted on the face or back of the certificate either the full text of the restriction or a statement of the existence of such restriction.

If the corporation shall be authorized to issue more than one class of stock or more than one series of any class, the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights shall be set forth in full or summarized on the face or back of each certificate representing shares of such class or series of stock, provided that in lieu of the foregoing requirements there may be set forth on the face or back of each certificate representing shares of such class or series of stock a statement that the corporation will furnish without charge to each stockholder who so requests a copy of the full text of the powers, designations, preferences and relative, participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

Within a reasonable time after the issuance or transfer of uncertificated stock, the corporation shall send to the registered owner thereof a written notice containing the information required to be set forth or stated on certificates pursuant to Sections 151, 202(a) or 218(a) of the General Corporation Law of the State of Delaware or, with respect to Section 151 of General Corporation Law of the State of Delaware, a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

4.3 Transfers. Shares of stock of the corporation shall be transferable in the manner prescribed by law and in these By-laws. Transfers of shares of stock of the corporation shall be made only on the books of the corporation or by transfer agents designated to transfer shares of stock of the corporation. Subject to applicable law, shares of stock represented by certificates shall be transferred only on the books of the corporation by the surrender to the corporation or its transfer agent of the certificate representing such shares properly endorsed or accompanied by a written assignment or power of attorney properly executed, and with such proof of authority or the authenticity of signature as the corporation or its transfer agent may reasonably require. Except as may be otherwise required by law, by the Certificate of Incorporation or by these By-laws, the corporation shall be entitled to treat the record holder of stock as shown on its books as the owner of such stock for all purposes, including the payment of dividends and the right to vote with respect to such stock, regardless of any transfer, pledge or other disposition of such stock until the shares have been transferred on the books of the corporation in accordance with the requirements of these By-laws.

4.4 Lost, Stolen or Destroyed Certificates. The corporation may issue a new certificate of stock in place of any previously issued certificate alleged to have been lost, stolen or destroyed, upon such terms and conditions as the Board of Directors may prescribe, including the presentation of reasonable evidence of such loss, theft or destruction and the giving of such indemnity and posting of such bond as the Board of Directors may require for the protection of the corporation or any transfer agent or registrar.

4.5 Record Date. The Board of Directors may fix in advance a date as a record date for the determination of the stockholders entitled to notice of or to vote at any meeting of stockholders or to express consent (or dissent) to corporate action without a meeting, or entitled to receive payment of any dividend or other distribution or allotment of any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action. Such record date shall not precede the date on which the resolution fixing the record date is adopted, and such record date shall not be more than 60 nor less than 10 days before the date of such meeting, nor more than 10 days after the date of adoption of a record date for a consent without a meeting, nor more than 60 days prior to any other action to which such record date relates.

If no record date is fixed, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day before the day on which notice is given, or, if notice is waived, at the close of business on the day before the day on which the meeting is held. If no record date is fixed, the record date for determining stockholders entitled to express consent to corporate action without a meeting, when no prior action by the Board of Directors is necessary, shall be the day on which the first consent is properly delivered to the corporation. If no record date is fixed, the record date for determining stockholders for any other purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating to such purpose.

A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for the adjourned meeting.

4.6 Regulations. The issue, transfer, conversion and registration of shares of stock of the corporation shall be governed by such other regulations as the Board of Directors may establish.

## ARTICLE V

## GENERAL PROVISIONS

5.1 Fiscal Year. Except as from time to time otherwise designated by the Board of Directors, the fiscal year of the corporation shall begin on the first day of January of each year and end on the last day of December in each year.

5.2 Corporate Seal. The corporate seal shall be in such form as shall be approved by the Board of Directors.

5.3 Waiver of Notice. Whenever notice is required to be given by law, by the Certificate of Incorporation or by these By-laws, a written waiver, signed by the person entitled to notice, or a waiver by electronic transmission by the person entitled to notice, whether before, at or after the time of the event for which notice is to be given, shall be deemed equivalent to notice required to be given to such person. Neither the business nor the purpose of any meeting need be specified in any such waiver. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting, except when the person attends a meeting for the express purpose of objecting at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened.

5.4 Voting of Securities. Except as the Board of Directors may otherwise designate, the Chief Executive Officer, the President or the Treasurer may waive notice of, vote, or appoint any person or persons to vote, on behalf of the corporation at, and act as, or appoint any person or persons to act as, proxy or attorney-in-fact for this corporation (with or without power of substitution) at, any meeting of stockholders or securityholders of any other entity, the securities of which may be held by this corporation.

5.5 Evidence of Authority. A certificate by the Secretary, or an Assistant Secretary, or a temporary Secretary, as to any action taken by the stockholders, directors, a committee or any officer or representative of the corporation shall as to all persons who rely on the certificate in good faith be conclusive evidence of such action.

5.6 Certificate of Incorporation. All references in these By-laws to the Certificate of Incorporation shall be deemed to refer to the Certificate of Incorporation of the corporation, as amended and in effect from time to time.

5.7 Severability. Any determination that any provision of these By-laws is for any reason inapplicable, illegal or ineffective shall not affect or invalidate any other provision of these By-laws.

5.8 Pronouns. All pronouns used in these By-laws shall be deemed to refer to the masculine, feminine or neuter, singular or plural, as the identity of the person or persons may require.

## ARTICLE VI

## AMENDMENTS

6.1 By the Board of Directors. These By-laws may be altered, amended or repealed, in whole or in part, or new by-laws may be adopted by the Board of Directors.

6.2 By the Stockholders. These By-laws may be altered, amended or repealed, in whole or in part, or new by-laws may be adopted by the affirmative vote of the holders of a majority of the shares of the capital stock of the corporation issued and outstanding and entitled to vote at any annual meeting of stockholders, or at any special meeting of stockholders, provided notice of such alteration, amendment, repeal or adoption of new by-laws shall have been stated in the notice of such special meeting.

**Exhibit 4.2**

**Execution Copy**

# AGIOS PHARMACEUTICALS, INC.

# SECOND AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT

November 16, 2011

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AGIOS PHARMACEUTICALS, INC.

SECOND AMENDED AND RESTATED
INVESTOR RIGHTS AGREEMENT

This Agreement dated as of November 16, 2011 is entered into by and among Agios Pharmaceuticals, Inc., a Delaware corporation (the "Company"), Lewis Cantley, Tak Mak, Craig Thompson and Michael Su (individually, a "Founder" and collectively, the "Founders"), and the individuals and entities listed on Exhibit A attached hereto (the "Purchasers").

Recitals

WHEREAS, the Company and certain Purchasers (the "Existing Purchasers") have previously entered into that certain Amended and Restated Investor Rights Agreement, dated as of April 14, 2010 (the "Prior Agreement"), which provides for certain arrangements with respect to (i) the registration of shares of capital stock of the Company under the Securities Act (as defined below), (ii) certain Purchasers' right of first refusal with respect to certain issuances of securities of the Company, and (iii) certain covenants of the Company;

WHEREAS, the Company and certain Purchasers have entered into a Series C-1 Convertible Preferred Stock and Series C-2 Convertible Preferred Stock Purchase Agreement of even date herewith (the "Purchase Agreement"); and

WHEREAS, the Company and the Existing Purchasers desire to amend and restate the Prior Agreement, to add new Purchasers as parties to this Agreement and to accept the rights created pursuant hereto in lieu of the rights created under the Prior Agreement.

NOW, THEREFORE, in consideration of the mutual promises and covenants contained in this Agreement, the parties hereto agree as follows:

1. Certain Definitions.

As used in this Agreement, the following terms shall have the following respective meanings:

"Affiliated Party" means, with respect to any Purchaser, any person or entity which, directly or indirectly, controls, is controlled by or is under common control with such Purchaser, including, without limitation, any general partner, officer or director of such Purchaser and any venture capital fund now or hereafter existing which is controlled by one or more general partners of, or shares the same management company as, such Purchaser.

"Available Undersubscription Amount" means the difference between the total of all of the Basic Amounts available for purchase by Qualified Purchasers pursuant to Section 3.1 and the Basic Amounts subscribed for pursuant to Section 3.1.

"Basic Amount" means, with respect to a Qualified Purchaser, its pro rata portion of the Offered Securities determined by multiplying the number of Offered Securities by a fraction, the numerator of which is the aggregate number of shares of Common Stock issuable upon conversion of all Shares then held by such Qualified Purchaser and the denominator of which is the total number of shares of Common Stock then outstanding (giving effect to the conversion into Common Stock of all outstanding shares of convertible preferred stock but excluding all shares of Common Stock (including shares issued upon exercise of options) issued to employees of the Company after the date hereof).

"Code" means the Internal Revenue Code of 1986, as amended.

"Commission" means the Securities and Exchange Commission, or any other federal agency at the time administering the Securities Act.

"Common Stock" means the common stock, $0.001 par value per share, of the Company.

"Company" has the meaning ascribed to it in the introductory paragraph hereto.

"Company Sale" means: (a) a merger or consolidation in which (i) the Company is a constituent party, or (ii) a Company Subsidiary is a constituent party and the Company issues shares of its capital stock pursuant to such merger or consolidation, except in the case of either clause (i) or (ii) any such merger or consolidation involving the Company or a Company Subsidiary in which the shares of capital stock of the Company outstanding immediately prior to such merger or consolidation continue to represent, or are converted into or exchanged for shares of capital stock which represent, immediately following such merger or consolidation, more than 50% by voting power of the capital stock of (A) the surviving or resulting corporation or (B) if the surviving or resulting corporation is a wholly owned subsidiary of another corporation immediately following such merger or consolidation, the parent corporation of such surviving or resulting corporation; (b) the sale, lease, transfer, exclusive license or other disposition, in a single transaction or series of related transactions, by the Company or a Company Subsidiary of all or substantially all the assets of the Company and the Company Subsidiaries taken as a whole (except where such sale, lease, transfer, exclusive license or other disposition is to a wholly owned Company Subsidiary); or (c) the sale or transfer, in a single transaction or series of related transactions, by the stockholders of the Company of more than 50% by voting power of the then-outstanding capital stock of the Company to any person or entity or group of affiliated persons or entities in which (i) the Company is party to such transaction or transactions or (ii) the acquiring persons or entities are not Affiliated Parties of holders of Series A Convertible Preferred Stock of the Company.

"Company Subsidiary" means any corporation, partnership, trust, limited liability company or other non-corporate business enterprise in which the Company (or another Company Subsidiary) holds stock or other ownership interests representing (a) more than 50% of the voting power of all outstanding stock or ownership interests of such entity or (b) the right to receive more than 50% of the net assets of such entity available for distribution to the holders of outstanding stock or ownership interests upon a liquidation or dissolution of such entity.

"Confidential Information" means any information that is labeled as confidential, proprietary or secret which a Purchaser obtains from the Company pursuant to financial statements, reports and other materials provided by the Company to such Purchaser pursuant to this Agreement or pursuant to visitation or inspection rights granted hereunder.

"Exchange Act" means the Securities Exchange Act of 1934, as amended, or any successor federal statute, and the rules and regulations of the Commission issued under such Act, as they each may, from time to time, be in effect.

"Fidelity Purchasers" means each of Fidelity Select Portfolios: Pharmaceuticals Portfolio, Fidelity Select Portfolios: Biotechnology Portfolio, Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund, Fidelity Mt. Vernon Street Trust: Fidelity Growth Company Fund, Fidelity Contrafund: Fidelity Advisor New Insights Fund, Fidelity Securities Fund: Fidelity Small Cap Opportunities Fund and Fidelity Capital Trust: Fidelity Small Cap Independence Fund.

"Indemnified Party" means a party entitled to indemnification pursuant to Section 2.5.

"Indemnifying Party" means a party obligated to provide indemnification pursuant to Section 2.5.

"Independent Directors" has the meaning given to such term in the Second Amended and Restated Stockholders' Voting Agreement by and among the Company, the Purchasers and the Founders, dated on or about the date hereof.

"Initial Public Offering" means the initial underwritten public offering of shares of Common Stock pursuant to an effective Registration Statement.

"Initiating Holders" means the Purchasers initiating a request for registration pursuant to Section 2.1(a) or 2.1(b), as the case may be.

"Notice of Acceptance" means a written notice from a Purchaser to the Company containing the information specified in Section 3.1(b).

"Offer" means a written notice of any proposed or intended issuance, sale or exchange of Offered Securities containing the information specified in Section 3.1(a).

"Offered Securities" means (a) any shares of Common Stock, (b) any other equity securities of the Company, including, without limitation, shares of preferred stock, (c) any option, warrant or other right to subscribe for, purchase or otherwise acquire any equity securities of the Company, or (d) any debt securities convertible into capital stock of the Company.

"Other Holders" means holders of securities of the Company (other than Purchasers) who are entitled, by contract with the Company, to have securities included in a Registration Statement.

"Prospectus" means the prospectus included in any Registration Statement, as amended or supplemented by an amendment or prospectus supplement, including post-effective amendments, and all material incorporated by reference or deemed to be incorporated by reference in such Prospectus.

"Purchase Agreement" has the meaning ascribed to it in the recitals hereto.

"Purchaser" has the meaning ascribed to it in the introductory paragraph hereto.

"Qualified Public Offering" means the closing of the sale of shares of Common Stock to the public in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act resulting in at least $30,000,000 of gross proceeds to the Corporation and with either (a) a price of at least $5.00 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Common Stock) or (b) a listing of the Common Stock on a nationally recognized securities exchange or trading system.

"Qualified Purchaser" means a Purchaser that is an "accredited investor" within the meaning of Rule 501(a) under the Securities Act.

"Refused Securities" means those Offered Securities as to which a Notice of Acceptance has not been given by the Qualified Purchasers pursuant to Section 3.1.

"Registrable Shares" means (a) the shares of Common Stock issued or issuable upon conversion of the Shares, (b) any IPO Shares (as defined in the Series B Purchase Agreement) purchased

in a Private Placement (as defined in the Series B Purchase Agreement), and (c) any other shares of Common Stock issued in respect of such shares (because of stock splits, stock dividends, reclassifications, recapitalizations or similar events); provided, however, that shares of Common Stock which are Registrable Shares shall cease to be Registrable Shares (i) upon any sale pursuant to a Registration Statement or Rule 144 under the Securities Act or (ii) upon any sale in any manner to a person or entity which is not entitled, pursuant to Section 6.1, to the rights under this Agreement or (iii) at such time, following an Initial Public Offering, as they become eligible for sale pursuant to Rule 144(b)(1)(i) under the Securities Act; provided, however, with respect to clause (iii), a period of at least one year, as determined in accordance with paragraph (d) of Rule 144 under the Securities Act, has elapsed since the later of the date such shares were acquired from the Company or an affiliate of the Company. Wherever reference is made in this Agreement to a request or consent of holders of a certain percentage of Registrable Shares, the determination of such percentage shall include shares of Common Stock issuable upon conversion of the Shares even if such conversion has not been effected.

"Registration Expenses" means all expenses incurred by the Company in complying with the provisions of Section 2, including, without limitation, all registration and filing fees, exchange listing fees, printing expenses, fees and expenses of counsel for the Company and the fees and expenses of one counsel selected by the Selling Stockholders to represent the Selling Stockholders, state Blue Sky fees and expenses, and the expense of any special audits incident to or required by any such registration, but excluding underwriting discounts, selling commissions and the fees and expenses of Selling Stockholders' own counsel (other than the counsel selected to represent all Selling Stockholders).

"Registration Statement" means a registration statement filed by the Company with the Commission for a public offering and sale of securities of the Company (other than a registration statement on Form S-8 or Form S-4, or their successors, or any other form for a similar limited purpose, or any registration statement covering only securities proposed to be issued in exchange for securities or assets of another corporation).

"Securities Act" means the Securities Act of 1933, as amended, or any successor federal statute, and the rules and regulations of the Commission issued under such Act, as they each may, from time to time, be in effect.

"Selling Stockholder" means any Purchaser owning Registrable Shares included in a Registration Statement.

"Series A Directors" means the directors designated by the holders of Series A Convertible Preferred Stock of the Company pursuant to the Second Amended and Restated Stockholders' Voting Agreement by and among the Company, the Purchasers and the Founders, dated on or about the date hereof.

"Series B Purchase Agreement" means the Series B Convertible Preferred Stock Purchase Agreement, dated as of April 14, 2010, by and between the Company and Celgene Corporation.

"Shares" means shares of Series A Convertible Preferred Stock, $0.001 par value per share, of the Company, shares of Series B Convertible Preferred Stock, $0.001 par value per share, of the Company, Series C-1 Convertible Preferred Stock, $0.001 par value per share, of the Company and Series C-2 Convertible Preferred Stock, $0.001 par value per share, of the Company.

"Undersubscription Amount" means, with respect to a Qualified Purchaser, any additional portion of the Offered Securities attributable to the Basic Amounts of other Qualified Purchasers as such Qualified Purchaser indicates it will purchase or acquire should the other Qualified Purchasers subscribe for less than their Basic Amounts.

2. Registration Rights.

2.1 Required Registrations.

(a) At any time after the earlier of (i) five years after the date hereof or (ii) six months after the closing of the Initial Public Offering, a Purchaser or Purchasers holding in the aggregate a majority of the Registrable Shares then outstanding may request, in writing, that the Company effect the registration on Form S-1 (or any successor form) of Registrable Shares owned by such Purchaser or Purchasers having an aggregate value of at least $5,000,000 (based on the market price or fair value on the date of such request).

(b) At any time after the Company becomes eligible to file a Registration Statement on Form S-3 (or any successor form relating to secondary offerings), a Purchaser or Purchasers holding in the aggregate at least 25% of the Registrable Shares may request, in writing, that the Company effect the registration on Form S-3 (or such successor form), of Registrable Shares having an aggregate value of at least $5,000,000 (based on the public market price on the date of such request).

(c) Upon receipt of any request for registration pursuant to this Section 2, the Company shall promptly give written notice of such proposed registration to all other Purchasers. Such Purchasers shall have the right, by giving written notice to the Company within 30 days after the Company provides its notice, to elect to have included in such registration such of their Registrable Shares as such Purchasers may request in such notice of election, subject in the case of an underwritten offering to the terms of Section 2.1(d). Thereupon, the Company shall, as expeditiously as possible, use its best efforts to effect the registration on an appropriate registration form of all Registrable Shares which the Company has been requested to so register; provided, however, that in the case of a registration requested under Section 2.1(b), the Company will only be obligated to effect such registration on Form S-3 (or any successor form).

(d) If the Initiating Holders intend to distribute the Registrable Shares covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to Section 2.1(a) or (b), as the case may be, and the Company shall include such information in its written notice referred to in Section 2.1(c). In such event, (i) the right of any other Purchaser to include its Registrable Shares in such registration pursuant to Section 2.1(a) or (b), as the case may be, shall be conditioned upon such other Purchaser's participation in such underwriting on the terms set forth herein, and (ii) all Purchasers including Registrable Shares in such registration shall enter into an underwriting agreement upon customary terms with the underwriter or underwriters managing the offering; provided that such underwriting agreement shall not provide for indemnification or contribution obligations on the part of the Purchasers materially greater than the obligations of the Purchasers pursuant to Section 2.5. The Initiating Holders shall have the right to select the managing underwriter(s) for any underwritten offering requested pursuant to Section 2.1(a) or (b), subject to the approval of the Company, which approval will not be unreasonably withheld, conditioned or delayed. If any Purchaser who has requested inclusion of its Registrable Shares in such registration as provided above disapproves of the terms of the underwriting, such Purchaser may elect, by written notice to the Company, to withdraw its Registrable Shares from such Registration Statement and underwriting. If the Company desires that any officers or directors of the Company holding securities of the Company be included in any registration for an underwritten offering requested pursuant to Section 2.1 or if Other Holders request such inclusion, the Company may include the securities of such officers, directors and Other Holders in such registration and underwriting on the terms set forth herein applicable to the Purchasers. If the managing underwriter

advises the Company in writing that marketing factors require a limitation on the number of shares to be underwritten, the shares held by officers or directors of the Company and by Other Holders (other than Registrable Shares) shall be excluded from such Registration Statement and underwriting to the extent deemed advisable by the managing underwriter, and if a further reduction of the number of shares is required, the number of shares that may be included in such Registration Statement and underwriting shall be allocated among all Purchasers requesting registration in proportion, as nearly as practicable, to the respective number of Registrable Shares held by them on the date of the request for registration made by the Initiating Holders pursuant to Section 2.1(a) or (b), as the case may be. If any such stockholder would thus be entitled to include more shares than such stockholder requested to be registered, the excess shall be allocated among other participating stockholders pro rata in the manner described in the preceding sentence. If the managing underwriter has not limited the number of Registrable Shares or other securities to be underwritten, the Company may include securities for its own account in such registration if the managing underwriter so agrees and if the number of Registrable Shares and other securities which would otherwise have been included in such registration and underwriting will not thereby be limited.

(e) The Company shall not be required to effect more than (i) two registrations pursuant to Section 2.1(a) or (ii) in any 12-month period, two registrations pursuant to Section 2.1(b). In addition, the Company shall not be required to effect any registration within six months after the effective date of the Registration Statement relating to the Initial Public Offering. For purposes of this Section 2.1(e), a Registration Statement shall not be counted until such time as such Registration Statement has been declared effective by the Commission (unless the Initiating Holders withdraw their request for such registration (other than as a result of information concerning the business or financial condition of the Company which is made known to the Purchasers after the date on which such registration was requested) and elect not to pay the Registration Expenses therefor pursuant to Section 2.4). For purposes of this Section 2.1(e), a Registration Statement shall not be counted if, as a result of an exercise of the underwriter's cut-back provisions, less than 50% of the total number of Registrable Shares that Purchasers have requested to be included in such Registration Statement are so included.

(f) If at the time of any request to register Registrable Shares by Initiating Holders pursuant to this Section 2.1, the Company is engaged or has plans to engage in a registered public offering or is engaged in any other activity which, in the good faith determination of the Company's Board of Directors, would be adversely affected by the requested registration, then the Company may at its option direct that such request be delayed for a period not in excess of 30 days from the date of such request, such right to delay a request to be exercised by the Company not more than twice in any 12-month period.

2.2 Incidental Registration.

(a) Whenever the Company proposes to file a Registration Statement covering shares of Common Stock at any time and from time to time, it will, prior to such filing, give written notice to all Purchasers of its intention to do so. Upon the written request of a Purchaser or Purchasers given within 20 days after the Company provides such notice (which request shall state the intended method of disposition of such Registrable Shares), unless (i) the Registration Statement is to be filed pursuant to Section 2.1 hereof, (ii) the Registration Statement covers shares to be sold solely for the account of Other Holders, which shares were acquired pursuant to either (I) an acquisition of a company of which they were formerly stockholders, (II) a "private placement" under the Securities Act or (III) Rule 144A under the Securities Act, or (iii) no Registrable Shares are to be included in the Registration Statement as a result of a written notice from the managing underwriter pursuant to Section 2.2(b), the Company shall use its best efforts to cause all Registrable Shares which the Company has been requested by such Purchaser or Purchasers to register to be registered under the Securities Act to the extent

necessary to permit their sale or other disposition in accordance with the intended methods of distribution specified in the request of such Purchaser or Purchasers; provided that the Company shall have the right to postpone or withdraw any registration effected pursuant to this Section 2.2 without obligation to any Purchaser.

(b) If the registration for which the Company gives notice pursuant to Section 2.2(a) is a registered public offering involving an underwriting, the Company shall so advise the Purchasers as a part of the written notice given pursuant to Section 2.2(a). In such event, (i) the right of any Purchaser to include its Registrable Shares in such registration pursuant to this Section 2.2 shall be conditioned upon such Purchaser's participation in such underwriting on the terms set forth herein and (ii) all Purchasers including Registrable Shares in such registration shall enter into an underwriting agreement upon customary terms with the underwriter or underwriters selected for the underwriting by the Company. If any Purchaser who has requested inclusion of its Registrable Shares in such registration as provided above disapproves of the terms of the underwriting, such person may elect, by written notice to the Company, to withdraw its shares from such Registration Statement and underwriting. If the managing underwriter advises the Company in writing that marketing factors require a limitation on the number of shares to be underwritten, the shares held by holders of securities of the Company other than Purchasers and Other Holders shall be excluded from such Registration Statement and underwriting to the extent deemed advisable by the managing underwriter, and, if a further reduction of the number of shares is required, the shares held by Other Holders shall be excluded from such Registration Statement and underwriting to the extent deemed advisable by the managing underwriter, and, if a further reduction of the number of shares is required, the number of shares that may be included in such Registration Statement and underwriting shall be allocated among all Purchasers requesting registration in proportion, as nearly as practicable, to the respective number of shares of Common Stock (on an as-converted basis) held by them on the date the Company gives the notice specified in Section 2.2(a). If any Purchaser would thus be entitled to include more shares than such holder requested to be registered, the excess shall be allocated among other requesting Purchasers pro rata in the manner described in the preceding sentence.

2.3 Registration Procedures.

(a) If and whenever the Company is required by the provisions of this Agreement to use its best efforts to effect the registration of any Registrable Shares under the Securities Act, the Company shall:

(i) file with the Commission a Registration Statement with respect to such Registrable Shares and use its best efforts to cause that Registration Statement to become effective as soon as possible;

(ii) as expeditiously as possible prepare and file with the Commission any amendments and supplements to the Registration Statement and the prospectus included in the Registration Statement as may be necessary to comply with the provisions of the Securities Act (including the anti-fraud provisions thereof) and to keep the Registration Statement effective for 12 months from the effective date or such lesser period until all such Registrable Shares are sold;

(iii) as expeditiously as possible furnish to each Selling Stockholder such reasonable numbers of copies of the Prospectus, including any preliminary Prospectus, in conformity with the requirements of the Securities Act, and such other documents as such Selling Stockholder may reasonably request in order to facilitate the public sale or other disposition of the Registrable Shares owned by such Selling Stockholder;

(iv) as expeditiously as possible use its best efforts to register or qualify the Registrable Shares covered by the Registration Statement under the securities or Blue Sky laws of such states as the Selling Stockholders shall reasonably request, and do any and all other acts and things that may be necessary or desirable to enable the Selling Stockholders to consummate the public sale or other disposition in such states of the Registrable Shares owned by the Selling Stockholders; provided, however, that the Company shall not be required in connection with this paragraph (iv) to qualify as a foreign corporation or to execute a general consent to service of process in any jurisdiction or to amend its Certificate of Incorporation or By-laws in a manner that the Board of Directors of the Company determines is inadvisable;

(v) as expeditiously as possible, cause all such Registrable Shares to be listed on each securities exchange or automated quotation system on which similar securities issued by the Company are then listed;

(vi) promptly provide a transfer agent and registrar for all such Registrable Shares not later than the effective date of such Registration Statement;

(vii) promptly make available for inspection by the Selling Stockholders, any managing underwriter participating in any disposition pursuant to such Registration Statement, and any attorney or accountant or other agent retained by any such underwriter or selected by the Selling Stockholders, all financial and other records, pertinent corporate documents and properties of the Company and cause the Company's officers, directors, employees and independent accountants to supply all information reasonably requested by any such seller, underwriter, attorney, accountant or agent in connection with such Registration Statement;

(viii) notify each Selling Stockholder, promptly after it shall receive notice thereof, of the time when such Registration Statement has become effective or a supplement to any Prospectus forming a part of such Registration Statement has been filed; and

(ix) as expeditiously as possible following the effectiveness of such Registration Statement, notify each seller of such Registrable Shares of any request by the Commission for the amending or supplementing of such Registration Statement or Prospectus.

(b) If the Company has delivered a Prospectus to the Selling Stockholders and after having done so the Prospectus is amended to comply with the requirements of the Securities Act, the Company shall promptly notify the Selling Stockholders and, if requested, the Selling Stockholders shall immediately cease making offers of Registrable Shares and return all Prospectuses to the Company. The Company shall promptly provide the Selling Stockholders with revised Prospectuses and, following receipt of the revised Prospectuses, the Selling Stockholders shall be free to resume making offers of the Registrable Shares.

(c) In the event that, in the judgment of the Company, it is advisable to suspend use of a Prospectus included in a Registration Statement due to pending material developments or other events that have not yet been publicly disclosed and as to which the Company believes public disclosure would be detrimental to the Company, the Company shall notify all Selling Stockholders to such effect, and, upon receipt of such notice, each such Selling Stockholder shall immediately discontinue any sales of Registrable Shares pursuant to such Registration Statement until such Selling Stockholder has received copies of a supplemented or amended Prospectus or until such Selling Stockholder is advised in writing by the Company that the then current Prospectus may be used and has received copies of any additional or supplemental filings that are incorporated or deemed incorporated by reference in such Prospectus. Notwithstanding anything to the contrary herein, the Company shall not exercise its rights under this Section 2.3(c) to suspend sales of Registrable Shares for a period in excess of 30 days consecutively or 60 days in any 365-day period.

2.4 Allocation of Expenses. The Company will pay all Registration Expenses for all registrations under this Agreement; provided, however, that if a registration under Section 2.1 is withdrawn at the request of the Initiating Holders (other than as a result of information concerning the business or financial condition of the Company which is made known to the Selling Stockholders after the date on which such registration was requested) and if the Initiating Holders elect not to have such registration counted as a registration requested under Section 2.1, the Selling Stockholders shall pay the Registration Expenses of such registration pro rata in accordance with the number of their Registrable Shares included in such registration.

2.5 Indemnification and Contribution.

(a) In the event of any registration of any of the Registrable Shares under the Securities Act pursuant to this Agreement, the Company will indemnify and hold harmless each Selling Stockholder, each underwriter of such Registrable Shares, and each other person, if any, who controls such Selling Stockholder or underwriter within the meaning of the Securities Act or the Exchange Act against any losses, claims, damages or liabilities, joint or several, to which such Selling Stockholder, underwriter or controlling person may become subject under the Securities Act, the Exchange Act, state securities or Blue Sky laws or otherwise, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon (i) any untrue statement or alleged untrue statement of any material fact contained in any Registration Statement under which such Registrable Shares were registered under the Securities Act, any preliminary prospectus or final prospectus contained in the Registration Statement, or any amendment or supplement to such Registration Statement, (ii) the omission or alleged omission to state a material fact required to be stated therein or necessary to make the statements therein not misleading, or (iii) any violation or alleged violation by the Company of the Securities Act, the Exchange Act, any state securities law or any rule or regulation promulgated under the Securities Act, the Exchange Act or any state securities law in connection with the Registration Statement or the offering contemplated thereby; and the Company will reimburse such Selling Stockholder, underwriter and each such controlling person for any legal or any other expenses reasonably incurred by such Selling Stockholder, underwriter or controlling person in connection with investigating or defending any such loss, claim, damage, liability or action; provided, however, that the Company will not be liable in any such case to the extent that any such loss, claim, damage or liability arises out of or is based upon any untrue statement or omission made in such Registration Statement, preliminary prospectus or prospectus, or any such amendment or supplement, in reliance upon and in conformity with information furnished to the Company, in writing, by or on behalf of such Selling Stockholder, underwriter or controlling person specifically for use in the preparation thereof.

(b) In the event of any registration of any of the Registrable Shares under the Securities Act pursuant to this Agreement, each Selling Stockholder, severally and not jointly, will indemnify and hold harmless the Company, each of its directors and officers and each underwriter (if any) and each person, if any, who controls the Company or any such underwriter within the meaning of the Securities Act or the Exchange Act, against any losses, claims, damages or liabilities, joint or several, to which the Company, such directors and officers, underwriter or controlling person may become subject under the Securities Act, Exchange Act, state securities or Blue Sky laws or otherwise, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon (i) any untrue statement or alleged untrue statement of a material fact contained in any Registration Statement under which such Registrable Shares were registered under the Securities Act, any preliminary prospectus or final prospectus contained in the Registration Statement, or any amendment or supplement to the Registration Statement, or (ii) any omission or alleged omission to state a material fact required to be

stated therein or necessary to make the statements therein not misleading, if and to the extent (and only to the extent), in the case of both clauses (i) and (ii), that the statement or omission was made in reliance upon and in conformity with information relating to such Selling Stockholder furnished in writing to the Company by or on behalf of such Selling Stockholder specifically for use in connection with the preparation of such Registration Statement, prospectus, amendment or supplement; provided, however, that the obligations of a Selling Stockholder hereunder shall be limited to an amount equal to the net proceeds to such Selling Stockholder of Registrable Shares sold in connection with such registration.

(c) Each Indemnified Party shall give notice to the Indemnifying Party promptly after such Indemnified Party has actual knowledge of any claim as to which indemnity may be sought, and shall permit the Indemnifying Party to assume the defense of any such claim or any litigation resulting therefrom; provided, that counsel for the Indemnifying Party, who shall conduct the defense of such claim or litigation, shall be approved by the Indemnified Party (whose approval shall not be unreasonably withheld, conditioned or delayed); and, provided, further, that the failure of any Indemnified Party to give notice as provided herein shall not relieve the Indemnifying Party of its obligations under this Section 2.5 except to the extent that the Indemnifying Party is adversely affected by such failure. The Indemnified Party may participate in such defense at such party's expense; provided, however, that the Indemnifying Party shall pay such expense if the Indemnified Party reasonably concludes that representation of such Indemnified Party by the counsel retained by the Indemnifying Party would be inappropriate due to actual or potential differing interests between the Indemnified Party and any other party represented by such counsel in such proceeding; provided further that in no event shall the Indemnifying Party be required to pay the expenses of more than one law firm per jurisdiction as counsel for the Indemnified Party. The Indemnifying Party also shall be responsible for the expenses of such defense if the Indemnifying Party does not elect to assume such defense. No Indemnifying Party, in the defense of any such claim or litigation shall, except with the consent of each Indemnified Party, consent to entry of any judgment or enter into any settlement which does not include as an unconditional term thereof the giving by the claimant or plaintiff to such Indemnified Party of a release from all liability in respect of such claim or litigation, and no Indemnified Party shall consent to entry of any judgment or settle such claim or litigation without the prior written consent of the Indemnifying Party, which consent shall not be unreasonably withheld, conditioned or delayed.

(d) In order to provide for just and equitable contribution in circumstances in which the indemnification provided for in this Section 2.5 is due in accordance with its terms but for any reason is held to be unavailable to an Indemnified Party in respect to any losses, claims, damages and liabilities referred to herein, then the Indemnifying Party shall, in lieu of indemnifying such Indemnified Party, contribute to the amount paid or payable by such Indemnified Party as a result of such losses, claims, damages or liabilities to which such party may be subject in such proportion as is appropriate to reflect the relative fault of the Company on the one hand and each Selling Stockholder on the other in connection with the statements or omissions which resulted in such losses, claims, damages or liabilities, as well as any other relevant equitable considerations. The relative fault of the Company and each Selling Stockholder shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of material fact related to information supplied by the Company or a Selling Stockholder and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission. The Company and the Selling Stockholders agree that it would not be just and equitable if contribution pursuant to this Section 2.5(d) were determined by pro rata allocation or by any other method of allocation which does not take account of the equitable considerations referred to above. Notwithstanding the provisions of this Section 2.5(d), (i) in no case shall any one Selling Stockholder be liable or responsible for any amount in excess of the net proceeds received by such Selling Stockholder from the offering of Registrable Shares and (ii) the Company shall be liable and responsible for any amount in excess of such proceeds; provided, however, that no person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to

contribution from any person who was not guilty of such fraudulent misrepresentation. Any party entitled to contribution will, promptly after receipt of notice of commencement of any action, suit or proceeding against such party in respect of which a claim for contribution may be made against another party or parties under this Section 2.5(d), notify such party or parties from whom contribution may be sought, but the omission so to notify such party or parties from whom contribution may be sought shall not relieve such party from any other obligation it or they may have thereunder or otherwise under this Section 2.5(d). No party shall be liable for contribution with respect to any action, suit, proceeding or claim settled without its prior written consent, which consent shall not be unreasonably withheld, conditioned or delayed.

(e) The rights and obligations of the Company and the Selling Stockholders under this Section 2.5 shall survive the termination of this Agreement.

2.6 Other Matters with Respect to Underwritten Offerings. In the event that Registrable Shares are sold pursuant to a Registration Statement in an underwritten offering pursuant to Section 2.1, the Company agrees to (a) enter into an underwriting agreement containing customary representations and warranties with respect to the business and operations of the Company and customary covenants and agreements to be performed by the Company, including without limitation customary provisions with respect to indemnification by the Company of the underwriters of such offering; (b) use its best efforts to cause its legal counsel to render customary opinions to the underwriters with respect to the Registration Statement; and (c) use its best efforts to cause its independent public accounting firm to issue customary "cold comfort letters" to the underwriters with respect to the Registration Statement.

2.7 Information by Holder. Each holder of Registrable Shares included in any registration shall furnish to the Company such information regarding such holder and the distribution proposed by such holder as the Company may reasonably request in writing and as shall be required in connection with any registration, qualification or compliance referred to in this Agreement.

2.8 "Lock-Up" Agreement; Confidentiality of Notices. Each Purchaser agrees, if requested by the Company and the managing underwriter of the Initial Public Offering, (i) not to (a) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly (other than as a result of a change of control of a holder of Registrable Shares where such holder survives the change of control), any Registrable Shares or other securities of the Company (excluding securities acquired in the Initial Public Offering or in the public market after such offering) or (b) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of any Registrable Shares or other securities of the Company (excluding securities acquired in the Initial Public Offering or in the public market after such offering), whether any transaction described in clause (a) or (b) is to be settled by delivery of securities, in cash or otherwise, during the period beginning on the date of the filing of such registration statement with the Securities and Exchange Commission and ending 180 days after the date of the final prospectus relating to the Initial Public Offering (plus up to an additional 34 days to the extent requested by the managing underwriters for such offering in order to address NASD Rule 2711(f) of the Financial Industry Regulatory Authority, Inc. or NYSE Rule 472(f)(4) or any similar successor provision) and (ii) to execute any agreement reflecting clause (i) above as may be requested by the Company or the managing underwriters at the time of such offering; provided, that all stockholders of the Company then holding at least 1% of the outstanding Common Stock (on an as-converted basis) and all officers and directors of the Company enter into similar agreements.

The Company may impose stop-transfer instructions with respect to the Registrable Shares or other securities subject to the foregoing restriction until the end of such "lock-up" period.

As a condition to the obligation of the Purchasers under this Section 2.8, the Company agrees to use reasonable efforts to ensure that the "lock-up" obligation of the Purchasers under this Section 2.8, and any agreement entered into by the Purchasers as a result of their obligations under this Section 2.8, shall allow for periodic early releases of portions of the securities subject to such "lock-up" obligations, which may be conditioned upon the trading price of the Company's Common Stock. The Company also agrees to use its best efforts to ensure that the "lock-up" obligation of the Purchasers under this Section 2.8, and any agreement entered into by the Purchasers as a result of their obligation under this Section 2.8, shall provide that all Purchasers will participate on a pro-rata basis in any early release of any stockholder.

Any Purchaser receiving any written notice from the Company regarding the Company's plans to file a Registration Statement shall treat such notice confidentially and shall not disclose such information to any person other than as necessary to exercise its rights under this Agreement.

2.9 Limitations on Subsequent Registration Rights. The Company shall not, prior to the Initial Public Offering, without the prior written consent of Purchasers holding at least a majority of the Registrable Shares then held by all Purchasers, enter into any agreement (other than this Agreement) with any holder or prospective holder of any securities of the Company which grants such holder or prospective holder rights to include securities of the Company in any Registration Statement, unless (a) such rights to include securities in a registration initiated by the Company or by Purchasers are not more favorable than the rights granted to Other Holders under Sections 2.1 and 2.2, and (b) no rights are granted to initiate a registration, other than registration pursuant to a registration statement on Form S-3 (or its successor) in which Purchasers are entitled to include Registrable Shares on a pro rata basis with such holders based on the number of shares of Common Stock (on an as-converted basis) owned by Purchasers and such holders.

2.10 Reports Under Exchange Act. After the earliest of (i) the closing of the sale of securities of the Company pursuant to a Registration Statement, (ii) the registration by the Company of a class of securities under Section 12 of the Exchange Act, or (iii) the issuance by the Company of an offering circular pursuant to Regulation A under the Securities Act and with a view to making available to the holders of Registrable Shares the benefits of Rule 144 and any other rule or regulation of the SEC that may at any time permit such holders to sell securities of the Company to the public without registration or pursuant to a registration on Form S-3, the Company agrees to:

(a) make and keep current public information about the Company available, as those terms are understood and defined in Rule 144;

(b) use its best efforts to file with the Commission in a timely manner all reports and other documents required of the Company under the Securities Act and the Exchange Act (at any time after it has become subject to such reporting requirements); and

(c) furnish to any holder of Registrable Shares upon request (i) a written statement by the Company as to its compliance with the reporting requirements of Rule 144 and of the Securities Act and the Exchange Act (at any time after it has become subject to such reporting requirements), (ii) a copy of the most recent annual or quarterly report of the Company, and (iii) such other reports and documents of the Company as such holder may reasonably request to avail itself of any similar rule or regulation of the Commission allowing it to sell any such securities without registration (at any time after the Company has become subject to the reporting requirements under the Exchange Act) or pursuant to Form S-3 (at any time after the Company so qualifies to use such form).

2.11 Termination. All of the Company's obligations to register Registrable Shares under Sections 2.1 and 2.2 shall terminate upon the earliest of (a) five years after the closing of the Initial Public Offering, (b) the date on which no Purchaser holds any Registrable Shares or (c) a Company Sale.

3. Right of First Refusal.

3.1 Rights of Purchasers to Acquire Offered Securities.

(a) The Company shall not issue, sell or exchange, agree to issue, sell or exchange, or reserve or set aside for issuance, sale or exchange, any Offered Securities, unless in each such case the Company shall have first complied with this Section 3.1. The Company shall deliver to each Purchaser an Offer, which shall (i) identify and describe the Offered Securities, (ii) describe the price and other terms upon which they are to be issued, sold or exchanged, and the number or amount of the Offered Securities to be issued, sold or exchanged, (iii) identify the persons or entities (if known) to which or with which the Offered Securities are to be offered, issued, sold or exchanged, and (iv) offer to issue and sell to or exchange with such Purchaser that is a Qualified Purchaser (A) such Qualified Purchaser's Basic Amount and (B) such Qualified Purchaser's Undersubscription Amount. Notwithstanding the other provisions of this Section 3.1, after delivery of the Offer, the Company may issue, sell or exchange, agree to issue, sell or exchange, or reserve or set aside for issuance, sale or exchange, Offered Securities to the offerees or purchasers described in the Offer and upon the terms and conditions (including, without limitation, unit prices and interest rates) which are not more favorable, in the aggregate, to the acquiring person or persons or less favorable to the Company than those set forth in the Offer without complying with the terms of this Section 3.1, provided that the Company permits each Qualified Purchaser to purchase the number of Offered Securities that such Qualified Purchaser is entitled to purchase pursuant to this Section 3.1 (calculated in the same manner as if such Qualified Purchasers purchased such Offered Securities on the same date as the offerees or purchasers described in the Offer) on substantially the same terms as the Company sold the Offered Securities in the initial transaction, within 10 days after the Company receives a Notice of Acceptance from such Qualified Purchaser.

(b) To accept an Offer, in whole or in part, a Qualified Purchaser must deliver to the Company, on or prior to the date 30 days after the date of delivery of the Offer, a Notice of Acceptance providing a representation letter certifying that such Qualified Purchaser is an accredited investor within the meaning of Rule 501 under the Securities Act and indicating the portion of the Qualified Purchaser's Basic Amount that such Qualified Purchaser elects to purchase and, if such Qualified Purchaser shall elect to purchase all of its Basic Amount, the Undersubscription Amount (if any) that such Qualified Purchaser elects to purchase. If the Basic Amounts subscribed for by all Qualified Purchasers are less than the total of all of the Basic Amounts available for purchase, then each Qualified Purchaser who has set forth an Undersubscription Amount in its Notice of Acceptance shall be entitled to purchase, in addition to the Basic Amounts subscribed for, the Undersubscription Amount it has subscribed for; provided, however, that if the Undersubscription Amounts subscribed for exceed the Available Undersubscription Amount, each Qualified Purchaser who has subscribed for any Undersubscription Amount shall be entitled to purchase only that portion of the Available Undersubscription Amount as the Undersubscription Amount subscribed for by such Qualified Purchaser bears to the total Undersubscription Amounts subscribed for by all Purchasers, subject to rounding by the Board of Directors to the extent it deems reasonably necessary.

(c) The Company shall have 90 days from the expiration of the period set forth in Section 3.1(b) to issue, sell or exchange all or any part of the Refused Securities other than previously sold under the last sentence of Section 3.1(a), but only to the offerees or purchasers described in the Offer (if so described therein) and only upon terms and conditions (including, without limitation, unit prices and interest rates) which are not more favorable, in the aggregate, to the acquiring person or persons or less favorable to the Company than those set forth in the Offer.

(d) In the event the Company shall propose to sell less than all the Refused Securities, then each Qualified Purchaser may, at its sole option and in its sole discretion, reduce the number or amount of the Offered Securities specified in its Notice of Acceptance to an amount that shall be not less than the number or amount of the Offered Securities that the Qualified Purchaser elected to purchase pursuant to Section 3.1(b) multiplied by a fraction, (i) the numerator of which shall be the number or amount of Offered Securities the Company actually proposes to issue, sell or exchange (including Offered Securities to be issued or sold to Qualified Purchasers pursuant to Section 3.1(b) prior to such reduction) and (ii) the denominator of which shall be the original amount of the Offered Securities. In the event that any Qualified Purchaser so elects to reduce the number or amount of Offered Securities specified in its Notice of Acceptance, the Company may not issue, sell or exchange more than the reduced number or amount of the Offered Securities unless and until such securities have again been offered to the Qualified Purchasers in accordance with Section 3.1(a).

(e) Upon (i) the closing of the issuance, sale or exchange of all or less than all of the Refused Securities or (ii) such other date agreed to by the Company and Qualified Purchasers who have subscribed for a majority of the Offered Securities subscribed for by the Qualified Purchasers, such Qualified Purchaser or Purchasers shall acquire from the Company and the Company shall issue to such Qualified Purchaser or Purchasers, the number or amount of Offered Securities specified in the Notices of Acceptance, as reduced pursuant to Section 3.1(d) if any of the Qualified Purchasers has so elected, upon the terms and conditions specified in the Offer.

(f) The purchase by the Qualified Purchasers of any Offered Securities is subject in all cases to the preparation, execution and delivery by the Company and the Qualified Purchasers of a purchase agreement relating to such Offered Securities reasonably satisfactory in form and substance to the Qualified Purchasers and their respective counsel.

(g) Any Offered Securities not acquired by the Qualified Purchasers or other persons in accordance with Section 3.1(c) may not be issued, sold or exchanged until they are again offered to the Qualified Purchasers under the procedures specified in this Agreement.

(h) The rights of the Qualified Purchasers under this Section 3.1 shall not apply to:

(i) the issuance of any shares of Common Stock as a stock dividend to holders of Common Stock or upon any subdivision or combination of shares of Common Stock;

(ii) the issuance of any shares of Common Stock upon conversion of shares of outstanding convertible preferred stock;

(iii) the issuance of up to an aggregate of 10,669,018 shares (including shares issued prior to the date hereof) of Common Stock (or such greater number as is approved by the Board of Directors of the Company, including at least a majority of the Series A Directors and all of the Independent Directors) or options with respect thereto (subject in either case to appropriate adjustment for stock splits, stock dividends, recapitalizations and similar events occurring after the date of this Agreement), issued or issuable to employees, directors or officers of, or consultants to, the Company or any Company Subsidiary pursuant to any plan, agreement or arrangement approved by the Board of Directors of the Company, including at least a majority of the Series A Directors and all of the Independent Directors (it being understood that any shares subject to options that expire or

terminate unexercised or any restricted stock repurchased by the Company shall not be counted towards the maximum number set forth in this clause (iii) unless and until regranted or reissued pursuant to any such plan, agreement or arrangement);

(iv) the issuance of securities solely in consideration for the acquisition (whether by merger or otherwise) by the Company or any Company Subsidiary of all or substantially all of the stock or assets of any other entity (which issuance is approved by the Board of Directors, including at least a majority of the Series A Directors and all of the Independent Directors);

(v) the issuance of shares of Common Stock by the Company in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act; or

(vi) the issuance of shares of Common Stock, or the grant of options or warrants therefor, in connection with any present or future borrowing, line of credit, leasing or similar financing arrangement approved by the Board of Directors of the Company, including at least a majority of the Series A Directors and all of the Independent Directors;

(vii) the issuance of shares of Common Stock, or the grant of options or warrants therefor, pursuant to a joint venture agreement, provided, that such issuances are approved by the Board of Directors of the Corporation, including at least a majority of the Series A Directors and all of the Independent Directors; or

(viii) the issuance of shares of Common Stock, or the grant of options or warrants therefor, in connection with sponsored research, collaboration, technology license, development, OEM, marketing or other similar agreements or strategic partnerships approved by the Board of Directors of the Corporation, including at least a majority of the Series A Directors and all of the Independent Directors.

3.2 Termination. This Section 3 shall terminate upon the earlier of the closing of a Company Sale or the closing of the Initial Public Offering.

4. Covenants.

4.1 Negative Covenants. So long as at least 1,000,000 Shares (subject to appropriate adjustment for stock splits, stock dividends, recapitalizations and similar events occurring after the date of this Agreement) are outstanding, the Company shall not, without the consent of the Board of Directors, including at least a majority of the Series A Directors and all of the Independent Directors:

(a) increase the size of the Board of Directors above nine (9) members;

(b) hire or fire any senior executives or change the compensation of (including approving the payment of bonuses to) senior executives not contemplated in the Budget (as defined below) or such executives' employment agreements;

(c) make any investment other than investments in prime commercial paper, money market funds, certificates of deposit in any United States bank having a net worth in excess of $100,000,000 or obligations issued or guaranteed by the United States of America, in each case having a maturity not in excess of one year;

(d) enter into any lines of business that are not primarily related to the business of the Company as conducted on the date hereof, exit the business of the Company as conducted on the date hereof, or change the principal business of the Company;

(e) grant an exclusive license to any of the Company's material intellectual property rights;

(f) acquire all or substantially all of the properties, assets or stock of any other company or entity;

(g) incur indebtedness in excess of $100,000 in the aggregate that is not covered by the Budget, other than trade credit incurred in the ordinary course of business;

(h) make any loan or advance to, or own any stock or other securities of, any subsidiary or other corporation, partnership, or other entity unless it is wholly owned by the Company;

(i) make any loan or advance to any person, including, any employee or director, except advances and similar expenditures in the ordinary course of business or under the terms of a employee stock or option plan approved by the Board of Directors;

(j) guarantee, any indebtedness except for trade accounts of the Company or any subsidiary arising in the ordinary course of business; or

(k) enter into or be a party to any transaction with any director, officer or employee of the Company or any "associate" (as defined in Rule 12b-2 promulgated under the Exchange Act) of any such person.

4.2 Observation.

(a) The Company will permit one designee of the Founders, who shall be a Founder then serving on the Company's scientific advisory board who is not an employee of or a member of the Board of Directors of the Company, to attend all meetings of the Board of Directors of the Company, and shall provide such Founder with such notice and other information with respect to such meetings as are delivered to the directors of the Company. Notwithstanding the foregoing, the Company may prevent such Founder from attending a Board of Directors meeting (or portion thereof) or receiving certain information with respect thereto if the Company's Board of Directors reasonably believes that the delivery of such information or the attendance at such meeting (i) would result in the loss of trade secret protection or otherwise compromise confidential information or (ii) would adversely affect attorney-client privilege.

(b) As long as the Fidelity Purchasers do not have a representative serving on the Board of Directors of the Company, the Company will permit one designee of the Fidelity Purchasers (the "Fidelity Designee"), who shall be reasonably acceptable to the Company, to attend meetings of the Board of Directors of the Company, and shall provide the Fidelity Designee with such notice and other information with respect to such meetings as are delivered to the directors of the Company. Notwithstanding the foregoing, the Board of Directors of the Company may prevent the Fidelity Designee from attending a Board of Directors meeting (or portion thereof) or receiving certain information with respect thereto if the Company's Board of Directors reasonably believes that the delivery of such information or the attendance at such meeting (i) would result in the loss of trade secret protection or otherwise compromise confidential information or (ii) would adversely affect attorney-client privilege.

4.3 Financial Statements and Budget. The Company shall deliver to each Purchaser:

(a) within 120 days after the end of each fiscal year of the Company, an audited balance sheet of the Company as at the end of such year and audited statements of income and of cash flows of the Company for such year, certified by certified public accountants of established regional or national reputation selected by the Company, and prepared in accordance with generally accepted accounting principles consistently applied;

(b) within 30 days after the end of each of the first three fiscal quarters of the Company and within 60 days after the end of the fourth fiscal quarter of the Company, an unaudited balance sheet of the Company as at the end of such quarter, and unaudited statements of income and of cash flows of the Company for such fiscal quarter and for the current fiscal year to the end of such fiscal quarter;

(c) within 30 days after the end of each month (other than the last month of any fiscal quarter), an unaudited balance sheet of the Company as at the end of such month and unaudited statements of income and of cash flows of the Company for such month and for the current fiscal year to the end of such month, setting forth in comparative form the Company's projected financial statements for the corresponding periods for the current fiscal year;

(d) at least 30 days prior to the commencement of each new fiscal year, a budget (the "Budget") approved by the Board of Directors of the Company for such fiscal year; provided that any budget provided to Celgene may be revised to exclude any information that the Company reasonably believes would (i) identify parties to existing business transactions or business transactions under negotiation (provided that the budget shall retain information sufficient for Celgene to understand the impact of the budget on the Company's financial condition) or (ii) reveal sensitive or strategic information related to a potential or existing conflict of interest between Celgene and the Company with respect to the Collaboration Agreement; and

(e) promptly following the end of each fiscal quarter of the Company, an updated capitalization table of the Company certified by the Treasurer of the Company.

Upon the request of any Purchaser, the Company will use commercially reasonable efforts to advise such Purchaser if the Company believes there may be material non-public information about any other company that has any class of its equity securities traded publicly in any part of the world in any of the materials provided to such Purchaser under this Section 4.3.

4.4 Agreements with Employees; Options.

(a) Subject to the policies of any academic or research institutions with whom the Company's consultants or advisors may be affiliated, the Company (A) shall require all persons now or hereafter employed by the Company to enter into non-competition, non-solicitation confidentiality and assignment agreements substantially in the form of Exhibit G to the Purchase Agreement and (B) shall require all consultants utilized by the Company to enter into such invention and non-disclosure agreements and/or non-competition and non-solicitation agreements as may be required by the Board of Directors of the Company.

(b) Unless otherwise approved by the Board of Directors, including at least a majority of the Series A Directors and all of the Independent Directors, all options or restricted stock granted or issued by the Company after the date hereof to employees or consultants shall become exercisable at the rate of 25% on the first anniversary of the date of grant or issue and 2.0833% per month thereafter over the subsequent three (3) years, so long as the holder continues to be an employee or consultant of the Company.

4.5 Board of Directors.

(a) The Company shall promptly reimburse in full each director of the Company who is not an employee of the Company for all of his or her reasonable out-of-pocket expenses incurred in attending each meeting of the Board of Directors of the Company or any committee thereof.

(b) The Board of Directors shall meet at least eight (8) times per year (whether in person or by teleconference), unless otherwise agreed by a majority of the members of the Board of Directors.

(c) The Company shall obtain as promptly as practicable following the date of this Agreement and shall maintain, until otherwise approved by a majority of the Board of Directors who are not employees of the Company, a director and officer liability insurance policy on terms approved by a majority of the members of the Board of Directors who are not employees of the Company.

(d) The Company hereby acknowledges that one or more of the Series A Directors may have certain rights to indemnification, advancement of expenses and/or insurance provided by one or more of the Investors and certain of their affiliates (collectively, the "Fund Indemnitors"). The Company hereby agrees (i) that it is the indemnitor of first resort (i.e., its obligations to any such Series A Director are primary and any obligation of the Fund Indemnitors to advance expenses or to provide indemnification for the same expenses or liabilities incurred by such Series A Director are secondary), (ii) that it shall be required to advance the full amount of expenses incurred by such Series A Director and shall be liable for the full amount of all expenses, judgments, penalties, fines and amounts paid in settlement by or on behalf of any such Series A Director to the extent legally permitted and as required by the Certificate of Incorporation or Bylaws of the Company (or any agreement between the Company and such Series A Director), without regard to any rights such Series A Director may have against the Fund Indemnitors, and, (iii) that it irrevocably waives, relinquishes and releases the Fund Indemnitors from any and all claims against the Fund Indemnitors for contribution, subrogation or any other recovery of any kind in respect thereof. The Company further agrees that no advancement or payment by the Fund Indemnitors on behalf of any such Series A Director with respect to any claim for which such Series A Director has sought indemnification from the Company shall affect the foregoing and the Fund Indemnitors shall have a right of contribution and/or be subrogated to the extent of such advancement or payment to all of the rights of recovery of such Series A Director against the Company.

(e) In the event that the Company or any of its successors or assigns (i) consolidates with or merges into any other entity and shall not be the continuing or surviving corporation in such consolidation or merger or (ii) transfers or conveys all or substantially all of its properties and assets to any entity, then, and in each such case, to the extent necessary, proper provision shall be made so that the successors and assigns of the Company to assume the obligations of the Company with respect to indemnification of members of the Board of Directors as contained in the Company's Third Amended and Restated Certificate of Incorporation, as amended and/or restated from time to time.

(f) Each committee of the Board of Directors shall contain at least one Series A Director and at least one Independent Director.

4.6 Termination of Covenants. All covenants of the Company contained in this Section 4 (except the covenants set forth in Section 4.5(d) and (e)) shall terminate upon the earlier of the closing of a Company Sale or the closing of the Initial Public Offering.

5. Confidentiality; Acknowledgement of Investor Activity.

(a) Each Purchaser agrees that he, she or it will keep confidential and will not disclose, divulge or use for any purpose, other than to monitor its investment in the Company, any Confidential Information, unless such Confidential Information (a) is known or becomes known to the public in general (other than as a result of a breach of this Section 5.1 by such Purchaser), (b) is or has been independently developed or conceived by the Purchaser without use of the Company's Confidential Information or (c) is or has been made known or disclosed to the Purchaser by a third party without a breach of any obligation of confidentiality such third party may have to the Company; provided, however, that a Purchaser may disclose Confidential Information (i) to its attorneys, accountants, consultants, and other professionals to the extent necessary to obtain their services in connection with monitoring its investment in the Company, (ii) to any prospective purchaser of any Shares from such Purchaser as long as such prospective purchaser agrees to be bound by the provisions of this Section 5.1, (iii) to any Affiliated Party of such Purchaser, provided that such party is obligated not to disclose, divulge or use any Confidential Information to the same extent as the Purchasers, or (iv) as may otherwise be required by law, regulation or legal process, provided that the Purchaser takes reasonable steps to minimize the extent of any such required disclosure. Notwithstanding the foregoing, such information shall not be deemed confidential for the purpose of enforcing this Agreement.

(b) The Company acknowledges that certain of the Investors are registered Investment Companies under the Investment Company Act of 1940, as amended, other investment funds or in the business of venture capital investing and therefore review the business plans and related proprietary information of many enterprises, including enterprises that may have products or services that compete directly or indirectly with those of the Company. Nothing in this Agreement shall preclude or in any way restrict the Investors from investing or participating in any particular enterprise whether or not such enterprise has products or services which compete with those of the Company; provided that the Investors remain in compliance with the confidentiality obligations set forth above in Section 5.1.

6. Transfers of Rights; Calculation of Share Numbers.

6.1 Transfer of Rights. This Agreement, and the rights and obligations of each Purchaser hereunder, may be assigned by such Purchaser to (a) any person or entity to which at least 600,000 Shares (subject to appropriate adjustment for stock splits, stock dividends, recapitalizations and similar events occurring after the date of this Agreement) or all of the Shares owned by such Purchaser (if fewer than 600,000) are transferred by such Purchaser, or (b) to any Affiliated Party of such Purchaser, and, in each case, such transferee shall be deemed a "Purchaser" for purposes of this Agreement; provided that such assignment of rights shall be contingent upon the transferee providing a written instrument to the Company notifying the Company of such transfer and assignment and agreeing in writing to be bound by the terms of this Agreement. Notwithstanding the foregoing, any person or entity to which any Shares or Registrable Shares are transferred by a Purchaser, whether voluntarily or by operation of law, shall be bound by the obligations under Section 2.8 to the same extent as if such transferee were a Purchaser hereunder and no Purchaser shall transfer any Shares or Registrable Shares unless the transferee provides a written instrument to the Company notifying the Company of such transfer and agreeing in writing to be bound by the terms of Section 2.8.

6.2 Calculation of Share Numbers. In determining the number of Shares owned by a Purchaser for purposes of exercising rights under this Agreement, (a) Shares owned by a Purchaser shall be deemed to include Shares which have been converted into Common Stock so long as such Common Stock is owned by such Purchaser and (b) all Shares held by affiliated entities or persons shall be aggregated together (provided that no shares shall be attributed to more than one entity or person within any such group of affiliated entities or persons).

7. General.

7.1 Massachusetts Business Trust. A copy of the Agreement and Declaration of Trust of each of Fidelity Purchaser or any affiliate thereof is on file with the Secretary of State of the Commonwealth of Massachusetts and notice is hereby given that this Agreement is executed on behalf of the trustees of such Fidelity Purchaser or any affiliate thereof as trustees and not individually and that the obligations of this Agreement are not binding on any of the trustees, officers or stockholders of such Fidelity Purchaser or any affiliate thereof individually but are binding only upon such Fidelity Purchaser or any affiliate thereof and its assets and property.

7.2 Severability. The invalidity or unenforceability of any provision of this Agreement shall not affect the validity or enforceability of any other provision of this Agreement.

7.3 Specific Performance. In addition to any and all other remedies that may be available at law in the event of any breach of this Agreement, each Purchaser shall be entitled to specific performance of the agreements and obligations of the Company hereunder and to such other injunctive or other equitable relief as may be granted by a court of competent jurisdiction.

7.4 Governing Law. This Agreement shall be governed by and construed in accordance with the General Corporation Law of the State of Delaware, as to matters within the scope thereof, and the internal laws of the Commonwealth of Massachusetts (without reference to the conflicts of law provisions thereof), as to all other matters.

7.5 Notices. All notices, requests, consents and other communications under this Agreement shall be in writing and shall be deemed delivered (i) three business days after being sent by registered or certified mail, return receipt requested, postage prepaid, (ii) one business day after being sent via a reputable nationwide overnight courier service guaranteeing next business day delivery or (iii) immediately upon confirmation of receipt if delivered by e-mail, in each case to the intended recipient as set forth below:

If to the Company, at 38 Sidney Street, 2nd Floor, Cambridge, Massachusetts 02139, Attention: President, or at such other address as may have been furnished in writing by the Company to the other parties hereto, with a copy to Wilmer Cutler Pickering Hale and Dorr LLP, 399 Park Avenue, New York, NY 10022, Attention: Steven D. Singer, Esq.;

If to a Purchaser, at its address set forth on Exhibit A, or at such other address as may have been furnished in writing by such Purchaser to the other parties hereto; or

If to a Founder, at the address set forth below such Founder's signature to this Agreement, or at such other address as may have been furnished in writing by such Founder to the other parties hereto.

For purposes of clarity, any notice to Salthill Partners, L.P., Salthill Investors (Bermuda) L.P. and Hawkes Bay Master Investors (Cayman) LP (each a "Wellington Purchaser") shall be exclusively delivered to the Wellington Management Company, LLP at the address set forth on Exhibit A hereto unless otherwise directed by such Wellington Purchaser.

Any party may give any notice, request, consent or other communication under this Agreement using any other means (including, without limitation, personal delivery, messenger service, telecopy, first class mail or electronic mail), but no such notice, request, consent or other communication shall be deemed to have been duly given unless and until it is actually received by the party for whom it is intended. Any party may change the address to which notices, requests, consents or other communications hereunder are to be delivered by giving the other parties notice in the manner set forth in this Section 7.4.

7.6 Amendment and Restatement of Prior Agreement; Complete Agreement. The Company and the Purchasers (as defined in the Prior Agreement) holding Shares representing a majority of the voting power of all Shares held by Purchasers (as defined in the Prior Agreement) agree that, as of the date of this Agreement, (i) the Prior Agreement is hereby amended and restated in its entirety by this Agreement, (ii) the provisions of the Prior Agreement shall no longer be of any force or effect, and (iii) this Agreement constitutes the entire agreement and understanding of the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings relating to such subject matter.

7.7 Amendments and Waivers. This Agreement may be amended or terminated and the observance of any term of this Agreement may be waived with respect to all parties to this Agreement (either generally or in a particular instance and either retroactively or prospectively), with the written consent of the Company and Purchasers holding Shares representing a majority of the voting power of all Shares then held by Purchasers; provided that any amendment, termination or waiver to the terms of Section 2 (or a defined term used therein) that occurs after the closing of the Initial Public Offering shall instead require the written consent of the Company and Purchasers holding Registrable Shares representing a majority of the voting power of all Registrable Shares then held by all Purchasers. Notwithstanding the foregoing, (a) this Agreement may not be amended or terminated and the observance of any term hereunder may not be waived with respect to any Purchaser without the written consent of such Purchaser unless such amendment, termination or waiver applies to all Purchasers in the same fashion (it being agreed that a waiver of the provisions of Section 3 with respect to a particular transaction shall be deemed to apply to all Purchasers in the same fashion if such waiver does so by its terms, notwithstanding the fact that certain Purchasers may nonetheless, by agreement with the Company, purchase securities in such transaction), (b) this Agreement may not be amended or terminated and the observance of any term hereunder may not be waived in a manner that is adverse to the holders of Series C-1 Convertible Preferred Stock and not similarly adverse to the other holders of Preferred Stock without the written consent of the holders of a majority of the outstanding shares of Series C-1 Convertible Preferred Stock (the "Requisite Series C-1 Vote"), (c) Section 4.2(a) may not be amended or waived without the written consent of holders of at least a majority of the Founders then employed by or engaged as a consultant or advisor to the Company, (d) Sections 4.2(b) and 4.3 may not be amended and the observance thereof may not be waived without the written consent of the Requisite Series C-1 Vote, and (e) any requirement to obtain to the approval of all of the Independent Directors may not be amended or terminated and the observance thereof may not be waived without the written consent of the Requisite Series C-1 Vote. The Company shall give prompt written notice of any amendment or termination hereof or waiver hereunder to any party hereto that did not consent in writing to such amendment, termination or waiver. Any amendment, termination or waiver effected in accordance with this Section 7.7 shall be binding on all parties hereto, even if they do not execute such consent. No waivers of or exceptions to any term, condition or provision of this Agreement, in any one or more instances, shall be deemed to be, or construed as, a further or continuing waiver of any such term, condition or provision.

7.8 Pronouns. Whenever the context may require, any pronouns used in this Agreement shall include the corresponding masculine, feminine or neuter forms, and the singular form of nouns and pronouns shall include the plural, and vice versa.

7.9 Counterparts; Facsimile Signatures. This Agreement may be executed in any number of counterparts, each of which shall be deemed to be an original, and all of which together shall constitute one and the same document. This Agreement may be executed by facsimile signatures.

7.10 Section Headings and References. The section headings are for the convenience of the parties and in no way alter, modify, amend, limit or restrict the contractual obligations of the parties. Any reference in this agreement to a particular section or subsection shall refer to a section or subsection of this Agreement, unless specified otherwise.

[Remainder of Page Intentionally Left Blank]

Executed as of the date first written above.

**COMPANY:**

AGIOS PHARMACEUTICALS, INC.

By: /s/ David Schenkein
Name: David Schenkein
Title: Chief Executive Officer

**FOUNDERS:**

/s/ Lewis Cantley
Lewis Cantley
Address: 43 Larch Road
Cambridge, MA 02138

/s/ Tak Mak
Tak Mak
Address: The Campbell Family Institute for Breast Cancer Research
620 University Avenue, Suite 706
Toronto, Ontario
Canada M5G 2C1

/s/ Craig Thompson
Craig Thompson
Address: 304 Mallwyd Road
Merion, PA 19066

/s/ Michael Su
Michael Su
Address: 346 Hartman Road
Newton, MA 02459

**PURCHASERS:**

ARCH VENTURE FUND VII, L.P.

By: ARCH Venture Partners VII, L.P.
Its: General Partner

By: ARCH Venture Partners VII, LLC
Its: General Partner

By: /s/ Robert Nelsen
Name:
Title:

FLAGSHIP VENTURES FUND 2007, L.P.

By: Flagship Ventures 2007 General Partner LLC
Its: General Partner

By: /s/ Noubar Afeyan
Name:
Title:

THIRD ROCK VENTURES, L.P.

By: Third Rock Ventures GP, L.P.
Its: General Partner

By: TRV GP, LLC
Its: General Partner

By: /s/ Kevin Starr
Name:
Title: Manager

PRINCESS MARGARET HOSPITAL FOUNDATION

By: /s/ Paul Alofs
Name: Paul Alofs
Title: President and CEO

BIOTECHNOLOGY VALUE FUND, L.P.

By: BVF Partners, L.P.
Its: General Partner

By: BVF, Inc.
Its: General Partner

By: /s/ Mark Lampert
Name: Mark Lampert
Title: President

BIOTECHNOLOGY VALUE FUND II, L.P.

By: BVF Partners, L.P.
Its: General Partner

By: BVF, Inc.
Its: General Partner

By: /s/ Mark Lampert
Name: Mark Lampert
Title: President

BVF INVESTMENTS, L.L.C.

By: BVF Partners, L.P.
Its: Manager

By: BVF, Inc.
Its: General Partner

By: /s/ Mark Lampert
Name: Mark Lampert
Title: President

INVESTMENT 10, LLC

By: BVF Partners, L.P.
Its: Attorney-in-fact

By: BVF, Inc.
Its: General Partner

By: /s/ Mark Lampert
Name: Mark Lampert
Title: President

CELGENE EUROPEAN INVESTMENT COMPANY LLC

By: /s/ Paul D'Angio
Name: Paul D'Angio
Title: Managing Director

HAWKES BAY MASTER INVESTORS (CAYMAN) LP

By: /s/ Steven Hoffman
Name: Steven Hoffman
Title: Vice President and Counsel
By: Wellington Management Company, LLP, as Investment Advisor for and on behalf of Hawkes Bay Master Investors (Cayman) LP

SALTHILL INVESTORS (BERMUDA) L.P.

By: /s/ Steven Hoffman
Name: Steven Hoffman
Title: Vice President and Counsel
By: Wellington Management Company, LLP, as Investment Advisor for and on behalf of Salthill Investors (Bermuda) L.P.

SALTHILL PARTNERS, L.P.

By: /s/ Steven Hoffman
Name: Steven Hoffman
Title: Vice President and Counsel
By: Wellington Management Company, LLP, as Investment Advisor for and on behalf of Salthill Partners, L.P.

WUXI PHARMATECH HEALTHCARE FUND I L.P.

By: /s/ Edward Hu

For and on behalf of
WuXi PharmaTech Investments (Cayman) INC.
As General Partner for and on behalf of
WuXi PharmaTech Fund I General Partner L.P.

FIDELITY SELECT PORTFOLIOS: PHARMACEUTICALS PORTFOLIO

By: /s/ Jeffrey Christian
Name: Jeffrey Christian
Title: Deputy Treasurer

FIDELITY SELECT PORTFOLIOS: BIOTECHNOLOGY PORTFOLIO

By: /s/ Jeffrey Christian
Name: Jeffrey Christian
Title: Deputy Treasurer

FIDELITY ADVISOR SERIES VII: FIDELITY ADVISOR BIOTECHNOLOGY FUND

By: /s/ Jeffrey Christian
Name: Jeffrey Christian
Title: Deputy Treasurer

FIDELITY MT. VERNON STREET TRUST: FIDELITY GROWTH COMPANY FUND

By: /s/ Jeffrey Christian
Name: Jeffrey Christian
Title: Deputy Treasurer

FIDELITY CONTRAFUND: FIDELITY ADVISOR NEW INSIGHTS FUND

By: /s/ Jeffrey Christian
Name: Jeffrey Christian
Title: Deputy Treasurer

FIDELITY SECURITIES FUND: FIDELITY SMALL CAP OPPORTUNITIES FUND

By: /s/ Jeffrey Christian
Name: Jeffrey Christian
Title: Deputy Treasurer

FIDELITY CAPITAL TRUST: FIDELITY SMALL CAP INDEPENDENCE FUND

By: /s/ Jeffrey Christian
Name: Jeffrey Christian
Title: Deputy Treasurer

Exhibit A

List of Purchasers

Name and Address

ARCH Venture Fund VII, L.P.
c/o ARCH Venture Partners
8725 West Higgins Road
Suite 290
Chicago, IL 60631

Flagship Ventures Fund 2007, L.P.
One Memorial Drive
7th Floor
Cambridge, MA 02142

Third Rock Ventures, L.P.
29 Newbury Street, Suite 401
Boston, MA 02116
ATTN: Kevin Starr

Princess Margaret Hospital Foundation
8th Floor, 700 University Avenue
M5G 1Z5
Toronto, Ontario, Canada
Attn: Paul Alofs, President and CEO

Celgene European Investment Company LLC
86 Morris Avenue
Summit, NJ 07901
Attention: George S. Golumbeski

With a copy to:
Celgene Corporation
86 Morris Avenue
Summit, NJ 07901
Attention: Legal Department

WuXi PharmaTech Healthcare Fund I L.P.
c/o WuXi AppTec Co. Ltd.
288 FuTe Zhong Road
Wai Gao Qiao Free Trade Zone
Shanghai 200131
P.R.CHINA
Attn: Ge Li

Fidelity Select Portfolios: Pharmaceuticals Portfolio
c/o Fidelity Investments
82 Devonshire Street, V13H
Boston, MA 02109
Attn: Andrew Boyd

With a copy (which shall not constitute notice) to:
H. David Henken, Esq.
Goodwin|Procter LLP
Exchange Place
Boston, MA 02109

Fidelity Select Portfolios: Biotechnology Portfolio
c/o Fidelity Investments
82 Devonshire Street, V13H
Boston, MA 02109
Attn: Andrew Boyd

With a copy (which shall not constitute notice) to:
H. David Henken, Esq.
Goodwin|Procter LLP
Exchange Place
Boston, MA 02109

Fidelity Advisor Series VII: Fidelity Advisor
Biotechnology Fund
c/o Fidelity Investments
82 Devonshire Street, V13H
Boston, MA 02109
Attn: Andrew Boyd

With a copy (which shall not constitute notice) to:
H. David Henken, Esq.
Goodwin|Procter LLP
Exchange Place
Boston, MA 02109

Fidelity Mt. Vernon Street Trust: Fidelity Growth
Company Fund
c/o Fidelity Investments
82 Devonshire Street, V13H
Boston, MA 02109
Attn: Andrew Boyd

With a copy (which shall not constitute notice) to:
H. David Henken, Esq.
Goodwin|Procter LLP
Exchange Place
Boston, MA 02109

Fidelity Contrafund: Fidelity Advisor New Insights Fund
c/o Fidelity Investments
82 Devonshire Street, V13H
Boston, MA 02109
Attn: Andrew Boyd

With a copy (which shall not constitute notice) to:
H. David Henken, Esq.
Goodwin|Procter LLP
Exchange Place
Boston, MA 02109

Fidelity Securities Fund: Fidelity Small Cap Opportunities Fund
Ball & Co
c/o Fidelity Investments
82 Devonshire Street, V13H
Boston, MA 02109
Attn: Andrew Boyd

With a copy (which shall not constitute notice) to:
H. David Henken, Esq.
Goodwin|Procter LLP
Exchange Place
Boston, MA 02109

Fidelity Capital Trust: Fidelity Small Cap
Independence Fund
c/o Fidelity Investments
82 Devonshire Street, V13H
Boston, MA 02109
Attn: Andrew Boyd

With a copy (which shall not constitute notice) to:
H. David Henken, Esq.
Goodwin|Procter LLP
Exchange Place
Boston, MA 02109

Biotechnology Value Fund II, L.P.
Attn: Scott Perlen, VP – Finance
Grosvenor Capital Management, L.P.
900 N. Michigan Avenue, Suite 1100
Chicago, IL 60611

Biotechnology Value Fund, L.P.
Attn: Scott Perlen, VP – Finance
Grosvenor Capital Management, L.P.
900 N. Michigan Avenue, Suite 1100
Chicago, IL 60611

BVF Investments, L.L.C.
Attn: Scott Perlen, VP – Finance
Grosvenor Capital Management, L.P.
900 N. Michigan Avenue, Suite 1100
Chicago, IL 60611

Investment 10, LLC
Attn: Scott Perlen, VP – Finance
Grosvenor Capital Management, L.P.
900 N. Michigan Avenue, Suite 1100
Chicago, IL 60611

Salthill Partners, L.P.
c/o Wellington Management Company, LLP
280 Congress Street
Boston, MA 02210
Attention: Steven Hoffman, VP and Counsel
email: seclaw@wellington.com

Salthill Investors (Bermuda) L.P.
c/o Wellington Management Company, LLP
280 Congress Street
Boston, MA 02210
Attention: Steven Hoffman, VP and Counsel
email: seclaw@wellington.com

Hawkes Bay Master Investors (Cayman) LP
c/o Wellington Management Company, LLP
280 Congress Street
Boston, MA 02210
Attention: Steven Hoffman, VP and Counsel
email: seclaw@wellington.com

**Exhibit 10.1**

AGIOS PHARMACEUTICALS, INC.

2007 STOCK INCENTIVE PLAN[1]

1. Purpose

The purpose of this 2007 Stock Incentive Plan (the "Plan") of Agios Pharmaceuticals, Inc., a Delaware corporation (the "Company"), is to advance the interests of the Company's stockholders by enhancing the Company's ability to attract, retain and motivate persons who are expected to make important contributions to the Company and by providing such persons with equity ownership opportunities and performance-based incentives that are intended to better align the interests of such persons with those of the Company's stockholders. Except where the context otherwise requires, the term "Company" shall include any of the Company's present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code") and any other business venture (including, without limitation, joint venture or limited liability company) in which the Company has a controlling interest, as determined by the Board of Directors of the Company (the "Board").

2. Eligibility

All of the Company's employees, officers, directors, consultants and advisors are eligible to be granted options, restricted stock, restricted stock units ("RSUs") and other stock-based awards (each, an "Award") under the Plan. Each person who receives an Award under the Plan is deemed a "Participant".

3. Administration and Delegation

(a) Administration by Board of Directors. The Plan will be administered by the Board. The Board shall have authority to grant Awards and to adopt, amend and repeal such administrative rules, guidelines and practices relating to the Plan as it shall deem advisable. The Board may construe and interpret the terms of the Plan and any Award agreements entered into under the Plan. The Board may correct any defect, supply any omission or reconcile any inconsistency in the Plan or any Award in the manner and to the extent it shall deem expedient to carry the Plan into effect and it shall be the sole and final judge of such expediency. All decisions by the Board shall be made in the Board's sole discretion and shall be final and binding on all persons having or claiming any interest in the Plan or in any Award. No director or person acting pursuant to the authority delegated by the Board shall be liable for any action or determination relating to or under the Plan made in good faith.

(b) Appointment of Committees. To the extent permitted by applicable law, the Board may delegate any or all of its powers under the Plan to one or more committees or subcommittees of the Board (a "Committee"). All references in the Plan to the "Board" shall mean the Board or a Committee of the Board or the officers referred to in Section 3(c) to the extent that the Board's powers or authority under the Plan have been delegated to such Committee or officers.

[1] As amended on March 27, 2012.

(c) Delegation to Officers. To the extent permitted by applicable law, the Board may delegate to one or more officers of the Company the power to grant Awards (subject to any limitations under the Plan) to employees or officers of the Company or any of its present or future subsidiary corporations and to exercise such other powers under the Plan as the Board may determine, provided that the Board shall fix the terms of the Awards to be granted by such officers (including the exercise price of such Awards, which may include a formula by which the exercise price will be determined) and the maximum number of shares subject to Awards that the officers may grant; provided further, however, that no officer shall be authorized to grant Awards to any "executive officer" of the Company (as defined by Rule 3b-7 under the Securities Exchange Act of 1934, as amended (the "Exchange Act")) or to any "officer" of the Company (as defined by Rule 16a-1 under the Exchange Act).

4. Stock Available for Awards.

(a) Number of Shares. Subject to adjustment under Section 8, Awards may be made under the Plan for up to 13,969,018 shares of common stock, $0.001 par value per share, of the Company (the "Common Stock"). If any Award expires or is terminated, surrendered or canceled without having been fully exercised, is forfeited in whole or in part (including as the result of shares of Common Stock subject to such Award being repurchased by the Company at the original issuance price pursuant to a contractual repurchase right), or results in any Common Stock not being issued, the unused Common Stock covered by such Award shall again be available for the grant of Awards under the Plan. Further, shares of Common Stock tendered to the Company by a Participant to exercise an Award shall be added to the number of shares of Common Stock available for the grant of Awards under the Plan. However, in the case of Incentive Stock Options (as hereinafter defined), the foregoing provisions shall be subject to any limitations under the Code. Shares issued under the Plan may consist in whole or in part of authorized but unissued shares or treasury shares. At no time while there is any Option (as defined below) outstanding and held by a Participant who was a resident of the State of California on the date of grant of such Option, shall the total number of shares of Common Stock issuable upon exercise of all outstanding options and the total number of shares provided for under any stock bonus or similar plan or agreement of the Company exceed the applicable percentage as calculated in accordance with the conditions and exclusions of Section 260.140.45 of the California Code of Regulations (the "California Regulations"), based on the shares of the Company which are outstanding at the time the calculation is made.

(b) Substitute Awards. In connection with a merger or consolidation of an entity with the Company or the acquisition by the Company of property or stock of an entity, the Board may grant Awards in substitution for any options or other stock or stock-based awards granted by such entity or an affiliate thereof. Substitute Awards may be granted on such terms as the Board deems appropriate in the circumstances, notwithstanding any limitations on Awards contained in the Plan. Substitute Awards shall not count against the overall share limit set forth in Section 4(a), except as may be required by reason of Section 422 and related provisions of the Code.

5. Stock Options

(a) General. The Board may grant options to purchase Common Stock (each, an "Option") and determine the number of shares of Common Stock to be covered by each Option,

the exercise price of each Option and the conditions and limitations applicable to the exercise of each Option, including conditions relating to applicable federal or state securities laws, as it considers necessary or advisable. An Option that is not intended to be an Incentive Stock Option (as hereinafter defined) shall be designated a "Nonstatutory Stock Option".

(b) Incentive Stock Options. An Option that the Board intends to be an "incentive stock option" as defined in Section 422 of the Code (an "Incentive Stock Option") shall only be granted to employees of Agios Pharmaceuticals, Inc., any of Agios Pharmaceuticals, Inc.'s present or future parent or subsidiary corporations as defined in Sections 424(e) or (f) of the Code, and any other entities the employees of which are eligible to receive Incentive Stock Options under the Code, and shall be subject to and shall be construed consistently with the requirements of Section 422 of the Code. The Company shall have no liability to a Participant, or any other party, if an Option (or any part thereof) that is intended to be an Incentive Stock Option is not an Incentive Stock Option or for any action taken by the Board, including without limitation the conversion of an Incentive Stock Option to a Nonstatutory Stock Option.

(c) Exercise Price. The Board shall establish the exercise price of each Option and specify the exercise price in the applicable option agreement.

(d) Duration of Options. Each Option shall be exercisable at such times and subject to such terms and conditions as the Board may specify in the applicable option agreement.

(e) Exercise of Option. Options may be exercised by delivery to the Company of a written notice of exercise signed by the proper person or by any other form of notice (including electronic notice) approved by the Board together with payment in full as specified in Section 5(f) for the number of shares for which the Option is exercised. Shares of Common Stock subject to the Option will be delivered by the Company as soon as practicable following exercise.

(f) Payment Upon Exercise. Common Stock purchased upon the exercise of an Option granted under the Plan shall be paid for as follows:

(1) in cash or by check, payable to the order of the Company;

(2) when the Common Stock is registered under the Exchange Act, except as may otherwise be provided in the applicable option agreement, by (i) delivery of an irrevocable and unconditional undertaking by a creditworthy broker to deliver promptly to the Company sufficient funds to pay the exercise price and any required tax withholding or (ii) delivery by the Participant to the Company of a copy of irrevocable and unconditional instructions to a creditworthy broker to deliver promptly to the Company cash or a check sufficient to pay the exercise price and any required tax withholding;

(3) when the Common Stock is registered under the Exchange Act and to the extent provided for in the applicable option agreement or approved by the Board, in its sole discretion, by delivery (either by actual delivery or attestation) of shares of Common Stock owned by the Participant valued at their fair market value as determined by (or in a manner approved by) the Board ("Fair Market Value"), provided (i) such method of payment is then permitted under applicable law, (ii) such Common Stock, if acquired directly from the Company,

was owned by the Participant for such minimum period of time, if any, as may be established by the Board in its discretion and (iii) such Common Stock is not subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements;

(4) to the extent permitted by applicable law and provided for in the applicable option agreement or approved by the Board, in its sole discretion, by (i) delivery of a promissory note of the Participant to the Company on terms determined by the Board, or (ii) payment of such other lawful consideration as the Board may determine; or

(5) by any combination of the above permitted forms of payment.

6. Restricted Stock; Restricted Stock Units

(a) General. The Board may grant Awards entitling recipients to acquire shares of Common Stock ("Restricted Stock"), subject to the right of the Company to repurchase all or part of such shares at their issue price or other stated or formula price (or to require forfeiture of such shares if issued at no cost) from the recipient in the event that conditions specified by the Board in the applicable Award are not satisfied prior to the end of the applicable restriction period or periods established by the Board for such Award. Instead of granting Awards for Restricted Stock, the Board may grant Awards entitling the recipient to receive shares of Common Stock or cash to be delivered at the time such Award vests ("Restricted Stock Units") (Restricted Stock and Restricted Stock Units are each referred to herein as a "Restricted Stock Award").

(b) Terms and Conditions for All Restricted Stock Awards. The Board shall determine the terms and conditions of a Restricted Stock Award, including the conditions for vesting and repurchase (or forfeiture) and the issue price, if any.

(c) Additional Provisions Relating to Restricted Stock.

(1) Dividends. Participants holding shares of Restricted Stock will be entitled to all ordinary cash dividends paid with respect to such shares, unless otherwise provided by the Board. Unless otherwise provided, by the Board, if any dividends or distributions are paid in shares, or consist of a dividend or distribution to holders of Common Stock other than an ordinary cash dividend, the shares, cash or other property will be subject to the same restrictions on transferability and forfeitability as the shares of Restricted Stock with respect to which they were paid. Each dividend payment will be made no later than the end of the calendar year in which the dividends are paid to shareholders of that class of stock or, if later, the 15th day of the third month following the date the dividends are paid to shareholders of that class of stock.

(2) Stock Certificates. The Company may require that any stock certificates issued in respect of shares of Restricted Stock shall be deposited in escrow by the Participant, together with a stock power endorsed in blank, with the Company (or its designee). At the expiration of the applicable restriction periods, the Company (or such designee) shall deliver the certificates no longer subject to such restrictions to the Participant or if the Participant has died, to the beneficiary designated, in a manner determined by the Board, by a Participant to receive amounts due or exercise rights of the Participant in the event of the Participant's death (the "Designated Beneficiary"). In the absence of an effective designation by a Participant, "Designated Beneficiary" shall mean the Participant's estate.

7. Other Stock-Based Awards

Other Awards of shares of Common Stock, and other Awards that are valued in whole or in part by reference to, or are otherwise based on, shares of Common Stock or other property, may be granted hereunder to Participants ("Other Stock-Based Awards"), including without limitation stock appreciation rights ("SARs") and Awards entitling recipients to receive shares of Common Stock to be delivered in the future. Such Other Stock-Based Awards shall also be available as a form of payment in the settlement of other Awards granted under the Plan or as payment in lieu of compensation to which a Participant is otherwise entitled. Other Stock-Based Awards may be paid in shares of Common Stock or cash, as the Board shall determine. Subject to the provisions of the Plan, the Board shall determine the terms and conditions of each Other Stock-Based Award, including any purchase price applicable thereto.

8. Adjustments for Changes in Common Stock and Certain Other Events

(a) Changes in Capitalization. In the event of any stock split, reverse stock split, stock dividend, recapitalization, combination of shares, reclassification of shares, spin-off or other similar change in capitalization or event, or any dividend or distribution to holders of Common Stock other than an ordinary cash dividend, (i) the number and class of securities available under this Plan, (ii) the number and class of securities and exercise price per share of each outstanding Option, (iii) the number of shares subject to and the repurchase price per share subject to each outstanding Restricted Stock Award, and (iv) the terms of each other outstanding Award shall be equitably adjusted by the Company (or substituted Awards may be made, if applicable) in the manner determined by the Board. Without limiting the generality of the foregoing, in the event the Company effects a split of the Common Stock by means of a stock dividend and the exercise price of and the number of shares subject to an outstanding Option are adjusted as of the date of the distribution of the dividend (rather than as of the record date for such dividend), then an optionee who exercises an Option between the record date and the distribution date for such stock dividend shall be entitled to receive, on the distribution date, the stock dividend with respect to the shares of Common Stock acquired upon such Option exercise, notwithstanding the fact that such shares were not outstanding as of the close of business on the record date for such stock dividend.

(b) Reorganization Events.

(1) Definition. A "Reorganization Event" shall mean: (a) any merger or consolidation of the Company with or into another entity as a result of which all of the Common Stock of the Company is converted into or exchanged for the right to receive cash, securities or other property or is cancelled, (b) any exchange of all of the Common Stock of the Company for cash, securities or other property pursuant to a share exchange transaction or (c) any liquidation or dissolution of the Company.

(2) Consequences of a Reorganization Event on Awards Other than Restricted Stock Awards. In connection with a Reorganization Event, the Board may take any one or more

of the following actions as to all or any (or any portion of) outstanding Awards other than Restricted Stock Awards on such terms as the Board determines: (i) provide that Awards shall be assumed, or substantially equivalent Awards shall be substituted, by the acquiring or succeeding corporation (or an affiliate thereof), (ii) upon written notice to a Participant, provide that the Participant's unexercised Awards will terminate immediately prior to the consummation of such Reorganization Event unless exercised by the Participant within a specified period following the date of such notice, (iii) provide that outstanding Awards shall become exercisable, realizable, or deliverable, or restrictions applicable to an Award shall lapse, in whole or in part prior to or upon such Reorganization Event, (iv) in the event of a Reorganization Event under the terms of which holders of Common Stock will receive upon consummation thereof a cash payment for each share surrendered in the Reorganization Event (the "Acquisition Price"), make or provide for a cash payment to a Participant equal to the excess, if any, of (A) the Acquisition Price times the number of shares of Common Stock subject to the Participant's Awards (to the extent the exercise price does not exceed the Acquisition Price) over (B) the aggregate exercise price of all such outstanding Awards and any applicable tax withholdings, in exchange for the termination of such Awards, (v) provide that, in connection with a liquidation or dissolution of the Company, Awards shall convert into the right to receive liquidation proceeds (if applicable, net of the exercise price thereof and any applicable tax withholdings) and (vi) any combination of the foregoing. In taking any of the actions permitted under this Section 8(b), the Board shall not be obligated by the Plan to treat all Awards, all Awards held by a Participant, or all Awards of the same type, identically.

For purposes of clause (i) above, an Option shall be considered assumed if, following consummation of the Reorganization Event, the Option confers the right to purchase, for each share of Common Stock subject to the Option immediately prior to the consummation of the Reorganization Event, the consideration (whether cash, securities or other property) received as a result of the Reorganization Event by holders of Common Stock for each share of Common Stock held immediately prior to the consummation of the Reorganization Event (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding shares of Common Stock); provided, however, that if the consideration received as a result of the Reorganization Event is not solely common stock of the acquiring or succeeding corporation (or an affiliate thereof), the Company may, with the consent of the acquiring or succeeding corporation, provide for the consideration to be received upon the exercise of Options to consist solely of common stock of the acquiring or succeeding corporation (or an affiliate thereof) equivalent in value (as determined by the Board) to the per share consideration received by holders of outstanding shares of Common Stock as a result of the Reorganization Event.

(3) Consequences of a Reorganization Event on Restricted Stock Awards. Upon the occurrence of a Reorganization Event other than a liquidation or dissolution of the Company, the repurchase and other rights of the Company under each outstanding Restricted Stock Award shall inure to the benefit of the Company's successor and shall, unless the Board determines otherwise, apply to the cash, securities or other property which the Common Stock was converted into or exchanged for pursuant to such Reorganization Event in the same manner and to the same extent as they applied to the Common Stock subject to such Restricted Stock Award. Upon the occurrence of a Reorganization Event involving the liquidation or dissolution of the Company, except to the extent specifically provided to the contrary in the instrument

evidencing any Restricted Stock Award or any other agreement between a Participant and the Company, all restrictions and conditions on all Restricted Stock Awards then outstanding shall automatically be deemed terminated or satisfied.

9. General Provisions Applicable to Awards

(a) Transferability of Awards. Except as the Board may otherwise determine or provide in an Award, Awards shall not be sold, assigned, transferred, pledged or otherwise encumbered by the person to whom they are granted, either voluntarily or by operation of law, except by will or the laws of descent and distribution or, other than in the case of an Incentive Stock Option, pursuant to a qualified domestic relations order, and, during the life of the Participant, shall be exercisable only by the Participant. References to a Participant, to the extent relevant in the context, shall include references to authorized transferees.

(b) Documentation. Each Award shall be evidenced in such form (written, electronic or otherwise) as the Board shall determine. Each Award may contain terms and conditions in addition to those set forth in the Plan.

(c) Board Discretion. Except as otherwise provided by the Plan, each Award may be made alone or in addition or in relation to any other Award. The terms of each Award need not be identical, and the Board need not treat Participants uniformly.

(d) Termination of Status. The Board shall determine the effect on an Award of the disability, death, termination or other cessation of employment, authorized leave of absence or other change in the employment or other status of a Participant and the extent to which, and the period during which, the Participant, or the Participant's legal representative, conservator, guardian or Designated Beneficiary, may exercise rights under the Award.

(e) Withholding. The Participant must satisfy all applicable federal, state, and local or other income and employment tax withholding obligations before the Company will deliver stock certificates or otherwise recognize ownership of Common Stock under an Award. The Company may decide to satisfy the withholding obligations through additional withholding on salary or wages. If the Company elects not to or cannot withhold from other compensation, the Participant must pay the Company the full amount, if any, required for withholding or have a broker tender to the Company cash equal to the withholding obligations. Payment of withholding obligations is due before the Company will issue any shares on exercise or release from forfeiture of an Award or, if the Company so requires, at the same time as is payment of the exercise price unless the Company determines otherwise. If provided for in an Award or approved by the Board in its sole discretion, a Participant may satisfy such tax obligations in whole or in part by delivery of shares of Common Stock, including shares retained from the Award creating the tax obligation, valued at their Fair Market Value; provided, however, except as otherwise provided by the Board, that the total tax withholding where stock is being used to satisfy such tax obligations cannot exceed the Company's minimum statutory withholding obligations (based on minimum statutory withholding rates for federal and state tax purposes, including payroll taxes, that are applicable to such supplemental taxable income). Shares surrendered to satisfy tax withholding requirements cannot be subject to any repurchase, forfeiture, unfulfilled vesting or other similar requirements.

(f) Amendment of Award. The Board may amend, modify or terminate any outstanding Award, including but not limited to, substituting therefor another Award of the same or a different type, changing the date of exercise or realization, and converting an Incentive Stock Option to a Nonstatutory Stock Option. The Participant's consent to such action shall be required unless (i) the Board determines that the action, taking into account any related action, would not materially and adversely affect the Participant's rights under the Plan or (ii) the change is permitted under Section 8 hereof.

(g) Conditions on Delivery of Stock. The Company will not be obligated to deliver any shares of Common Stock pursuant to the Plan or to remove restrictions from shares previously delivered under the Plan until (i) all conditions of the Award have been met or removed to the satisfaction of the Company, (ii) in the opinion of the Company's counsel, all other legal matters in connection with the issuance and delivery of such shares have been satisfied, including any applicable securities laws and any applicable stock exchange or stock market rules and regulations, and (iii) the Participant has executed and delivered to the Company such representations or agreements as the Company may consider appropriate to satisfy the requirements of any applicable laws, rules or regulations.

(h) Acceleration. The Board may at any time provide that any Award shall become immediately exercisable in full or in part, free of some or all restrictions or conditions, or otherwise realizable in full or in part, as the case may be.

10. Miscellaneous

(a) No Right To Employment or Other Status. No person shall have any claim or right to be granted an Award, and the grant of an Award shall not be construed as giving a Participant the right to continued employment or any other relationship with the Company. The Company expressly reserves the right at any time to dismiss or otherwise terminate its relationship with a Participant free from any liability or claim under the Plan, except as expressly provided in the applicable Award.

(b) No Rights As Stockholder. Subject to the provisions of the applicable Award, no Participant or Designated Beneficiary shall have any rights as a stockholder with respect to any shares of Common Stock to be distributed with respect to an Award until becoming the record holder of such shares.

(c) Effective Date and Term of Plan. The Plan shall become effective on the date on which it is adopted by the Board. No Awards shall be granted under the Plan after the expiration of 10 years from the earlier of (i) the date on which the Plan was adopted by the Board or (ii) the date the Plan was approved by the Company's stockholders, but Awards previously granted may extend beyond that date.

(d) Amendment of Plan. The Board may amend, suspend or terminate the Plan or any portion thereof at any time; provided that if at any time the approval of the Company's stockholders is required as to any modification or amendment under Section 422 of the Code or any successor provision with respect to Incentive Stock Options, the Board may not effect such modification or amendment without such approval. Unless otherwise specified in the

amendment, any amendment to the Plan adopted in accordance with this Section 10(d) shall apply to, and be binding on the holders of, all Awards outstanding under the Plan at the time the amendment is adopted, provided the Board determines that such amendment does not materially and adversely affect the rights of Participants under the Plan.

(e) Authorization of Sub-Plans. The Board may from time to time establish one or more sub-plans under the Plan for purposes of satisfying applicable blue sky, securities or tax laws of various jurisdictions. The Board shall establish such sub-plans by adopting supplements to this Plan containing (i) such limitations on the Board's discretion under the Plan as the Board deems necessary or desirable or (ii) such additional terms and conditions not otherwise inconsistent with the Plan as the Board shall deem necessary or desirable. All supplements adopted by the Board shall be deemed to be part of the Plan, but each supplement shall apply only to Participants within the affected jurisdiction and the Company shall not be required to provide copies of any supplement to Participants in any jurisdiction which is not the subject of such supplement.

(f) Compliance with Code Section 409A. No Award shall provide for deferral of compensation that does not comply with Section 409A of the Code, unless the Board, at the time of grant, specifically provides that the Award is not intended to comply with Section 409A of the Code. The Company shall have no liability to a Participant, or any other party, if an Award that is intended to be exempt from, or compliant with, Section 409A is not so exempt or compliant or for any action taken by the Board.

(g) Governing Law. The provisions of the Plan and all Awards made hereunder shall be governed by and interpreted in accordance with the laws of the State of Delaware, excluding choice-of-law principles of the law of such state that would require the application of the laws of a jurisdiction other than such state.

**AGIOS PHARMACEUTICALS, INC.**

**2007 STOCK INCENTIVE PLAN**

**CALIFORNIA SUPPLEMENT**

Pursuant to Section 10(e) of the Plan, the Board has adopted this supplement for purposes of satisfying the requirements of Section 25102(o) of the California Law:

Any Awards granted under the Plan to a Participant who is a resident of the State of California on the date of grant (a "California Participant") shall be subject to the following additional limitations, terms and conditions:

1. Additional Limitations on Options.

(a) Minimum Vesting Rate. Except in the case of Options granted to California Participants who are officers, directors, managers, consultants or advisors of the Company or its affiliates (which Options may become exercisable at whatever rate is determined by the Board), Options granted to California Participants shall become exercisable at a rate of not less than 20% per year over five years from the date of grant; provided, that, such Options may be subject to such reasonable forfeiture conditions as the Board may choose to impose and which are not inconsistent with Section 260.140.41 of the California Regulations.

(b) Minimum Exercise Price. The exercise price of Options granted to California Participants may not be less than 85% of the Fair Market Value of the Common Stock on the date of grant in the case of a Nonstatutory Stock Option or less than 100% of the Fair Market Value of the Common Stock on the date of grant in the case of an Incentive Stock Option; provided, however, that if the California Participant is a person who owns stock possessing more than 10% of the total combined voting power of all classes of stock of the Company or its parent or subsidiary corporations, the exercise price shall be not less than 110% of the Fair Market Value of the Common Stock on the date of grant.

(c) Maximum Duration of Options. No Options granted to California Participants shall have a term in excess of 10 years measured from the Option grant date.

(d) Minimum Exercise Period Following Termination. Unless a California Participant's employment is terminated for cause (as defined by applicable law, the terms of any contract of employment between the Company and such Participant, or in the instrument evidencing the grant of such Participant's Option), in the event of termination of employment of such Participant, such Participant shall have the right to exercise an Option, to the extent that he or she was otherwise entitled to exercise such Option on the date employment terminated, as follows: (i) at least six months from the date of termination, if termination was caused by such Participant's death or "permanent and total disability" (within the meaning of Section 22(e)(3) of the Code) and (ii) at least 30 days from the date of termination, if termination was caused other than by such Participant's death or "permanent and total disability" (within the meaning of Section 22(e)(3) of the Code).

(e) Limitation on Repurchase Rights. If an Option granted to a California Participant gives the Company the right to repurchase shares of Common Stock issued pursuant to the Plan upon termination of employment of such Participant, the terms of such repurchase right must comply with Section 260.140.41(k) of the California Regulations.

2. Additional Limitations for Restricted Stock Awards.

(a) Minimum Purchase Price. The purchase price for a Restricted Stock Award granted to a California Participant shall be not less than 85% of the Fair Market Value of the Common Stock at the time such Participant is granted the right to purchase shares under the Plan or at the time the purchase is consummated; provided, however, that if such Participant is a person who owns stock possessing more than 10% of the total combined voting power or value of all classes of stock of the Company or its parent or subsidiary corporations, the purchase price shall be not less than 100% of the Fair Market Value of the Common Stock at the time such Participant is granted the right to purchase shares under the Plan or at the time the purchase is consummated.

(b) Limitation of Repurchase Rights. If a Restricted Stock Award granted to a California Participant gives the Company the right to repurchase shares of Common Stock issued pursuant to the Plan upon termination of employment of such Participant, the terms of such repurchase right must comply with Section 260.140.42(h) of the California Regulations.

3. Additional Limitations for Other Stock-Based Awards. The terms of all Awards granted to a California Participant under Section 7 of the Plan shall comply, to the extent applicable, with Section 260.140.41 or Section 260.140.42 of the California Regulations.

4. Additional Requirement to Provide Information to California Participants. The Company shall provide to each California Participant and to each California Participant who acquires Common Stock pursuant to the Plan, not less frequently than annually, copies of annual financial statements (which need not be audited). The Company shall not be required to provide such statements to key employees whose duties in connection with the Company assure their access to equivalent information.

5. Additional Limitations on Timing of Awards. No Award granted to a California Participant shall become exercisable, vested or realizable, as applicable to such Award, unless the Plan has been approved by the holders of a majority of the Company's outstanding voting securities within 12 months before or after the date the Plan was adopted by the Board.

6. Additional Limitations Relating to Definition of Fair Market Value. For purposes of Section 1(b) and 2(a) of this supplement, "Fair Market Value" shall be determined in a manner not inconsistent with Section 260.140.50 of the California Regulations.

7. Additional Restriction Regarding Recapitalizations, Stock Splits, Etc. For purposes of Section 8 of the Plan, in the event of a stock split, reverse stock split, stock dividend, recapitalization, combination, reclassification or other distribution of the Company's securities, the number of securities allocated to each California Participant must be adjusted proportionately and without the receipt by the Company of any consideration from any California Participant.

**Exhibit 10.2**

AGIOS PHARMACEUTICALS, INC.

Incentive Stock Option Agreement
Granted Under 2007 Stock Incentive Plan

1. Grant of Option.

This agreement evidences the grant by Agios Pharmaceuticals, Inc., a Delaware corporation (the "Company"), on , 20 (the "Grant Date") to , an employee of the Company (the "Participant"), of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2007 Stock Incentive Plan (the "Plan"), a total of shares (the "Shares") of common stock, $0.001 par value per share, of the Company ("Common Stock") at $ per Share. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on (the "Final Exercise Date").

It is intended that the option evidenced by this agreement shall be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code"). Except as otherwise indicated by the context, the term "Participant", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable ("vest") as to [25%] of the original number of Shares on the [first] anniversary of the Vesting Commencement Date (as defined below) and as to an additional [2.0833%] of the original number of Shares at the end of each successive [month] following the [first] anniversary of the Vesting Commencement Date until the [fourth] anniversary of the Vesting Commencement Date. For purposes of this Agreement, "Vesting Commencement Date" shall mean .

The right of exercise shall be cumulative so that to the extent the option is not exercised in any period to the maximum extent permissible it shall continue to be exercisable, in whole or in part, with respect to all Shares for which it is vested until the earlier of the Final Exercise Date or the termination of this option under Section 3 hereof or the Plan.

3. Exercise of Option.

(a) Form of Exercise. Each election to exercise this option shall be accompanied by a completed Notice of Stock Option Exercise in the form attached hereto as Exhibit A, signed by the Participant, and received by the Company at its principal office, accompanied by this agreement, and payment in full in the manner provided in the Plan. The Participant may purchase less than the number of shares covered hereby, provided that no partial exercise of this option may be for any fractional share or for fewer than ten whole shares.

(b) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee or officer of, or consultant or advisor to, the Company or any parent or subsidiary of the Company as defined in Section 424(e) or (f) of the Code (an "Eligible Participant").

(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for "cause" as specified in paragraph (e) below, this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment. If the Participant is party to an employment or severance agreement with the Company that contains a definition of "cause" for termination of employment, "Cause" shall have the meaning ascribed to such term in such agreement. Otherwise, "Cause" shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant shall be considered to have been discharged for Cause if the Company determines, within 30 days after the Participant's resignation, that discharge for cause was warranted.

4. Company Right of First Refusal.

(a) Notice of Proposed Transfer. If the Participant proposes to sell, assign, transfer, pledge, hypothecate or otherwise dispose of, by operation of law or otherwise (collectively, "transfer") any Shares acquired upon exercise of this option, then the Participant shall first give written notice of the proposed transfer (the "Transfer Notice") to the Company. The Transfer Notice shall name the proposed transferee and state the number of such Shares the Participant proposes to transfer (the "Offered Shares"), the price per share and all other material terms and conditions of the transfer.

(b) Company Right to Purchase. For 30 days following its receipt of such Transfer Notice, the Company shall have the option to purchase all or part of the Offered Shares at the price and upon the terms set forth in the Transfer Notice. In the event the Company elects to purchase all or part of the Offered Shares, it shall give written notice of such election to the Participant within such 30-day period. Within 10 days after his or her receipt of such notice, the Participant shall tender to the Company at its principal offices the certificate or certificates representing the Offered Shares to be purchased by the Company, duly endorsed in blank by the Participant or with duly endorsed stock powers attached thereto, all in a form suitable for transfer of the Offered Shares to the Company. Promptly following receipt of such certificate or certificates, the Company shall deliver or mail to the Participant a check in payment of the purchase price for such Offered Shares; provided that if the terms of payment set forth in the Transfer Notice were other than cash against delivery, the Company may pay for the Offered Shares on the same terms and conditions as were set forth in the Transfer Notice; and provided further that any delay in making such payment shall not invalidate the Company's exercise of its option to purchase the Offered Shares.

(c) Shares Not Purchased By Company. If the Company does not elect to acquire all of the Offered Shares, the Participant may, within the 30-day period following the expiration of the option granted to the Company under subsection (b) above, transfer the Offered Shares which the Company has not elected to acquire to the proposed transferee, provided that such transfer shall not be on terms and conditions more favorable to the transferee than those contained in the Transfer Notice. Notwithstanding any of the above, all Offered Shares transferred pursuant to this Section 4 shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(d) Consequences of Non-Delivery. After the time at which the Offered Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Offered Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Offered Shares, but shall, insofar as permitted by law, treat the Company as the owner of such Offered Shares.

(e) Exempt Transactions. The following transactions shall be exempt from the provisions of this Section 4:

(1) any transfer of Shares to or for the benefit of any spouse, child or grandchild of the Participant, or to a trust for their benefit;

(2) any transfer pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended (the "Securities Act"); and

(3) the sale of all or substantially all of the outstanding shares of capital stock of the Company (including pursuant to a merger or consolidation);

provided, however, that in the case of a transfer pursuant to clause (1) above, such Shares shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(f) Assignment of Company Right. The Company may assign its rights to purchase Offered Shares in any particular transaction under this Section 4 to one or more persons or entities.

(g) Termination. The provisions of this Section 4 shall terminate upon the earlier of the following events:

(1) the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement filed by the Company under the Securities Act; or

(2) the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a merger or consolidation in which all or substantially all of the individuals and entities who were beneficial owners of the Company's voting securities immediately prior to such transaction beneficially own, directly or indirectly, more than 50% (determined on an as-converted basis) of the outstanding securities entitled to vote generally in the election of directors of the resulting, surviving or acquiring corporation in such transaction).

(h) No Obligation to Recognize Invalid Transfer. The Company shall not be required (1) to transfer on its books any of the Shares which shall have been sold or transferred in violation of any of the provisions set forth in this Section 4, or (2) to treat as owner of such Shares or to pay dividends to any transferee to whom any such Shares shall have been so sold or transferred.

(i) Legends. The certificate representing Shares shall bear a legend substantially in the following form (in addition to, or in combination with, any legend required by applicable federal and state securities laws and agreements relating to the transfer of the Company securities):

> "The shares represented by this certificate are subject to a right of first refusal in favor of the Company, as provided in a certain stock option agreement with the Company."

5. Agreement in Connection with Initial Public Offering.

The Participant agrees, in connection with the initial underwritten public offering of the Common Stock pursuant to a registration statement under the Securities Act, (i) not to (a) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable for shares of Common Stock or (b) enter into any swap or other agreement that transfers, in whole or in part, any of the economic

consequences of ownership of shares of Common Stock, whether any transaction described in clause (a) or (b) is to be settled by delivery of shares of Common Stock or other securities, in cash or otherwise, during the period beginning on the date of the filing of such registration statement with the Securities and Exchange Commission and ending 180 days from the date of the final prospectus relating to the offering (plus up to an additional 34 days to the extent requested by the managing underwriters for such offering in order to address Rule 2711(f) of the National Association of Securities Dealers, Inc. or any similar successor provision), and (ii) to execute any agreement reflecting clause (i) above as may be requested by the Company or the managing underwriters at the time of such offering. The Company may impose stop-transfer instructions with respect to the shares of Common Stock or other securities subject to the foregoing restriction until the end of the "lock-up" period.

6. Tax Matters.

(a) Withholding. No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

(b) Disqualifying Disposition. If the Participant disposes of Shares acquired upon exercise of this option within two years from the Grant Date or one year after such Shares were acquired pursuant to exercise of this option, the Participant shall notify the Company in writing of such disposition.

7. Nontransferability of Option.

This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

8. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

IN WITNESS WHEREOF, the Company has caused this option to be executed under its corporate seal by its duly authorized officer. This option shall take effect as a sealed instrument.

AGIOS PHARMACEUTICALS, INC.

By: _____

Name: _____

Title: _____

PARTICIPANT'S ACCEPTANCE

The undersigned hereby accepts the foregoing option and agrees to the terms and conditions thereof. The undersigned hereby acknowledges receipt of a copy of the Company's 2007 Stock Incentive Plan.

PARTICIPANT:

_____

Address: _____

_____

**Exhibit A**

**NOTICE OF STOCK OPTION EXERCISE**

Date: [1]

Agios Pharmaceuticals, Inc.
38 Sidney Street, 2nd Floor
Cambridge, MA 02139

Attention: Treasurer

Dear Sir or Madam:

I am the holder of [2] Stock Option granted to me under the Agios Pharmaceuticals, Inc. (the "Company") 2007 Stock Incentive Plan on [3] for the purchase of [4] shares of Common Stock of the Company at a purchase price of $ [5] per share.

I hereby exercise my option to purchase [6] shares of Common Stock (the "Shares"), for which I have enclosed [7] in the amount of [8]. Please register my stock certificate as follows:

Name(s): _____ [9]

_____

Address: _____

---

1 Enter the date of exercise.

2 Enter either "an Incentive" or "a Nonstatutory".

3 Enter the date of grant.

4 Enter the total number of shares of Common Stock for which the option was granted.

5 Enter the option exercise price per share of Common Stock.

6 Enter the number of shares of Common Stock to be purchased upon exercise of all or part of the option.

7 Enter "cash", "personal check" or if permitted by the option or Plan, "stock certificates No. XXXX and XXXX".

8 Enter the dollar amount (price per share of Common Stock times the number of shares of Common Stock to be purchased), or the number of shares tendered. Fair market value of shares tendered, together with cash or check, must cover the purchase price of the shares issued upon exercise.

9 Enter name(s) to appear on stock certificate: (a) Your name only; (b) Your name and other name (i.e., John Doe and Jane Doe, Joint Tenants With Right of Survivorship); or (c) In the case of a Nonstatutory option only, a Child's name, with you as custodian (i.e., Jane Doe, Custodian for Tommy Doe). Note: There may be income and/or gift tax consequences of registering shares in a Child's name.

Tax I.D. #: _____[10]

I represent, warrant and covenant as follows:

1. I am purchasing the Shares for my own account for investment only, and not with a view to, or for sale in connection with, any distribution of the Shares in violation of the Securities Act of 1933 (the "Securities Act"), or any rule or regulation under the Securities Act.

2. I have had such opportunity as I have deemed adequate to obtain from representatives of the Company such information as is necessary to permit me to evaluate the merits and risks of my investment in the Company.

3. I have sufficient experience in business, financial and investment matters to be able to evaluate the risks involved in the purchase of the Shares and to make an informed investment decision with respect to such purchase.

4. I can afford a complete loss of the value of the Shares and am able to bear the economic risk of holding such Shares for an indefinite period.

5. I understand that (i) the Shares have not been registered under the Securities Act and are "restricted securities" within the meaning of Rule 144 under the Securities Act, (ii) the Shares cannot be sold, transferred or otherwise disposed of unless they are subsequently registered under the Securities Act or an exemption from registration is then available; (iii) in any event, the exemption from registration under Rule 144 will not be available for at least one year and even then will not be available unless a public market then exists for the Common Stock, adequate information concerning the Company is then available to the public, and other terms and conditions of Rule 144 are complied with; and (iv) there is now no registration statement on file with the Securities and Exchange Commission with respect to any stock of the Company and the Company has no obligation or current intention to register the Shares under the Securities Act.

Very truly yours,

_____

(Signature)

[10] Social Security Number of Holder(s).

**Exhibit 10.3**

AGIOS PHARMACEUTICALS, INC.

Nonstatutory Stock Option Agreement
Granted Under 2007 Stock Incentive Plan

1. Grant of Option.

This agreement evidences the grant by Agios Pharmaceuticals, Inc., a Delaware corporation (the "Company"), on , 20 (the "Grant Date") to , an employee, consultant, or director of the Company (the "Participant"), of an option to purchase, in whole or in part, on the terms provided herein and in the Company's 2007 Stock Incentive Plan (the "Plan"), a total of shares (the "Shares") of common stock, $0.001 par value per share, of the Company ("Common Stock") at $ per Share. Unless earlier terminated, this option shall expire at 5:00 p.m., Eastern time, on (the "Final Exercise Date").

It is intended that the option evidenced by this agreement shall not be an incentive stock option as defined in Section 422 of the Internal Revenue Code of 1986, as amended, and any regulations promulgated thereunder (the "Code"). Except as otherwise indicated by the context, the term "Participant", as used in this option, shall be deemed to include any person who acquires the right to exercise this option validly under its terms.

2. Vesting Schedule.

This option will become exercisable ("vest") as follows: .

3. Exercise of Option.

(a) Form of Exercise. Each election to exercise this option shall be accompanied by a completed Notice of Stock Option Exercise in the form attached hereto as Exhibit A, signed by the Participant, and received by the Company at its principal office, accompanied by this agreement, and payment in full in the manner provided in the Plan. The Participant may purchase less than the number of shares covered hereby, provided that no partial exercise of this option may be for any fractional share or for fewer than ten whole shares.

(b) Continuous Relationship with the Company Required. Except as otherwise provided in this Section 3, this option may not be exercised unless the Participant, at the time he or she exercises this option, is, and has been at all times since the Grant Date, an employee, officer or director of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants, or advisors of which are eligible to receive option grants under the Plan (an "Eligible Participant").

(c) Termination of Relationship with the Company. If the Participant ceases to be an Eligible Participant for any reason, then, except as provided in paragraphs (d) and (e) below, the right to exercise this option shall terminate three months after such cessation (but in no event after the Final Exercise Date), provided that this option shall be exercisable only to the extent that the Participant was entitled to exercise this option on the date of such cessation. Notwithstanding the foregoing, if the Participant, prior to the Final Exercise Date, violates the

non-competition or confidentiality provisions of any employment contract, confidentiality and nondisclosure agreement or other agreement between the Participant and the Company, the right to exercise this option shall terminate immediately upon such violation.

(d) Exercise Period Upon Death or Disability. If the Participant dies or becomes disabled (within the meaning of Section 22(e)(3) of the Code) prior to the Final Exercise Date while he or she is an Eligible Participant and the Company has not terminated such relationship for "cause" as specified in paragraph (e) below, this option shall be exercisable, within the period of one year following the date of death or disability of the Participant, by the Participant (or in the case of death by an authorized transferee), provided that this option shall be exercisable only to the extent that this option was exercisable by the Participant on the date of his or her death or disability, and further provided that this option shall not be exercisable after the Final Exercise Date.

(e) Termination for Cause. If, prior to the Final Exercise Date, the Participant's employment or other relationship with the Company is terminated by the Company for Cause (as defined below), the right to exercise this option shall terminate immediately upon the effective date of such termination of employment or other relationship. If the Participant is party to an employment, consulting or severance agreement with the Company that contains a definition of "cause" for termination of employment or other relationship, "Cause" shall have the meaning ascribed to such term in such agreement. Otherwise, "Cause" shall mean willful misconduct by the Participant or willful failure by the Participant to perform his or her responsibilities to the Company (including, without limitation, breach by the Participant of any provision of any employment, consulting, advisory, nondisclosure, non-competition or other similar agreement between the Participant and the Company), as determined by the Company, which determination shall be conclusive. The Participant shall be considered to have been discharged for "Cause" if the Company determines, within 30 days after the Participant's resignation, that discharge for cause was warranted.

4. Company Right of First Refusal.

(a) Notice of Proposed Transfer. If the Participant proposes to sell, assign, transfer, pledge, hypothecate or otherwise dispose of, by operation of law or otherwise (collectively, "transfer") any Shares acquired upon exercise of this option, then the Participant shall first give written notice of the proposed transfer (the "Transfer Notice") to the Company. The Transfer Notice shall name the proposed transferee and state the number of such Shares the Participant proposes to transfer (the "Offered Shares"), the price per share and all other material terms and conditions of the transfer.

(b) Company Right to Purchase. For 30 days following its receipt of such Transfer Notice, the Company shall have the option to purchase all or part of the Offered Shares at the price and upon the terms set forth in the Transfer Notice. In the event the Company elects to purchase all or part of the Offered Shares, it shall give written notice of such election to the Participant within such 30-day period. Within 10 days after his or her receipt of such notice, the Participant shall tender to the Company at its principal offices the certificate or certificates representing the Offered Shares to be purchased by the Company, duly endorsed in blank by the Participant or with duly endorsed stock powers attached thereto, all in a form suitable for transfer

of the Offered Shares to the Company. Promptly following receipt of such certificate or certificates, the Company shall deliver or mail to the Participant a check in payment of the purchase price for such Offered Shares; provided that if the terms of payment set forth in the Transfer Notice were other than cash against delivery, the Company may pay for the Offered Shares on the same terms and conditions as were set forth in the Transfer Notice; and provided further that any delay in making such payment shall not invalidate the Company's exercise of its option to purchase the Offered Shares.

(c) Shares Not Purchased By Company. If the Company does not elect to acquire all of the Offered Shares, the Participant may, within the 30-day period following the expiration of the option granted to the Company under subsection (b) above, transfer the Offered Shares which the Company has not elected to acquire to the proposed transferee, provided that such transfer shall not be on terms and conditions more favorable to the transferee than those contained in the Transfer Notice. Notwithstanding any of the above, all Offered Shares transferred pursuant to this Section 4 shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(d) Consequences of Non-Delivery. After the time at which the Offered Shares are required to be delivered to the Company for transfer to the Company pursuant to subsection (b) above, the Company shall not pay any dividend to the Participant on account of such Offered Shares or permit the Participant to exercise any of the privileges or rights of a stockholder with respect to such Offered Shares, but shall, insofar as permitted by law, treat the Company as the owner of such Offered Shares.

(e) Exempt Transactions. The following transactions shall be exempt from the provisions of this Section 4:

(1) any transfer of Shares to or for the benefit of any spouse, child or grandchild of the Participant, or to a trust for their benefit;

(2) any transfer pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended (the "Securities Act"); and

(3) the sale of all or substantially all of the outstanding shares of capital stock of the Company (including pursuant to a merger or consolidation);

provided, however, that in the case of a transfer pursuant to clause (1) above, such Shares shall remain subject to the right of first refusal set forth in this Section 4 and such transferee shall, as a condition to such transfer, deliver to the Company a written instrument confirming that such transferee shall be bound by all of the terms and conditions of this Section 4.

(f) Assignment of Company Right. The Company may assign its rights to purchase Offered Shares in any particular transaction under this Section 4 to one or more persons or entities.

(g) Termination. The provisions of this Section 4 shall terminate upon the earlier of the following events:

(1) the closing of the sale of shares of Common Stock in an underwritten public offering pursuant to an effective registration statement filed by the Company under the Securities Act; or

(2) the sale of all or substantially all of the outstanding shares of capital stock, assets or business of the Company, by merger, consolidation, sale of assets or otherwise (other than a merger or consolidation in which all or substantially all of the individuals and entities who were beneficial owners of the Company's voting securities immediately prior to such transaction beneficially own, directly or indirectly, more than 50% (determined on an as-converted basis) of the outstanding securities entitled to vote generally in the election of directors of the resulting, surviving or acquiring corporation in such transaction).

(h) No Obligation to Recognize Invalid Transfer. The Company shall not be required (1) to transfer on its books any of the Shares which shall have been sold or transferred in violation of any of the provisions set forth in this Section 4, or (2) to treat as owner of such Shares or to pay dividends to any transferee to whom any such Shares shall have been so sold or transferred.

(i) Legends. The certificate representing Shares shall bear a legend substantially in the following form (in addition to, or in combination with, any legend required by applicable federal and state securities laws and agreements relating to the transfer of the Company securities):

> "The shares represented by this certificate are subject to a right of first refusal in favor of the Company, as provided in a certain stock option agreement with the Company."

5. Agreement in Connection with Initial Public Offering.

The Participant agrees, in connection with the initial underwritten public offering of the Common Stock pursuant to a registration statement under the Securities Act, (i) not to (a) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of Common Stock or any securities convertible into or exercisable or exchangeable for shares of Common Stock or (b) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of shares of Common Stock, whether any transaction described in clause (a) or (b) is to be settled by delivery of shares of Common Stock or other securities, in cash or otherwise, during the period beginning on the date of the filing of such registration statement with the Securities and Exchange Commission and ending 180 days from the date of the final prospectus relating to the offering (plus up to an additional 34 days to the extent requested by the managing underwriters for such offering in order to address Rule 2711(f) of the National Association of Securities Dealers, Inc. or any similar successor provision), and (ii) to execute any agreement reflecting clause (i) above as may be requested by the Company or the managing underwriters at the time of such offering. The Company may impose stop-transfer instructions with respect to the shares of Common Stock or other securities subject to the foregoing restriction until the end of the "lock-up" period.

6. Withholding.

No Shares will be issued pursuant to the exercise of this option unless and until the Participant pays to the Company, or makes provision satisfactory to the Company for payment of, any federal, state or local withholding taxes required by law to be withheld in respect of this option.

7. Nontransferability of Option.

This option may not be sold, assigned, transferred, pledged or otherwise encumbered by the Participant, either voluntarily or by operation of law, except by will or the laws of descent and distribution, and, during the lifetime of the Participant, this option shall be exercisable only by the Participant.

8. Provisions of the Plan.

This option is subject to the provisions of the Plan (including the provisions relating to amendments to the Plan), a copy of which is furnished to the Participant with this option.

IN WITNESS WHEREOF, the Company has caused this option to be executed under its corporate seal by its duly authorized officer. This option shall take effect as a sealed instrument.

AGIOS PHARMACEUTICALS, INC.

By: _____

Name: _____

Title: _____

PARTICIPANT'S ACCEPTANCE

The undersigned hereby accepts the foregoing option and agrees to the terms and conditions thereof. The undersigned hereby acknowledges receipt of a copy of the Company's 2007 Stock Incentive Plan.

PARTICIPANT:

Address:

**Exhibit A**

**NOTICE OF STOCK OPTION EXERCISE**

Date: [1]

Agios Pharmaceuticals, Inc.
38 Sidney Street, 2nd Floor
Cambridge, MA 02139

Attention: Treasurer

Dear Sir or Madam:

I am the holder of [2] Stock Option granted to me under the Agios Pharmaceuticals, Inc. (the "Company") 2007 Stock Incentive Plan on [3] for the purchase of [4] shares of Common Stock of the Company at a purchase price of $ [5] per share.

I hereby exercise my option to purchase [6] shares of Common Stock (the "Shares"), for which I have enclosed [7] in the amount of [8]. Please register my stock certificate as follows:

Name(s): _____[9]

_____

Address: _____

Tax I.D. #: _____[10]

---

[1] Enter the date of exercise.

[2] Enter either "an Incentive" or "a Nonstatutory".

[3] Enter the date of grant.

[4] Enter the total number of shares of Common Stock for which the option was granted.

[5] Enter the option exercise price per share of Common Stock.

[6] Enter the number of shares of Common Stock to be purchased upon exercise of all or part of the option.

[7] Enter "cash", "personal check" or if permitted by the option or Plan, "stock certificates No. XXXX and XXXX".

[8] Enter the dollar amount (price per share of Common Stock times the number of shares of Common Stock to be purchased), or the number of shares tendered. Fair market value of shares tendered, together with cash or check, must cover the purchase price of the shares issued upon exercise.

[9] Enter name(s) to appear on stock certificate: (a) Your name only; (b) Your name and other name (i.e., John Doe and Jane Doe, Joint Tenants With Right of Survivorship); or (c) In the case of a Nonstatutory option only, a Child's name, with you as custodian (i.e., Jane Doe, Custodian for Tommy Doe). Note: There may be income and/or gift tax consequences of registering shares in a Child's name.

[10] Social Security Number of Holder(s).

I represent, warrant and covenant as follows:

1. I am purchasing the Shares for my own account for investment only, and not with a view to, or for sale in connection with, any distribution of the Shares in violation of the Securities Act of 1933 (the “Securities Act”), or any rule or regulation under the Securities Act.

2. I have had such opportunity as I have deemed adequate to obtain from representatives of the Company such information as is necessary to permit me to evaluate the merits and risks of my investment in the Company.

3. I have sufficient experience in business, financial and investment matters to be able to evaluate the risks involved in the purchase of the Shares and to make an informed investment decision with respect to such purchase.

4. I can afford a complete loss of the value of the Shares and am able to bear the economic risk of holding such Shares for an indefinite period.

5. I understand that (i) the Shares have not been registered under the Securities Act and are “restricted securities” within the meaning of Rule 144 under the Securities Act, (ii) the Shares cannot be sold, transferred or otherwise disposed of unless they are subsequently registered under the Securities Act or an exemption from registration is then available; (iii) in any event, the exemption from registration under Rule 144 will not be available for at least one year and even then will not be available unless a public market then exists for the Common Stock, adequate information concerning the Company is then available to the public, and other terms and conditions of Rule 144 are complied with; and (iv) there is now no registration statement on file with the Securities and Exchange Commission with respect to any stock of the Company and the Company has no obligation or current intention to register the Shares under the Securities Act.

Very truly yours,

_____

(Signature)

**Exhibit 10.11**

May 4, 2010

Glenn Goddard
12 Hartford Circle
Andover, MA 01810

Dear Glenn:

I am pleased to offer you the position of Vice President, Finance, at Agios Pharmaceuticals, Inc. reporting to Duncan Higgons, Chief Operating Officer. You will receive a semi-monthly salary of $10,000.00 which is equivalent to $240,000.00 annually.

You will be granted a stock option to purchase 125,000 shares of the company's Common stock, subject to Board of Directors approval. The stock option exercise price will be at fair market value as established by the Board and will be subject to the standard terms and conditions of the Agios Stock Option Plan. The option will vest over four years at the rate of 25% after twelve months of full time active employment and then an additional l/48$^{th}$ for each additional month of full time active employment after your first anniversary date until after four full years when the option is fully vested. A copy of the plan will be provided to you along with a Stock Option Grant Letter after the option grant has been approved.

You will be eligible to participate in all of the company's benefits plans, which include Medical and Dental Insurance Programs, Flexible Spending Program for medical and daycare expenses, Life Insurance, AD&D, and Short and Long Term Disability Plans, and 401(k). The company pays for 90% of the cost of the HMO medical plan and 85% of the PPO plan. It pays for 90% of the cost of the dental plan and will pay the full cost of Life and AD&D insurance as well as Short and Long Term Disability plans. You will accrue three weeks paid vacation each year and receive 11 paid holidays annually in accordance with the company holiday schedule.

The offer of employment is contingent upon your signing the company's standard Forms of Agreement Regarding Inventions, Confidentiality and Non-Competition (Copy attached) and 1-9 Employment Verification Form. You will be required to submit documentation that establishes identity and employment eligibility in accordance with the US Immigration and Naturalization requirements. If there are any other agreements of any type that you are aware of which may impact or limit your ability to perform your job at Agios Pharmaceuticals, please let us know as soon as possible.

This employment offer letter is not intended to create or constitute an employment agreement or contract between you and Agios Pharmaceuticals. It is also important for you to understand that Massachusetts is an "at will" employment state. This means that you will have the right to terminate your employment relationship with Agios Pharmaceuticals at any time for any reason. Similarly, Agios Pharmaceuticals will have the right to terminate its employment relationship with you at any time for any reason.

I am very excited about having you join our team and I anticipate that you will make many important contributions to our Company and strategic mission. Please acknowledge your acceptance of this offer by returning a signed copy of this letter. This offer will remain open until Thursday, May 6, 2010.

Best regards,

/s/ Duncan Higgons
J. Duncan Higgons
Chief Operating Officer
Agios Pharmaceuticals, Inc.

I accept this offer of employment with Agios Pharmaceuticals Inc. and will begin work on:
On or before July 1, 2010.

Signature:

| /s/ Glenn Goddard | 5/5/10 |
|---|---|
| Glenn Goddard | Date |

**Exhibit 10.12**

THE CLARK BUILDING

Cambridge, Massachusetts

LANDLORD

---

THIRTY-EIGHT SIDNEY STREET LIMITED PARTNERSHIP

TENANT

---

AGIOS PHARMACEUTICALS, INC.

THE CLARK BUILDING

Table of Contents

LEASE

ARTICLE I

RECITALS AND DEFINITIONS

Section 1.1 - Recitals.

This Lease (this "Lease") is entered into as of August 2, 2010, by and between THIRTY-EIGHT SIDNEY STREET LIMITED PARTNERSHIP, a Delaware limited partnership (the "Landlord") and AGIOS PHARMACEUTICALS, INC., a Delaware corporation ("Tenant").

In consideration of the mutual covenants herein set forth, the Landlord and the Tenant do hereby agree to the terms and conditions set forth in this Lease.

Section 1.2 - Definitions.

The following terms shall have the meanings indicated or referred to below:

"Additional Rent" means all charges payable by the Tenant pursuant to this Lease other than Annual Fixed Rent, including without implied limitation the Tenant's parking charges as provided in Section 2.4; the Tenant's Tax Expense Allocable to the Premises as provided in Section 3.2; the Tenant's Operating Expenses Allocable to the Premises in accordance with Section 3.3; amounts payable for special services pursuant to Section 3.5; the Landlord's share of any sublease or assignment proceeds pursuant to Section 6.8.

"Annual Fixed Rent" - See Exhibit A and Section 3.1.

"Building" means The Clark Building located at 38 Sidney Street, Cambridge, Massachusetts in which the Premises are located.

"Commencement Date" - See Section 2.5.

"Common Building Areas" means those portions of the Building which are not part of the Premises and to which the Tenant has appurtenant rights pursuant to Section 2.2.

"External Causes" means collectively, (i) Acts of God, war, civil commotion, fire, flood or other casualty, strikes or other extraordinary labor difficulties, shortages of labor or materials or equipment in the ordinary course of trade, government order or regulations or other cause not reasonably within the Landlord's or Tenant's control and not due to the fault or neglect of the Landlord or Tenant.

"Lease Year" means each period of one year during the Term commencing on the Commencement Date or on any anniversary thereof.

"Permitted Uses" - See Exhibit A.

"Premises" means approximately 38,536 rentable square feet as defined in Exhibit A. See Exhibit A, Exhibit B and Section 2.1.

"Property" means, collectively, the Building and the parcel of land on which the Building sits.

"Term" - See Exhibit A.

"University Park" means the area in Cambridge, Massachusetts, bounded on the North side by Massachusetts Avenue, Green and Blanche Streets, on the East side by Landsdowne, Cross and Purrington Streets, on the South side by Pacific Street and on the West side by Brookline Street.

## ARTICLE II
## PREMISES AND TERM

Section 2.1 - Premises.

Subject to the Expansion Premises Term Commencement set forth in Exhibit A below regarding the Expansion Premises, the Landlord hereby leases to the Tenant, and the Tenant hereby leases from the Landlord, for the Term, the Premises. The Premises shall exclude the entry and main lobby of the Building, first floor elevator lobby, first floor mail room, the common stairways and stairwells, elevators and elevator wills, boiler room, sprinklers, sprinkler rooms, elevator rooms, mechanical rooms, loading and receiving areas, electric and telephone closets, janitor closets, loading docks and bays, rooftop mechanical penthouses to the extent they house Building equipment, and pipes, ducts, conduits, wires and appurtenant fixtures and equipment serving exclusively or in common other parts of the Building. If the Premises at any time includes less than the entire rentable floor area of any floor of the Building, the Premises shall also exclude the common corridors, vestibules, elevator lobby and toilets located on such floor. The Tenant acknowledges that, except as expressly set forth in this Lease, there have been no representations or warranties made by or on behalf of the Landlord with respect to the Premises, the Building or the Property or with respect to the suitability of any of them for the conduct of the Tenant's business. Tenant acknowledges that, except as expressly set forth in this Lease, it is accepting the Premises in its present "as-is" condition with no expectation that Landlord will or should perform or contribute toward the cost of any leasehold improvements required to prepare the Premises for Tenant's occupancy. Landlord shall be responsible, at its sole cost and expense, to (i) demise the Second Floor Expansion Premises as shown on Exhibit B, (ii) demise the Third Floor Expansion Premises as shown on Exhibit B, (iii) create common areas and common area corridors for a multi-tenant third floor (after giving good faith consideration to Tenant's input and suggestions for the layout and configuration of such common areas and common area corridors); and (iv) to replace the roof of the Building during 2010, all in a manner which meets all City of Cambridge building code requirements. Landlord shall deliver to Tenant a copy of any report in its possession, including but not limited to any and all decommissioning documents and reports, that describes the environmental condition of any portion of the Expansion Premises prepared by or on behalf of Landlord or ETEX Corporation ("ETEX") in connection with the prior occupancy of the Expansion Premises by ETEX.

Section 2.2 - Appurtenant Rights.

The Tenant shall have, as appurtenant to the Premises, the nonexclusive right to use in common with others, subject to reasonable rules of general applicability to occupants of the Building from time to time made by the Landlord of which the Tenant is given notice: (i) the entry, vestibules and main lobby of the Building, first floor mailroom, the common stairways, elevators, elevator wells, boiler room, elevator rooms, sprinkler rooms, mechanical rooms, electric and telephone closets, janitor closets, loading docks and bays, rooftop mechanical penthouses and shafts to the extent they house Building equipment, and the pipes, sprinklers, ducts, conduits, wires and appurtenant fixtures and equipment serving the Premises in common with others, (ii) common walkways and driveways necessary or reasonably convenient for access to the Building, (iii) access to loading area and freight elevator subject to Rules and Regulations then in effect, and (iv) if the Premises at any time include less than the entire rentable floor area of any floor, the common toilets, corridors, vestibules, and elevator lobby of such floor.

Additionally, the Tenant shall have, as appurtenant to the Premises (and exclusively for use in connection with the occupancy of the Premises), the nonexclusive right of access to and proportionate use of the roof for the purpose of installing and maintaining mechanical equipment, antennae and dishes which, in each case, have been pre-approved by the Landlord pursuant to the terms of Article IV, subject however, to reasonable rules of general applicability to occupants of the Building from time to time made by the Landlord of which the Tenant is given notice, but only to the extent that the Tenant has assumed responsibility for maintenance and repair thereof.

Section 2.3 - Landlord’s Reservations.

(a) The Landlord reserves the right from time to time, without unreasonable interference with the Tenant’s use and with written notice to Tenant, except in emergencies (including the specialized needs of Tenant’s operations which Landlord hereby acknowledges): (i) to install, use, maintain, repair, replace and relocate for service to the Premises and other parts of the Building, or either, pipes, ducts, conduits, wires and appurtenant fixtures and equipment, wherever located in the Premises or the Building, and (ii) to alter or relocate any other common facility, provided that substitutions are substantially equivalent or better for Tenant’s use of the Premises consistent with the Permitted Uses.

(b) Tenant acknowledges that the Park is comprised of several buildings, including the Building and both life science/office buildings (“Commercial Buildings”) and residential buildings (“Residential Buildings”), together with common and publicly accessible landscaped areas, service drives, and sidewalks. Landlord has established a common scheme for the operation and maintenance of the Park to which this Lease and the other leases of space in the Park are subject pursuant to a legal instrument entitled the “Declaration of Covenants,” provided, however, that the terms and conditions of the Declaration of Covenants shall not diminish in any material and adverse manner any of Tenant’s rights and benefits with respect to the Premises, or materially and adversely increase any of Tenant’s obligations. Each Commercial Building, and certain of the Residential Buildings, are subject to the Declaration of Covenants, and contribute to the costs and expenses to be shared thereunder. However, Landlord and Tenant recognize that Residential Buildings may not contribute to such costs and expenses, and therefore, it is agreed

that allocation of costs and expenses payable under the Declaration of Covenants among the building owners, the Building's allocable share of which are Operating Expenses under this Lease, shall be based on an aggregation of all such costs and expenses, less whatever contributions can be collected from the Residential Buildings, and allocated to the Building based on a numerator comprised of the total rentable area of the Building, and the denominator of which is the total rentable area of all of the Commercial Buildings in existence from time to time, or by such other method as Landlord may reasonably determine.

Section 2.4 - Parking.

The Landlord shall provide and the Tenant shall pay for parking privileges for use by the Tenant's employees, business invitees and visitors in accordance with Exhibit A. The Landlord shall operate, or cause to be operated, a parking garage known as the 80 Landsdowne Street Garage (the "Garage") to serve the Building and other buildings in University Park. The Tenant's parking privileges shall be initially located in the Garage and shall be on a nonexclusive basis (i.e., no reserved spaces); provided, however, Landlord agrees that the Garage shall be operated so as to maintain therein sufficient spaces to accommodate Tenant's parking privileges described in Exhibit A. However, Tenant's parking privileges may be relocated by Landlord to Landlord's parking facility located at 55 Franklin Street, Cambridge, Massachusetts, upon reasonable prior notice to Tenant from Landlord. In the event that Tenant's parking privileges are so relocated, Tenant's parking privileges at such new location shall be consistent with the terms set forth in this Section 2.4. All monthly users will have unlimited access to the Garage twenty-four (24) hours per day, seven days per week. Additional parking passes may be provided to Tenant on a month-to-month basis, as available.

The Tenant agrees that it and all persons claiming by, through and under it, shall at all times abide by the reasonable rules and regulations promulgated by the Landlord, of which Tenant is given notice, with respect to the use of the parking facilities provided by the Landlord pursuant to this Lease. If there are any conflicts between the provisions of such rules and regulations and any provisions of this Lease, the provisions of this Lease shall govern.

Charges for Tenant's parking privileges hereunder shall be at current monthly parking rates (which rates shall be consistent with market parking rates in parking facilities of comparable quality at mixed use office/research parks in East Cambridge/Kendall Square/Cambridgeport) (currently at $235.00 per month per pass), and shall constitute Additional Rent and shall be payable monthly to Landlord at the time and in the fashion in which Annual Fixed Rent under this Lease is payable.

At any time during the Term Landlord shall have the right to assign Landlord's obligations to provide parking, as herein set forth, together with Landlord's right to receive Additional Rent for such parking spaces as herein provided, to a separate entity created for the purpose of providing the parking privileges set forth herein. In such event, Landlord and Tenant agree to execute and deliver appropriate documentation, including documentation with the new entity, reasonably necessary to provide for the new entity to assume Landlord's obligations to provide the parking privileges to Tenant as specified herein and for the Tenant to pay the Additional Rent attributable to the parking privileges directly to the new entity. Landlord shall, however, remain primarily liable for the provision of Tenant's parking privileges.

Section 2.5 - Commencement Date.

"Commencement Date" as defined in Exhibit A.

Section 2.6 - Extension Option.

Provided that there has been no Event of Default which is uncured and continuing on the part of the Tenant, and that Tenant is, as of the date of exercise of its rights under this Section 2.6, in occupancy of at least 67% of the Premises for its own business purposes, the Tenant shall have the right to extend the Term hereof for two (2) consecutive periods of five (5) years (the first such period being the "First Extension Term," the second such period being the "Second Extension Term" and, together with the First Extension Term, the "Full Extension Term") on the following terms and conditions:

(a) Such right to extend the Term shall be exercised by the giving of notice by Tenant to Landlord at least nine (9) months prior to the expiration of the Initial Term or First Extension Term, as applicable (the "Extension Notice Deadline Date"). Upon the giving of such notice on or before the Extension Notice Deadline Date, this Lease and the Term hereof shall be extended for an additional term, as specified above, without the necessity for the execution of any additional documents except a document memorializing the Annual Fixed Rent for the applicable Extension Term to be determined as set forth below. Time shall be of the essence with respect to the Tenant's giving notice to extend the Term on or before the Extension Notice Deadline Date. In no event may the Tenant extend the Term under this Section 2.6 for more than ten (10) years after the expiration of the Initial Term, unless Landlord and Tenant shall mutually agree to such an extension.

(b) The First Extension Term and the Second Extension Term shall be upon all the terms, conditions and provisions of this Lease, except the Annual Fixed Rent during each such Extension Term shall be the then Extension Rental Value of the Premises for such Extension Term, to be determined under this Section 2.6.

(c) For purposes of the First Extension Term and Second Extension Term described in this Section 2.6 the Extension Fair Rental Value of the Premises shall mean the then current fair market annual rent for leases of other space of a comparable nature and quality similarly improved, taking into account the condition to which such premises have been improved (excluding Removable Alterations) and the economic terms and conditions specified in this Lease that will be applicable thereto, including the savings, if any, due to the absence or reduction of brokerage commissions. The Landlord and Tenant shall endeavor to agree upon the Extension Fair Rental Value of the Premises within thirty (30) days after the Tenant has exercised an option for an Extension Term. If the Extension Fair Rental Value of the Premises is not agreed upon by the Landlord and the Tenant within this time frame, each of the Landlord and the Tenant shall retain a real estate professional with at least ten (10) years continuous experience in the business of appraising or marketing similar commercial real estate in the Cambridge, Massachusetts area who shall, within thirty (30) days of his or her selection, prepare a written report summarizing his or her conclusion as to the Extension Fair Rental Value. The Landlord and the Tenant shall simultaneously exchange such reports; provided, however, if

either party has not obtained such a report within forty-five (45) days after the last day of the thirty (30) day period referred to above in this Section 2.6, then the determination set forth in the other party's report shall be final and binding upon the parties. If both parties receive reports within such time and the lower determination is within ten percent (10%) of the higher determination, then the average of these determinations shall be deemed to be the Extension Fair Rental Value for the Premises. If these determinations differ by more than ten percent (10%), then the Landlord and the Tenant shall mutually select a person with the qualifications stated above (the "Final Professional") to resolve the dispute as to the Extension Fair Rental Value for the Premises. If the Landlord and the Tenant cannot agree upon the designation of the Final Professional within ten (10) days of the exchange of the first valuation reports, either party may apply to the American Arbitration Association, the Greater Boston Real Estate Board, or any successor thereto, for the designation of a Final Professional. Within ten (10) days of the selection of the Final Professional, the Landlord and the Tenant shall each submit to the Final Professional a copy of their respective real estate professional's determination of the Extension Fair Rental Value for the Premises. The Final Professional shall then, within thirty (30) days of his or her selection, prepare a written report summarizing his or her conclusion as to the Extension Fair Rental Value (the "Final Professional's Valuation"). The Final Professional shall give notice of the Final Professional's Valuation to the Landlord and the Tenant and such decision shall be final and binding upon the Landlord and the Tenant. In the event that the commencement of either of the First Extension Term or Second Extension Term occurs prior to a final determination of the Extension Fair Rental Value therefor (the "Extension Rent Determination Date"), then the Tenant shall pay the Annual Fixed Rental at the greater of (i) the rate specified by the Landlord in its proposed Extension Fair Rental Value or (ii) the then applicable Fixed Rental Rate (such greater amount being referred to as the "Interim Rent"). If the Annual Fixed Rent as finally determined for such Extension Term is determined to be greater than the Interim Rent, then the Tenant shall pay to the Landlord the amount of the underpayment for the period from the end of the Initial Term of this Lease until the Extension Rent Determination Date within thirty (30) days of the Extension Rent Determination Date. If the Annual Fixed Rent as finally determined for the Extension Term is determined to be less than the Interim Rent, then the Landlord shall credit the amount of such overpayment against the monthly installments of Annual Fixed Rent coming due after the Extension Rent Determination Date.

Section 2.7 - Right of First Offer.

Subject to the provisions of this Section 2.7 as well as the pre-existing rights of Sanofi Pasteur Biologics, Tenant shall have a continuing right of first offer for all or any portion of the portion of the Building which may hereafter become vacant and available (the "First Offer Space"). Landlord shall notify Tenant of the terms on which Landlord intends to offer to lease the First Offer Space ("Landlord's Notice"). Within ten (10) business days after receipt of Landlord's Notice, Tenant may, by written notice delivered to Landlord, (i) reject Landlord's Notice, or (ii) unconditionally and irrevocably accept Landlord's offer to lease such space for Tenant's own use on the terms set forth in Landlord's Notice. If Tenant fails to timely respond as aforesaid, such failure shall be deemed Tenant's rejection of Landlord's Notice. In the event Tenant exercises its right to the First Offer Space, Landlord and Tenant hereby agree to amend

those provisions of this Lease which are necessarily affected by the increase in the rentable area and leaving all other provisions of this Lease in full force and effect without modification. After Tenant takes possession of the First Offer Space, the term "Premises" as used in this Lease, shall be deemed to refer to and include the First Offer Space.

If Landlord's Notice is rejected under clause (i) above (or deemed rejected through the Tenant's failure to timely respond), then Landlord may enter into a lease for the First Offer Space providing for an effective Annual Fixed Rent equal to or less than five percent (5%) less than that specified in Landlord's Notice. For clarity, in the event that the Landlord proposes to enter into a lease for the First Offer Space providing for an effective Annual Fixed Rent greater than five percent (5%) less than that specified in Landlord's Notice, Landlord shall notify Tenant of such terms by sending an additional Landlord's Notice that will be subject to the terms of the preceding paragraph.

Except as may be set forth in Landlord's Notice, Landlord's failure to deliver, or delay in delivering, all or any part of the First Offer Space, for any reason, shall not constitute a default of Landlord, and shall not affect the validity of the Lease.

Notwithstanding any provision of this Section 2.7 to the contrary, Tenant's rights under this Section 2.7 shall be void, at Landlord's election, if Tenant is in default hereunder and beyond any applicable cure periods on the date Tenant makes any election with respect to the First Offer Space under this Section 2.7 or at the time the First Offer Space would be added to the Premises. Nothing in this Section shall be construed to grant to Tenant any rights or interest in any space in the Building, and any claims by Tenant alleging a failure of Landlord to comply herewith shall be limited to claims for monetary damages. Tenant may not assert any rights in any space nor file any lis pendens or similar notice with respect thereto.

## ARTICLE III

## RENT AND OTHER PAYMENTS

Section 3.1 - Annual Fixed Rent.

From and after the Annual Fixed Rent Commencement Date (as defined in Exhibit A), the Tenant shall pay, without notice or demand, monthly installments of one-twelfth (1/12th) of the Annual Fixed Rent in effect and applicable to the Premises in advance for each full calendar month of the Term following the Annual Fixed Rent Commencement Date and of the corresponding fraction of said one-twelfth (1/12th) for any fraction of a calendar month at the Rent Commencement Date or end of the Term. The Annual Fixed Rent applicable to the Premises during the Term shall be as set forth in Exhibit A.

Section 3.2 - Real Estate Taxes.

From and after the Commencement Date, during the Term, the Tenant shall pay to the Landlord, as Additional Rent, the Tenant's Tax Expenses Allocable to the Premises (as such term is hereinafter defined) in accordance with this Section 3.2. The terms used in this Section 3.2 are defined as follows:

(a) "Tax Year" means the 12-month period beginning July 1 each year or if the appropriate governmental tax fiscal period shall begin on any date other than July 1, such other date.

(b) "The Tenant's Tax Expense Allocable to the Premises" means (i) that portion of the Landlord's Tax Expenses for a Tax Year which bears the same proportion thereto as the Rentable Floor Area of the Premises (from time to time) bears to the Total Rentable Floor Area of the Building and (ii) in the event that the Premises are improved to a standard which is higher than other portions of the Property and the Property is re-assessed at a higher value, such portion of the Real Estate Taxes on the Property with respect to any Tax Year as is appropriate so that the Tenant bears the portion of the Real Estate Taxes which are properly allocable to the Premises, as reasonably determined by Landlord using good faith commercially reasonable judgment based on assessment values and other information with respect to the Premises and the Building made available by the assessing authorities (Landlord's determination of such allocation shall take into account the rate of appreciation, if any, of real property in the City of Cambridge from the date of the prior assessment to the date of the new assessment, and the portion of any increased assessment on the Property which is allocable to any such general increase in the value of the real property in the City of Cambridge shall not be allocated disproportionately to Tenant).

(c) "The Landlord's Tax Expenses" with respect to any Tax Year means the aggregate Real Estate Taxes on the Property with respect to that Tax Year, reduced by any abatement receipts with respect to that Tax Year.

(d) "Real Estate Taxes" means (i) all real property taxes and special assessments of every kind and nature assessed by any governmental authority on the applicable property, but excluding any income taxes payable by Landlord as a result of payments made to Landlord by Tenant or any other tenant at the Property; and (ii) reasonable expenses of any proceedings for abatement of such taxes or special assessments. Any special assessments to be included within the definition of "Real Estate Taxes" shall be limited to the amount of the installment (plus any interest thereon) of such special tax or special assessment (which shall be payable over the longest period permitted by law) required to be paid during the Tax Year in respect of which such taxes are being determined. There shall be excluded from such taxes all income, estate, succession, inheritance, excess profit, franchise and transfer taxes; provided, however, that if at any time during the Term the present system of ad valorem taxation of real property shall be changed so that in lieu of the whole or any part of the ad valorem tax on real property, there shall be assessed on the Landlord a capital levy or other tax on the gross rents received with respect to the Property, or a federal, state, county, municipal or other local income, franchise, excise or similar tax, assessment, levy or charge (distinct from any now in effect) based, in whole or in part, upon any such gross rents, then any and all of such taxes, assessments, levies or charges, to the extent so based, shall be deemed to be included within the term "Real Estate Taxes."

Payments by the Tenant on account of the Tenant's Tax Expenses Allocable to the Premises shall be made monthly at the time and in the fashion herein provided for the payment of Annual Fixed Rent and shall be in an amount of the greater of (i) one-twelfth (1/12th) of the Tenant's Tax Expenses Allocable to the Premises for the current Tax Year as reasonably estimated by the Landlord, or (ii) an amount reasonably estimated by any ground lessor of the Land or holder of a first mortgage on the Property, to be sufficient, if paid monthly, to pay the Landlord's Tax Expenses on the dates due to the taxing authority.

Not later than ninety (90) days after the Landlord's Tax Expenses are determinable for the first Tax Year of the Term or fraction thereof and for each succeeding Tax Year or fraction thereof during the Term, the Landlord shall render the Tenant a statement in reasonable detail showing for the preceding year or fraction thereof, as the case may be, real estate taxes on the Property, and any abatements or refunds of such taxes. Expenses incurred in obtaining any tax abatement or refund may be charged against such tax abatement or refund before the adjustments are made for the Tax Year. If at the time such statement is rendered it is determined with respect to any Tax Year, that the Tenant has paid (i) less than the Tenant's Tax Expenses Allocable to the Premises or (ii) more than the Tenant's Tax Expenses Allocable to the Premises, then, in the case of (i) the Tenant shall pay to the Landlord, as Additional Rent, within thirty (30) days of such statement the amount of such underpayment and, in the case of (ii) the Landlord shall credit the amount of such overpayment against the monthly installments of the Tenant's Tax Expenses Allocable to the Premises next thereafter coming due (or refund such overpayment within thirty (30) days if the Term has expired and the Tenant has no further obligation to the Landlord).

To the extent that real estate taxes shall be payable to the taxing authority in installments with respect to periods less than a Tax Year, the statement to be furnished by the Landlord shall be rendered and payments made on account of such installments. Notwithstanding the foregoing provisions, no decrease in Landlord's Tax Expenses with respect to any Tax Year shall result in a reduction of the amount otherwise payable by Tenant if and to the extent said decrease is attributable to vacancies in the Building, rather than to a reduction in the assessed value of the Property as a whole or a reduction in the tax rate. Landlord shall, upon Tenant's request therefor, provide Tenant with copies of all applicable tax bills, statements, records and the like, as well as copies of Landlord's calculations and all other relevant information.

Section 3.3 - Operating Expenses.

From and after the Commencement Date, during the Term the Tenant shall pay to the Landlord, as Additional Rent, the Tenant's Operating Expenses Allocable to the Premises, as hereinafter defined, in accordance with this Section 3.3. The terms used in this Section 3.3 are defined as follows:

(a) "The Tenant's Operating Expenses Allocable to the Premises" means that portion of the Operating Expenses for the Property which bears the same proportion thereto as the Rentable Floor Area of the Premises bears to the Total Rentable Floor Area of the Building.

(b) "Operating Expenses for the Property" means Landlord's reasonable cost of operating, cleaning, maintaining and repairing the Property, and shall include

without limitation, the cost of services on Exhibit C; premiums for insurance carried pursuant to Section 7.4; the amount deductible from any insurance claim actually made by Landlord during the time period in question (which amount is currently $10,000.00, and which amount may be increased during the Term and any Extension Term provided such increase is reasonable and customary); reasonable compensation and all fringe benefits, worker's compensation insurance premiums and payroll taxes paid to, for or with respect to all persons (University Park/Building general manager and below, provided that such charges shall be prorated to reflect the percentage of rentable square feet of the Building as compared to all of the commercial rentable square feet at University Park) directly engaged in the operating, maintaining or cleaning of the Property; interior landscaping and maintenance; steam, water, sewer, gas, oil, electricity, telephone and other utility charges (excluding such utility charges either separately metered or separately chargeable to tenants for additional or special services and those charges related to the cost of operating base Building equipment not used by Tenant, cost of providing conditioned water for HVAC services; cost of building and cleaning supplies; the costs of routine environmental management programs operated by Landlord; market rental costs for equipment used in the operating, cleaning, maintaining or repairing of the Property, or the applicable fair market rental charges in the case of equipment owned by the Landlord; cost of cleaning; cost of maintenance, repairs and replacements; cost of snow removal; cost of landscape maintenance; security services; payments under service contracts with independent contractors; management fees at market rates (currently $1.17 per rentable square foot); the cost of any capital improvement either required by law or regulation or which reduces the Operating Expenses for the Property or which improves the management and operation of the Property in a manner acceptable to Tenant, which cost shall be amortized in accordance with generally accepted accounting principles together with interest on the unamortized balance calculated at the rate from time to time announced by Bank of America, N.A. as its prime rate; charges reasonably allocated to the Building for the operating, cleaning, maintaining and repairing of University Park common areas and amenities; and all other reasonable and necessary expenses paid in connection with the operation, cleaning, maintenance and repair of the Property. If, for any reason portions of the Rentable Area of the Building not included in the Premises were not occupied by tenants or the Landlord was not supplying all tenants with the services being supplied under the Lease or any tenants in the Building were supplied with a lesser level of standard services than those supplied to the Tenant under this Lease, Landlord's Operating Expenses for the Property shall include the amounts reasonably determined by Landlord which would have been incurred if ninety- five percent (95%) of the rentable area in the Building were occupied and were supplied with the same level of standard services as supplied to the Tenant under this Lease. If the Tenant provides written notice to the Landlord of deficiencies in the performance of cleaning services within the Premises provided pursuant to the terms of this Lease, then Landlord shall have thirty (30) days within delivery of such notice to remedy the deficiencies identified by the Tenant. If such deficiencies have not been resolved to the reasonable satisfaction of the Tenant

within such thirty (30) day period, then the Tenant shall have the ability to enter into its own contract with a vendor of its own choosing to provide cleaning services to the Premises. In the event that the Tenant does enter into such a contract with a vendor to provide cleaning services to the Premises, the Tenant shall notify the Landlord prior to the commencement of such cleaning services, which notice shall include the commencement date of such services, and the Operating Expenses charged to the Tenant from the commencement date through the remainder of the Term of this Lease shall not include any charges related to cleaning services of the Premises.

Operating Expenses for the Property shall not include the following: the Landlord's Tax Expense; cost of repairs or replacements (i) resulting from eminent domain takings, (ii) to the extent reimbursed by insurance, or (iii) required, above and beyond ordinary periodic maintenance, to maintain in serviceable condition the major structural elements of the Building, including the roof, exterior walls and floor slabs; replacement or contingency reserves; ground lease rents or payment of debt obligations; costs incurred due to negligent acts or omissions of Landlord, Landlord's agents, contractors or employees, or any other tenant of the Building; legal and other professional fees for matters not relating to the normal administration and operation of the Property; promotional, advertising, public relations or brokerage fees and commissions paid in connection with services rendered for securing or renewing leases; lease up and tenant improvement costs for space other than the Premises in the Building; costs of capital improvements not permitted hereinabove; and separately metered or sub metered utilities for other tenants in the Building. The Landlord's Operating Expenses shall be reduced by the amount of any proceeds, payments, credits or reimbursements which the Landlord receives from sources other than tenants and which are applicable to such Operating Expenses for the Property.

Payments by the Tenant for its share of the Operating Expenses for the Property shall be made in monthly installments of one-twelfth (1/12$^{th}$) of Tenant's share of Operating Expenses. The amount so to be paid to the Landlord shall be an amount from time to time reasonably estimated by the Landlord to be sufficient to aggregate a sum equal to the Tenant's share of the Operating Expenses for the Property for each calendar year.

Not later than ninety (90) days after the end of each calendar year or fraction thereof during the Term or fraction thereof at the end of the Term, the Landlord shall render the Tenant a statement in reasonable detail and according to usual accounting practices certified by a representative of the Landlord, showing for the preceding calendar year or fraction thereof, as the case may be, the Operating Expenses for the Property and the Tenant's Operating Expenses Allocable to the Premises. Said statement to be rendered to the Tenant also shall show for the preceding calendar year or fraction thereof, as the case may be, the amounts of Operating Expenses already paid by the Tenant. If at the time such statement is rendered it is determined with respect to any calendar year, that the Tenant has paid (i) less than the Tenant's Operating Expenses Allocable to the Premises or (ii) more than the Tenant's Operating Expenses Allocable to the Premises, then, in the case of (i) the Tenant shall pay to the Landlord, as Additional Rent, within thirty (30) days of such statement the amounts of such underpayment and, in the case of

(ii) the Landlord shall credit the amount of such overpayment against the monthly installments of the Tenant's Operating Expenses Allocable to the Premises next thereafter coming due (or refund such overpayment within thirty (30) days if the Term has expired and the Tenant has no further obligation to the Landlord).

Section 3.4 - Other Utility Charges.

During the Term, the Tenant shall pay directly to the provider of the service all separately metered charges for steam, heat, gas, electricity, fuel and other services and utilities furnished to the Premises, and shall pay to Landlord as Additional Rent its pro rata share of water, sewer and other services and utilities which shall be prorated to reflect Tenant's proportional usage based upon Tenant's proportional occupancy of the Building. Landlord acknowledges that all other tenant spaces in the Building are separately metered.

Section 3.5 - Above-standard Services.

If the Tenant requests and the Landlord elects to provide any services to the Tenant in addition to those described in Exhibit C, the Tenant shall pay to the Landlord, as Additional Rent, the amount billed by Landlord for such services at Landlord's standard rates as from time to time in effect. If the Tenant has requested that such services be provided on a regular basis, the Tenant shall, if requested by the Landlord, pay for such services at the time and in the fashion in which Annual Fixed Rent under this Lease is payable. Otherwise, the Tenant shall pay for such additional services within thirty (30) days after receipt of an invoice from the Landlord. Landlord shall have the right from time to time to inspect Tenant's utility meters and to install timers thereon at Tenant's expense for purposes of monitoring above-standard service usage. Tenant shall pay for such work within thirty (30) days after receipt of an invoice from Landlord.

Section 3.6 - No Offsets.

Annual Fixed Rent and Additional Rent shall be paid by the Tenant without offset, abatement or deduction except as provided herein.

Section 3.7 - Net Lease.

It is understood and agreed that this Lease is a net lease and that the Annual Fixed Rent is absolutely net to the Landlord excepting only the Landlord's obligations to pay any debt service or ground rent on the Property, to provide the Landlord's services, and to pay the real estate taxes and operating expenses which the Tenant is not required to pay under this Lease.

## ARTICLE IV
## ALTERATIONS

Section 4.1 - Consent Required for Tenant's Alterations.

The Tenant shall not make alterations or additions to the Premises except in accordance with (i) construction rules and regulations from time to time promulgated by Landlord and applicable to Tenants in the Building (a current copy of which is attached hereto as Exhibit F),

and (ii) plans and specifications therefor first approved by the Landlord, which approval shall not be unreasonably withheld, conditioned or delayed. In addition, Tenant may make non-structural alterations affecting only the interior of the Premises, and not affecting building systems, costing less than $50,000.00 in any one instance (or in the aggregate with respect to related alterations) without Landlord's prior written consent, but subject to the other terms of this Lease and provided that Tenant provides notice of such alterations within a reasonable time after the completion of the same. The Landlord shall not be deemed unreasonable for withholding approval of any alterations or additions which (i) will affect any structural or exterior element of the Building, any area or element outside of the Premises, or any facility serving any area of the Building outside of the Premises or any publicly accessible major interior features of the Building, (ii) will require significant expense to readapt the Premises to substantially the same condition of the Premises as of the date hereof unless the Tenant first gives assurance acceptable to the Landlord that such readaptation will be made prior to such termination without expense to the Landlord, or (iii) which would not be compatible with existing mechanical or electrical, plumbing, HVAC or other systems in the Building, in each case, as reasonably determined by the Landlord.

Section 4.2 - Ownership of Alterations.

All alterations and additions shall be part of the Building and owned by the Landlord. With respect to alterations and additions requiring prior notice to Landlord, if Tenant fails to inform Landlord (as and to the extent required under this Lease) at least ten (10) days prior to the installation of the alteration or addition, thereby preventing Landlord from making a determination as to whether it will want such addition or alteration removed from the Premises prior to its installation, then Landlord may require such removal without exception. All movable trade fixtures and furnishings not attached to the Premises shall remain the property of the Tenant and shall be removed by the Tenant upon termination or expiration of this Lease. The Tenant shall repair any damage caused by the removal of any alterations, additions or personal property from the Premises, including the Removable Equipment (as defined below). Landlord and Tenant agree that prior to the Expansion Premises Rent Commencement Date, Tenant shall provide a list to Landlord of equipment that Tenant has installed in the Premises, together with evidence indicating that such equipment was not purchased with the Leasehold Improvements Allowance (the "Removable Equipment"). Notwithstanding the foregoing provisions of this Section 4.2, Tenant shall be permitted to remove the Removable Equipment from the Premises at the end of the Term, provided that such Removable Equipment shall be removed by Tenant with reasonable care and diligence, including the capping off of all utility connections behind the adjacent interior finish, and the restoration of such interior finish to the extent necessary so that the Premises are left with complete wall, ceiling and floor finishes.

Section 4.3 - Construction Requirements for Alterations.

All construction work by the Tenant shall be done in a good and workmanlike manner employing only first-class materials and in compliance with Landlord's construction rules and regulations and with all applicable laws and all lawful ordinances, regulations and orders of Governmental authority and insurers of the Building. The Landlord or Landlord's authorized agent may (but without any implied obligation to do so) inspect the work of the Tenant at reasonable times with prior notice to Tenant and shall give notice of observed defects. All of the

Tenant's alterations and additions and installation of furnishings shall be coordinated with any work being performed by the Landlord and in such manner as to maintain harmonious labor relations and not to damage the Building or interfere with Building construction or operation and, except for installation of furnishings, shall be performed by contractors or workmen first approved by the Landlord, which approval the Landlord agrees not to unreasonably withhold, condition or delay (Landlord shall provide its written consent or written notice of its reason for withholding consent within ten (10) days of any request for consent from Tenant). The Tenant, before starting any work, shall receive and comply with Landlord's construction rules and regulations applicable to all tenants in the Building and shall cause Tenant's contractors to comply therewith, shall secure all licenses and permits necessary therefor and shall deliver to the Landlord a statement of the names of all its contractors and subcontractors performing work with a value in excess of $50,000 and the estimated cost of all labor and material to be furnished by them and security satisfactory to the Landlord protecting the Landlord against liens arising out of the furnishing of such labor and material; and cause each contractor engaged to perform work to carry worker's compensation insurance in statutory amounts covering all the contractors' and subcontractors' employees and comprehensive general public liability insurance with limits of $1,000,000 (individual)/$3,000,000 (occurrence), or in such lesser amounts as Landlord may accept, covering personal injury and death and property damage (all such insurance to be written in companies approved reasonably by the Landlord and insuring the Landlord, such individuals and entities affiliated with the Landlord as the Landlord may designate, and the Tenant as well as the contractors and to contain a requirement for at least thirty (30) days' notice to the Landlord prior to cancellation, nonrenewal or material change), and to deliver to the Landlord certificates of all such insurance.

Section 4.4 - Payment for Tenant Alterations.

Except as otherwise set forth herein, Tenant agrees to pay promptly when due the entire cost of any work done on the Premises by the Tenant, its agents, employees or independent contractors, and not to cause or permit any liens for labor or materials performed or furnished in connection therewith to attach to the Premises or the Property and promptly to discharge any such liens which may so attach. If any such lien shall be filed against the Premises or the Property and the Tenant shall fail to cause such lien to be discharged within ten (10) business days after the filing thereof, the Landlord may cause such lien to be discharged by payment, bond or otherwise without investigation as to the validity thereof or as to any offsets or defenses which the Tenant may have with respect to the amount claimed. The Tenant shall reimburse the Landlord, as Additional Rent, for any cost so incurred and shall indemnify and hold harmless the Landlord from and against any and all claims, costs, damages, liabilities and expenses (including reasonable attorneys' fees) which may be incurred or suffered by the Landlord by reason of any such lien or its discharge.

Section 4.5 - Leasehold Improvements Allowance and Space Plan Allowance.

In connection with Tenant's execution of this Lease, Tenant shall perform certain improvements to the Premises, as mutually agreed upon by Landlord and Tenant (the "Improvements"). Tenant acknowledges and agrees that the Improvements shall include (but shall not be limited to) the creation of laboratory and potentially vivarium space with supporting office space in the Expansion Premises. Landlord shall provide to Tenant the Leasehold

Improvements Allowance set forth in Exhibit A, which shall be paid and used in accordance with the provisions of the Work Letter attached to this Lease as Exhibit E. In addition, Landlord shall provide Tenant with an allowance to be used toward the costs of preparation of its space plan, in an amount equal to $0.10 per rentable square foot of the Premises.

## ARTICLE V

## RESPONSIBILITY FOR CONDITION OF BUILDING AND PREMISES

Section 5.1 - Maintenance of Building and Common Areas by Landlord.

Except as otherwise provided in Article VIII, the Landlord shall make such repairs to the major structural elements of the Building, including the roof, exterior walls and floor slabs as may be necessary to keep and maintain the same in good condition and maintain and make such repairs to the Common Building Areas as may be necessary to keep them in good order, condition and repair, including without limitation, the glass in the exterior walls of the Building, and all mechanical systems and equipment serving the Building and not exclusively serving the Premises. The Landlord shall further perform the services on Exhibit C hereto. The Landlord shall in no event be responsible to the Tenant for any condition in the Premises or the Building caused by an act or neglect of the Tenant, or any invitee or contractor of the Tenant. Landlord's costs in performing such services shall be reimbursed by the Tenant to the extent provided in Section 3.3. Except as specifically set forth herein, Tenant accepts the Premises in its as-is condition. Landlord acknowledges that (i) an emergency generator is available in the Building for the Tenant, and (ii) Landlord possesses all licenses and permits required of Landlord so that Tenant may obtain its required licenses and permits to store and use on the Premises the flammable materials used by the Tenant to conduct its business and operations.

Section 5.2 - Maintenance of Premises by Tenant.

The Tenant shall keep neat and clean and maintain in good order, condition and repair the Premises and every part thereof and all Building and mechanical equipment exclusively serving the Premises, reasonable wear and tear excepted and further excepting those repairs for which the Landlord is responsible pursuant to Section 5.1 and damage by fire or other casualty and as a consequence of the exercise of the power of eminent domain, and shall surrender the Premises and all alterations and additions thereto, at the end of the Term, in such condition, first removing all goods and effects of the Tenant and, to the extent specified by the Landlord by notice to the Tenant, all alterations and additions made by the Tenant, which Tenant has not elected to retain in accordance with the terms of Sections 4.2 and 5.2, and repairing any damage caused by such removal and restoring the Premises and leaving them clean and neat. The Tenant shall not permit or commit any waste, and the Tenant shall be responsible for the cost of repairs which may be made necessary by reason of damages to common areas in the Building by the Tenant, or any of the contractors or invitees of the Tenant. Mechanical, HVAC, and all laboratory systems and equipment shall be maintained in good order, condition and repair. Tenant shall, upon request, provide evidence reasonably satisfactory to Landlord that it has available the necessary expertise to properly conduct and carry out this responsibility, either through persons employed by the Tenant or through contracts with independent service organizations, or a combination thereof. All charges incurred by Landlord in connection with such work, whether by independent organizations or in accordance with reasonable rates assigned to employees of Landlord or Landlord's affiliates, shall be promptly reimbursed by Tenant as Additional Rent.

Section 5.3 - Delays in Landlord's Services.

The Landlord shall not be liable to the Tenant for any compensation or reduction of rent by reason of inconvenience or annoyance or for loss of business arising from the necessity of the Landlord or its agents entering the Premises for any purposes authorized in this Lease, or for repairing the Premises or any portion of the Building. In case the Landlord is prevented or delayed from making any repairs, alterations or improvements, or furnishing any services or performing any other covenant or duty to be performed on the Landlord's part, by reason of any External Cause, the Landlord shall not be liable to the Tenant therefor, nor, except as expressly otherwise provided in this Lease, shall the Tenant be entitled to any abatement or reduction of rent by reason thereof, nor shall the same give rise to a claim in the Tenant's favor that such failure constitutes actual or constructive, total or partial, eviction from the Premises.

The Landlord reserves the right to stop any service or utility system when necessary by reason of accident or emergency, until necessary repairs have been completed; provided, however, that in each instance of stoppage, the Landlord shall exercise reasonable diligence to eliminate the cause thereof. Except in case of emergency repairs, the Landlord will give the Tenant reasonable advance written notice of any contemplated stoppage and will use reasonable efforts to avoid unnecessary inconvenience to the Tenant by reason thereof. In no event shall the Landlord have any liability to the Tenant for the unavailability of heat, light or any utility or service to be provided by the Landlord to the extent that such unavailability is caused by External Causes, provided, however, that the Landlord is obligated to exercise reasonable efforts to restore such services or utility systems' operation as soon as possible.

Notwithstanding anything contained herein to the contrary, in the event Landlord shall fail to provide the services it is required to provide to Tenant hereunder for any reason other than due to Tenant's acts or omissions, and as a result thereof, Tenant is reasonably unable to use or conduct its operations on part or all of the Premises, Tenant shall be entitled to (i) proportionate abatement of rent (including but not limited to abatement of Tenant's Tax Expenses and Tenant's Operating Expenses) for the period Tenant is reasonably unable to use or conduct its operations on part or all of the Premises, or (ii) terminate this Lease if Landlord is unable to restore such services within three (3) months from the date of interruption. Tenant shall have the right to terminate this Lease as aforesaid by written notice to Landlord at any time after the expiration of such three (3) month period, and such termination shall be effective as of the date of the interruption in service. To the extent any such unavailability is caused primarily by the action or inaction of Landlord, it's servants, agents, employees, contractors, licensees, invitees or any persons claiming by, through or under Landlord, and (i) Landlord fails to commence commercially reasonable corrective action within ten (10) days after Tenant notifies Landlord of such unavailability, or (ii) Landlord, upon commencing commercially reasonable corrective action within ten (10) days after Tenant notifies Landlord of such unavailability, fails to restore the services within thirty (30) days after Tenant notifies Landlord of such unavailability, Tenant shall have the right to restore such service at Landlord's cost and expense.

ARTICLE VI

TENANT COVENANTS

The Tenant covenants during the Term and for such further time as the Tenant occupies any part of the Premises:

Section 6.1 - Permitted Uses.

The Tenant shall occupy the Premises only for the Permitted Uses, which include, but are not limited to, general business and administrative offices, biotechnology research and development, animal experimentation and related activities thereto. The Tenant shall not injure or deface the Premises or the Property, nor permit in the Premises any auction sale. The Tenant shall give written notice to the Landlord of any materials on OSHA's right to know list or which are subject to regulation by any other federal, state, municipal or other governmental authority and which the Tenant intends to have present at the Premises. The Tenant shall comply with all requirements of pubic authorities and of the Board of Fire Underwriters in connection with methods of storage, use and disposal thereof. The Tenant shall not permit in the Premises any nuisance, or the emission from the Premises of any objectionable noise, odor or vibration, nor use or devote the Premises or any part thereof for any purpose which is contrary to law or ordinance or liable to invalidate or increase premiums for any insurance on the Building or its contents or liable to render necessary any alteration or addition to the Building, nor commit or permit any waste in or with respect to the Premises, nor generate, store or dispose of any oil, toxic substances, hazardous wastes, or hazardous materials (each a, "Hazardous Material"), or permit the same in or on the Premises or any parking areas provided for under this Lease, unless first giving Landlord notice thereof. The Tenant shall not dump, flush or in any way introduce any Hazardous Materials into septic, sewage or other waste disposal systems serving the Premises or any parking areas provided for under this Lease, except as specifically permitted by government license or permit. The Tenant will, indemnify the Landlord and its successors and assigns against all claims, loss, cost, and expenses including attorneys' fees, incurred as a result of any contamination of the Building or any other portion of University Park with Hazardous Materials by the Tenant or Tenant's contractors, licensees, invitees, agents, servants or employees. Tenant shall provide to Landlord herewith certified copies of all licenses and permits Tenant has been required to obtain prior to handling any such Hazardous Materials. Tenant shall further provide to Landlord evidence satisfactory to Landlord from Tenant's consultant preparing any regulatory filings for licensing or permitting to handle Hazardous Materials setting forth in reasonable detail all licenses and/or permits that Tenant is required to obtain or will obtain prior to the Commencement Date and that such licenses and/or permits are valid and in full force and effect. Tenant shall have received all such licenses and/or permits prior to commencement of its operations in the Premises. From time to time hereafter upon thirty (30) days advance notice from Landlord, Tenant will provide Landlord with such updated provisions of Sections 6.1 and 6.2 as the Landlord may reasonably request. Upon request by the Landlord, Tenant shall immediately remove any material or substances which are not in compliance with this Section 6.1. The Landlord represents and warrants to the Tenant that, to the best of Landlord's knowledge, the Permitted Uses are in compliance with all current land use and zoning restrictions applicable to the Premises, subject to the terms and conditions thereof. Tenant shall have no liability for any environmental condition or violation of law that exists in

the Existing Premises as of the date of this Lease unless such liability is due to Tenant's act of omission, or within the Expansion Premises as of the date of the applicable Expansion Premises Term Commencement Date.

Section 6.2 - Laws and Regulations.

The Tenant shall comply with all federal, state and local laws, regulations, ordinances, executive orders, federal guidelines, and similar requirements in effect from time to time, including, without limitation, City of Cambridge ordinances numbered 1005, 1053, 1086 and any subsequently adopted ordinance for employment and animal experimentation with respect to animal experiments and hazardous waste and any such requirements pertaining to employment opportunity, anti-discrimination and affirmative action. Tenant shall have the right to contest any notice of violation for any of the foregoing by appropriate proceedings diligently conducted in good faith.

Section 6.3 - Rules and Regulations.

The Tenant shall not obstruct in any manner any portion of the Property not hereby leased; shall not permit the placing of any signs, curtains, blinds, shades, awnings, aerials or flagpoles, or the like, visible from outside the Premises; and shall comply with all reasonable rules and regulations of uniform application to all occupants of the Building now or hereafter made by the Landlord, of which the Tenant has been given notice, for the care and use of the Property and the parking facilities relating thereto. The Landlord shall not be liable to the Tenant for the failure of other occupants of the Building to conform to any such rules and regulations, however Landlord shall uniformly enforce the Rules and Regulations. The Landlord shall provide, at the Landlord's expense, a Building standard tenant name sign at the entryway to the Premises. Notwithstanding anything contained in this Lease (including all exhibits) to the contrary, Tenant shall have the right to install a sign or signs with its corporate logo at the entrance to the Premises on each level of the Building occupied, in part or in full, by Tenant, and shall have its name listed in the Building directory located in the Building's main lobby, subject to the prior approval of such sign by Landlord, which approval shall not be unreasonably withheld or delayed.

Section 6.4 - Safety Compliance.

The Tenant shall keep the Premises equipped with all safety appliances required by law or ordinance or any other regulations of any public authority because of any non-office use made by the Tenant and to procure all licenses and permits so required because of such use and, if requested by the Landlord, do any work so required because of such use, it being understood that the foregoing provisions shall not be construed to broaden in any way the Tenant's Permitted Uses. Tenant shall conduct such periodic tests, evaluations or certifications of safety appliances and laboratory equipment as are required or recommended in accordance with generally accepted standards for good laboratory practice to ensure that such safety appliances and equipment remain in good working order, and shall provide to Landlord copies of such reports, evaluations and certifications as they are periodically obtained by Tenant or upon ten (10) days advance notice from Landlord (but only to the extent that Tenant has failed to previously provide any such reports). Landlord represents and warrants that the Premises are in compliance with applicable laws.

Section 6.5 - Landlord's Entry.

The Tenant shall permit the Landlord and its agents (which agents shall be identified to Tenant and reasonably approved by Tenant for entry), after 48 hours prior notice and at times reasonably acceptable to Tenant, except in the case of emergencies, to enter the Premises at all reasonable hours for the purpose of inspecting or of making repairs to the same, monitoring Tenant's compliance with the requirements and restrictions set forth in this Lease, and for the purpose of showing the Premises to prospective purchasers and mortgagees at all reasonable times and to prospective tenants (during the last nine (9) months of the Term or after notice of termination by the Tenant has been received by Landlord) provided that in connection with such entry, Tenant may provide procedures reasonably designed so as not to jeopardize Tenant's trade secrets, proprietary technology or critical business operations.

Section 6.6 - Floor Load.

The Tenant shall not place a load upon any floor in the Premises exceeding the floor load per square foot of area which such floor was designed to carry and which is allowed by law. Further, Tenant shall not move any safe, vault or other heavy equipment in, about or out of the Premises except in such manner and at such time as the Landlord shall in each instance authorize. The Tenant's machines and mechanical equipment shall be placed and maintained by the Tenant at the Tenant's expense in settings sufficient to absorb or prevent vibration or noise that may be transmitted to the Building structure or to any other space in the Building.

Section 6.7 - Personal Property Tax.

The Tenant shall pay promptly when due all taxes which may be imposed upon personal property (including, without limitation, fixtures and equipment) in the Premises to whomever assessed. Tenant shall have the right to contest the validity or amount of any such taxes by appropriate proceedings diligently conducted in good faith.

Section 6.8 - Assignment and Subleases.

The Tenant shall hot assign, mortgage, pledge, hypothecate or otherwise transfer this Lease, or sublet (which term, without limitation, shall include granting of concessions, licenses and the like) the whole or any part of the Premises without, in each instance, having first received the consent of the Landlord which consent shall not be unreasonably withheld, conditioned or delayed. Except as specifically permitted herein, any assignment or sublease made without such consent shall be void. The Landlord shall not be deemed to be unreasonable in withholding its consent to any proposed assignment or subletting by the Tenant based on any of the following factors:

(a) The business of the proposed occupant is not consistent with the image and character which the Landlord desires to promote for the Building,

(b) The proposed assignment, mortgage or pledge would in any way materially diminish Landlord's rights with respect to the Premises.

(c) The proposed occupant is not sufficiently creditworthy in the reasonable opinion of Landlord based on a comparison of the creditworthiness of other similarly-situated companies in the same industry as the proposed occupant.

Notwithstanding anything to the contrary contained in this Section, Tenant shall have the right to assign or otherwise transfer this Lease or the Premises, or part of the Premises, without obtaining the prior consent of Landlord, (a) to its parent corporation, to a wholly owned subsidiary, to a corporation which is wholly owned by the same corporation which wholly owns Tenant, to an entity directly or indirectly controlling, controlled by or under common control with Tenant, any entity owning or controlling fifty percent (50%) or more of the outstanding voting interest of Tenant, or any entity of which Tenant owns or controls fifty percent (50%) or more of the voting interests, provided that (i) the transferee shall, prior to the effective date of the transfer, deliver to Landlord instruments evidencing such transfer and its agreement to assume and be bound by all the terms, conditions and covenants of this Lease to be performed by Tenant, all in form reasonably acceptable to Landlord, and (ii) at the time of such transfer there shall not be an uncured Event of Default under this Lease; or (b) to the purchaser of all or substantially all of its assets, any entity resulting from the merger or consolidation of Tenant, any successor entity resulting from a bona fide reorganization or Tenant, or to any entity into which the Tenant may be merged or consolidated (along with all or substantially all of its assets) (the "Acquiring Company"), provided that (i) the net assets of the Acquiring Company at the time of the transfer or merger shall not be less than $25,000,000.00, (ii) the Acquiring Company continues to operate the business conducted in the Premises consistent with the Permitted Uses described in Exhibit A hereto, (iii) the Acquiring Company shall assume in Writing, in form reasonably acceptable to Landlord, all of Tenant's obligations under this Lease, (iv) Tenant shall provide to Landlord such additional information regarding the Acquiring Company as Landlord shall reasonably request, and (v) Tenant shall pay Landlord's reasonable expenses incurred in connection therewith (up to a maximum amount of $5,000,00). Unless Landlord shall have objected to such assignment or transfer by Tenant within ten (10) business days following Landlord's receipt of the information or items described in (b)(i) and (iii) above, Landlord shall be deemed to have waived its right to object thereto. The transfers described in this paragraph are referred to hereinafter as "Permitted Transfers." Notwithstanding any other provision of this Lease, any public offering of shares or other ownership interest in Tenant or any private equity financing of Tenant by one or more investors who regularly invest in private companies shall not be deemed an assignment and shall not be subject to Landlord approval.

Whether or not the Landlord consents, or is required to consent, to any assignment or subletting, the Tenant named herein (to the extent that the Tenant continues to exist as a distinct entity separate and apart from the entity to which the Lease is assigned) shall remain fully and primarily liable for the obligations of the tenant hereunder, including, without limitation, the obligation to pay Annual Fixed Rent and Additional Rent provided under this Lease.

The Tenant shall give the Landlord notice of any proposed sublease or assignment, whether or not the Landlord's consent is required hereunder, specifying the provisions of the

proposed subletting or assignment, including (i) the name and address of the proposed subtenant or assignee, (ii) a copy of the proposed subtenant's or assignee's most recent annual financial statement, (iii) all of the terms and provisions upon which the proposed subletting or assignment is to be made. The Tenant shall reimburse the Landlord promptly for reasonable legal and other expenses incurred by the Landlord in connection with any request by the Tenant for consent to any assignment or subletting, in the aggregate amount of up to $5,000.00. If this Lease is assigned, or if the Premises or any part thereof is sublet or occupied by anyone other than the Tenant, the Landlord may, at any time during the continuance of an Event of Default hereunder without cure, collect rent and other charges from the assignee, sublessee or occupant and apply the net amount collected to the rent and other charges herein reserved, but no such assignment, subletting, occupancy or collection shall be deemed a waiver of the prohibitions contained in this Section 6.8 or the acceptance of the assignee, sublessee or occupant as a tenant, or a release of the Tenant from the further performance by the Tenant of covenants on the part of the Tenant herein contained. After deducting reasonable and ordinary sublease transaction expenses (including, without limitation, any broker's commission), unamortized tenant improvements paid by the Tenant and rent abatement, the Tenant shall pay to the Landlord fifty percent (50%) of any amounts the Tenant receives from any subtenant or assignee as rent, additional rent or other forms of compensation or reimbursement other than those which are less than or equal to the then due and payable proportionate monthly share of Annual Fixed Rent, Additional Rent and all other monies due to Landlord pursuant to this Lease (allocable in the case of a sublease to that portion of the Premises being subleased). The consent by the Landlord to an assignment or subletting shall not be construed to relieve the Tenant from obtaining the express consent in writing of the Landlord to any further assignment or subletting.

Landlord may elect, prior to approving or disapproving any proposed assignment or sublease of more than 50% of the entire Premises, to repossess the Premises, provided that such repossession shall not take effect (i) until twelve (12) months after the proposal by Tenant of an assignment of the entire Premises or (ii) until thirty (30) days after the proposal by Tenant of a proposed sublease of the entire Premises. Landlord may thereafter lease the Premises in such a manner as the Landlord may in its sole discretion determine. In the event Landlord elects to repossess the Premises as provided above, then all of the Tenant's rights and obligations hereunder with respect to the Premises shall cease and shall be of no further force and effect. The provisions of this paragraph shall not apply to Permitted Transfers.

## ARTICLE VII

## INDEMNITY AND INSURANCE

Section 7.1 - Indemnity.

(a) To the maximum extent this agreement may be made effective according to law, the Tenant shall defend the Landlord from and against all claims, proceedings, causes of actions and suits brought by third parties (collectively, "Claims") and shall indemnify and hold harmless the Landlord from and against any resultant costs and expenses (including but not limited to reasonable attorneys' fees), losses or liabilities which the Landlord may be required to pay to third parties to the extent the Claim arises from any breach by Tenant of any obligation of Tenant under this Lease or from any act, omission or negligence of the Tenant, or the Tenant's

contractors, licensees, invitees, agents, servants or employees, or arising from any accident, injury or damage whatsoever caused to any person or property, occurring after the date that possession of the Premises is first delivered to the Tenant and until the end of the Term and thereafter, so long as the Tenant is in occupancy of any part of the Premises, in or about the Premises or arising from any accident, injury or damage occurring outside the Premises but within the Building, on the Land, on the access roads and ways, in the parking facilities provided pursuant to the Lease, within University Park or any adjacent area maintained by Landlord or any individual or entity affiliated with Landlord, where such accident, injury or damage results, from an act or omission on the part of the Tenant or the Tenant's agents or employees, licensees, invitees, servants or contractors. Notwithstanding the foregoing, the Tenant's obligations under this Section 7.1 (a) shall not apply to the extent such Claims arise or result from a matter for which the Landlord is obligated to indemnify the Tenant as set forth in Section 7.1 (b).

(b) To the maximum extent this agreement may be made effective according to law, the Landlord shall defend the Tenant from and against all Claims and shall indemnify and hold harmless the Tenant from and against any resultant costs and expenses (including but not limited to reasonable attorneys' fees), losses or liabilities which the Tenant may be required to pay to third parties to the extent due toloss of life, bodily or personal injury or property damage, arising from or out of all acts, failures, omissions or negligence of Landlord, its agents, employees or contractors which occur in or about the Premises or arising from any accident, injury or damage occurring outside the Premises but within the Building, on the Land, on the access roads and ways, in the parking facilities provided pursuant to the Lease, within University Park or any adjacent area maintained by Landlord or any individual or entity affiliated with Landlord., Notwithstanding the foregoing, the Landlord's obligations under this Section 7. l(b) shall not apply to the extent such Claims arise or result from a matter for which the Tenant is obligated to indemnify Landlord as set forth in Section 7.1 (a).

Section 7.2 - Liability Insurance.

The Tenant agrees to maintain in full force from the date upon which the Tenant first enters the Premises for any reason, throughout the Term, and thereafter, so long as the Tenant is in occupancy of any part of the Premises, a policy of commercial general liability insurance under which the Landlord (and any individuals or entities affiliated with the Landlord, any ground lessor and any holder of a mortgage on the Property of whom the Tenant is notified by the Landlord) and the Tenant are named as additional insureds, and under which the insurer provides a contractual liability endorsement insuring against all cost, expense and liability arising out of or based upon any and all claims, accidents, injuries and damages described in Section 7.1, in the broadest form of such coverage from time to time available. Each such policy shall be noncancellable and nonamendable (to the extent that any proposed amendment reduces the limits or the scope of the insurance required in this Lease) with respect to the Landlord and such ground lessors and mortgagees without thirty (30) days' prior notice to the Landlord and such ground lessors and mortgagees and at the election of the Landlord, either a certificate of insurance or a duplicate original policy shall be delivered to the Landlord. The minimum limits of liability of such insurance as of the Commencement Date shall be Five Million Dollars ($5,000,000.00) in the aggregate for combined bodily injury (or death) and damage to property ($3,000,000.00 per occurrence), and from time to time during the Term such limits of liability shall be increased to reflect such higher limits as are customarily required pursuant to new leases of space in the Boston-Cambridge area with respect to similar properties.

Section 7.3 - Personal Property at Risk.

The Tenant agrees that all of the furnishings, fixtures, equipment, effects and property of every kind, nature and description of the Tenant and of all persons claiming by, through or under the Tenant which, during the continuance of this Lease or any occupancy of the Premises by the Tenant or anyone claiming under the Tenant which, during the continuance of this Lease or any occupancy of the Premises by the Tenant or anyone claiming under the Tenant, may be on the Premises or elsewhere in the Building or on the Lot or parking facilities provided hereby, shall be at the sole risk and hazard of the Tenant, and if the whole or any part thereof shall be destroyed or damaged by fire, water or otherwise, or by the leakage or bursting of water pipes, steam pipes, or other pipes, by theft or from any other cause, no part of said loss or damage is to be charged to or be borne by the Landlord, except that the Landlord shall in no event be exonerated from any liability to the Tenant or to any person, for any injury, loss, damage or liability to the extent caused by Landlord's, its agents, employees, licensees, invitees, servants or contractors gross negligence or willful misconduct.

Section 7.4 - Landlord's Insurance.

The Landlord shall carry such casualty and liability insurance upon and with respect to operations at the Building, as may from time to time be deemed reasonably prudent by the Landlord or required by any mortgagee holding a mortgage thereon or any ground lessor of the Land, and in any event, insurance against loss by fire and the risks now covered by extended coverage endorsement No. 4 in an amount equal to the replacement value of the Building, exclusive of foundations, site preparation and other nonrecurring construction costs.

Section 7.5 - Waiver of Subrogation.

Any insurance carried by either party with respect to the Building, Land, Premises, parking facilities or any property therein or occurrences thereon shall, without further request by either party, if it can be so written without additional premium, or with an additional premium which the other party elects to pay, include a clause or endorsement denying to the insurer rights of subrogation against the other party to the extent rights have been waived by the insured prior to occurrence of injury or loss. Each party, notwithstanding any provisions of this Lease to the contrary, hereby waives any rights of recovery against the other for injury or loss, including, without limitation, injury or loss caused by negligence of such other party, due to hazards covered by insurance containing such clause or endorsement to the extent of the indemnification received thereunder.

## ARTICLE VIII

## CASUALTY AND EMINENT DOMAIN

Section 8.l - Restoration Following Casualties.

If, during the Term, the Building or Premises shall be damaged by fire or casualty, subject to the exceptions and limitations provided below, the Landlord shall proceed promptly to exercise reasonable efforts to restore the Building or Premises to substantially the condition thereof at the time of such damage, but the Landlord shall not be responsible for delay in such restoration which may result from any External Cause. The Landlord shall have no obligation to expend in the reconstruction of the Building more than the actual amount of the insurance proceeds made available to the Landlord by its insurer and not retained by the Landlord's mortgagee or ground lessor. Any restoration of the Building or the Premises shall be altered to the extent necessary to comply with then current laws and applicable codes.

Section 8.2 - Landlord's Termination Election.

If the Landlord reasonably determines that the amount of insurance proceeds available to the Landlord is insufficient to cover the cost of restoring the Building or if in the reasonable opinion of the Landlord the Building has been so damaged that it is appropriate for the Landlord to raze or substantially alter the Building, then the Landlord may terminate this Lease by giving notice to the Tenant within sixty (60) days after the date of the casualty or such later date as is required to allow the Landlord a reasonable time to make either such determination. Any such termination shall be effective on the date designated in such notice from the Landlord, but in any event, not later than sixty (60) days after such notice, and if no date is specified, effective upon the date of the Casualty or Taking.

Section 8.3 Tenant's Termination Election.

Unless the Landlord has earlier advised the Tenant of the Landlord's election to terminate this Lease pursuant to Section 8.2, or to restore the Premises and maintain this Lease in effect pursuant to Section 8.1, the Tenant shall have the right after the expiration of ninety (90) days after any casualty which materially impairs a material portion of the Premises to give a written notice to the Landlord requiring the Landlord within ten (10) days thereafter to exercise or waive any right of the Landlord to terminate this Lease pursuant to Section 8.2 as a result of such casualty and if the Landlord fails to give timely notice to the Tenant waiving any right under Section 8.2 to terminate this Lease based on such casualty, the Tenant shall be entitled, at any time until the Landlord has given notice to the Tenant waiving such termination right, to give notice to the Landlord terminating this Lease. Where the Landlord is obligated to exercise reasonable efforts to restore the Premises, unless such restoration is completed within nine (9) months from the date of the casualty or taking, such period to be subject, however, to extension where the delay in completion of such work is due to External Causes (but in no event beyond nine (9) months from the date of the casualty or taking), the Tenant shall have the right to terminate this Lease at any time after the expiration of such nine-month (as extended) period until the restoration is substantially completed, such termination to take effect as of the date of the Casualty or Taking.

Section 8.4 - Casualty at Expiration of Lease.

If the Premises shall be damaged by fire or casualty in such a manner that the Premises cannot, in the ordinary course, reasonably be expected to be repaired within one hundred and twenty (120) days from the commencement of repair work and such damage occurs within the last eighteen (18) months of the Term (as the same may have been extended prior to such fire or casualty), either party shall have the right, by giving notice to the other not later than sixty (60) days after such damage, to terminate this Lease, whereupon this Lease shall terminate as of the date of such Casualty.

Section 8.5 - Eminent Domain.

Except as hereinafter provided, if the Premises, or such portion thereof as to render the balance (if reconstructed to the maximum extent practicable in the circumstances) unsuitable for the Tenant's purposes, shall be taken by condemnation or right of eminent domain, the Landlord or the Tenant shall have the right to terminate this Lease by notice to the other of its desire to do so, provided that such notice is given not later than thirty (30) days after the effective date of such taking. If so much of the Building shall be so taken that the Landlord determines that it would be appropriate to raze or substantially alter the Building, the Landlord shall have the right to terminate this Lease by giving notice to the Tenant of the Landlord's desire to do so not later than thirty (30) days after the effective date of such taking.

Should any part of the Premises be so taken or condemned during the Term, and should this Lease be not terminated in accordance with the foregoing provisions, the Landlord agrees to use reasonable efforts to put what may remain of the Premises into proper condition for use and occupation as nearly like the condition of the Premises prior to such taking as shall be practicable, subject, however, to applicable laws and codes then in existence and to the availability of sufficient proceeds from the eminent domain taking not retained by any mortgagee or ground lessor.

Section 8.6 - Rent After Casualty or Taking.

If the Premises shall be damaged by fire or other casualty, except as provided below, the Annual Fixed Rent and Additional Rent shall be justly and equitably abated and reduced according to the nature and extent of the loss of use thereof suffered by the Tenant, from and after the date of the Casualty or Taking until the Premises shall be restored to substantially the same condition as immediately prior to such Casualty or Taking. In the event of a taking which permanently reduces the area of the Premises, a just proportion of the Annual Fixed Rent shall be abated for the remainder of the Term.

Section 8.7 - Taking Award.

Except as otherwise provided in Section 8.7, the Landlord shall have and hereby reserves and accepts, and the Tenant hereby grants and assigns to the Landlord, all rights to recover for damages to the Building and the Land, and the leasehold interest hereby created, and to compensation accrued or hereafter to accrue by reason of such taking, damage or destruction, as aforesaid, and by way of confirming the foregoing, the Tenant hereby grants and assigns to the Landlord, all rights to such damages or compensation. Nothing contained herein shall be

construed to prevent the Tenant from prosecuting in any condemnation proceedings a claim for relocation expenses, provided that such action shall not affect the amount of compensation otherwise recoverable by the Landlord from the taking authority pursuant to the preceding sentence.

## ARTICLE IX

## DEFAULT

Section 9.1 Tenant's Default.

Each of the following shall constitute an Event of Default:

(a) Failure on the part of the Tenant to pay the Annual Fixed Rent, Additional Rent or other charges for which provision is made herein on or before the date on which the same become due and payable, if such condition continues for five (5) business days after written notice that the same are due; provided, however if Tenant shall fail to pay any of the foregoing (after receipt by Tenant of written notice from Landlord) when due two (2) times in any period of twelve (12) consecutive months, then Landlord shall not be required to give notice to Tenant of any future failure to pay during the remainder of the Term and any extension thereof, and such failure shall thereafter constitute an Event of Default if not cured within five (5) business days after the same are due.

(b) Failure on the part of the Tenant to perform or observe any other term or condition contained in this Lease if the Tenant shall not cure such failure within thirty (30) days after written notice from the Landlord to the Tenant thereof, provided that in the case of breaches of obligations under this Lease which are susceptible to cure but cannot be cured within thirty (30) days through the exercise of due diligence, so long as the Tenant commences such cure within thirty (30) days, such breach remains susceptible to cure, and the Tenant diligently pursues such cure, such breach shall not be deemed to create an Event of Default.

(c) The taking of the estate hereby created on execution or by other process of law; or a judicial declaration that the Tenant is bankrupt or insolvent according to law; or any assignment of the property of the Tenant for the benefit of creditors; or the appointment of a receiver, guardian, conservator, trustee in bankruptcy or other similar officer to take charge of all or any substantial part of the Tenant's property by a court of competent jurisdiction; or the filing of an involuntary petition against the Tenant under any provisions of the bankruptcy act now or hereafter enacted if the same is not dismissed within ninety (90) days; the filing by the Tenant of any voluntary petition for relief under provisions of any bankruptcy law now or hereafter enacted.

If an Event of Default shall occur and be continuing without cure, then, in any such case, whether or not the Term shall have begun, the Landlord lawfully may, immediately or at any

time thereafter, give written notice to the Tenant specifying the Event of Default and this Lease shall come to an end on the date specified therein as fully and completely as if such date were the date herein originally fixed for the expiration of the Lease Term, and the Tenant will then quit and surrender the Premises to the Landlord, but the Tenant shall remain liable as hereinafter provided.

Section 9.2 - Damages.

In the event that this Lease is terminated, the Tenant covenants to pay to the Landlord forthwith on the Landlord's demand, as compensation, an amount (the Lump Sum Payment) equal to the excess, if any, of the discounted present value of the total rent reserved for the remainder of the Term over the then discounted present fair rental value of the Premises for the remainder of the Term. In calculating the rent reserved, there shall be included, in addition to the Annual Fixed Rent and all Additional Rent, the value of all other considerations agreed to be paid or performed by the Tenant over the remainder of the Term. In calculating the amounts to be paid by the Tenant under the foregoing covenant, the Tenant shall be credited with the net proceeds of any rent obtained by reletting the Premises, after deducting all the Landlord's expenses in connection with such reletting, including, without limitation, all repossession costs, brokerage commissions, fees for legal services and expenses of preparing the Premises for such reletting and Landlord shall use commercially reasonable efforts to relet the Premises. The Landlord shall use commercially reasonable efforts to relet the Premises, or any part or parts thereof, for a term or terms which may, at the Landlord's option, exceed or be equal to or less than the period which would otherwise have constituted the balance of the Term, and may grant such concessions and free rent as the Landlord in its reasonable commercial judgment considers advisable or necessary to relet the same and shall make such alterations, repairs and improvements in the Premises as the Landlord in its reasonable commercial judgment considers advisable or necessary to relet the same. No action of the Landlord in accordance with foregoing or failure to relet or to collect rent under reletting shall operate to release or reduce the Tenant's liability except as provided herein. The Landlord shall be entitled to seek to rent other properties of the Landlord prior to reletting the Premises.

Section 9.3 - Cumulative Rights.

The specific remedies to which the Landlord may resort under the terms of this Lease are cumulative and are not intended to be exclusive of any other remedies or means of redress to which it may be lawfully entitled in case of any breach or threatened breach by the Tenant of any provisions of this Lease. In addition to the other remedies provided in this Lease, the Landlord shall be entitled to the restraint by injunction of the violation or attempted or threatened violation of any of the covenants, conditions or provisions of this Lease or to a decree compelling specific performance of any such covenants, conditions or provisions. Nothing contained in this Lease shall limit or prejudice the right of the Landlord to prove for and obtain in proceedings for bankruptcy, insolvency or like proceedings by reason of the termination of this Lease, an amount equal to the maximum allowed by any statute or rule of law in effect at the time when, and governing the proceedings in which, the damages are to be proved, whether or not the amount be greater, equal to, or less than the amount of the loss or damages referred to above.

Section 9.4 - Landlord's Self-help.

If the Tenant shall at any time default in the performance of any obligation under this Lease, the Landlord shall have the right, but not the obligation, after any applicable cure period and upon reasonable, but in no event more than ten (10) days', notice to the Tenant (except in case of emergency in which case no notice need be given), to perform such obligation. The Landlord may exercise its rights under this Section without waiving any other of its rights or releasing the Tenant from any of its obligations under this Lease.

Section 9.5 - Enforcement Expenses; Litigation.

In the event that either party prevails in litigation commenced to enforce any right or obligation hereunder, such party shall be entitled to recover from the other party all reasonable costs and expenses incurred by such party in connection with the litigation.

If either party hereto be made or becomes a party to any litigation commenced by or against the other party by or against a third party, or incurs costs or expenses related to such litigation, involving any part of the Property and the enforcement of any of the rights, obligations or remedies of such party, then the party becoming involved in any such litigation because of a claim against such other party hereto shall receive from such other party hereto all costs and reasonable attorneys' fees incurred by such party in such litigation.

Section 9.6 - Interest on Overdue Payments.

Any Annual Fixed Rent and Additional Rent not paid within any applicable grace period shall bear interest from the date due to the Landlord until paid at the variable rate (the "Default Interest Rate") equal to the higher of (i) the rate at which interest accrues on amounts not paid when due under the terms of the Landlord's financing for the Building, as from time to time in effect, and (ii) one and one-half percent (1.5%) per month.

Section 9.7 - Landlord's Right to Notice and Cure.

The Landlord shall in no event be in default in the performance of any of the Landlord's obligations hereunder unless and until the Landlord shall have failed to perform such obligations within thirty (30) days after notice by the Tenant to the Landlord expressly specifying wherein the Landlord has failed to perform any such obligation, provided that in the case of breaches of obligations under this Lease which are susceptible to cure but cannot be cured within thirty (30) days through the exercise of due diligence, so long as the Landlord commences such cure within thirty (30) days, such breach remains susceptible to cure, and the Landlord diligently pursues such cure, such breach shall not be deemed an event of default, under this Agreement. In the event of a breach or default of this Agreement by the Landlord, Tenant shall be afforded any and all rights and remedies afforded at law or in equity.

ARTICLE X

MORTGAGEES' AND GROUND LESSORS' RIGHTS

Section 10.1 - Subordination.

This Lease shall, at the election of the holder of any mortgage or ground lease on the Property, be subject and subordinate to any and all mortgages or ground leases on the Property, so that the lien of any such mortgage or ground lease shall be superior to all rights hereby or hereafter vested in the Tenant. Notwithstanding the foregoing, Tenant's rights under this Lease and use and enjoyment of the Premises shall not be disturbed by any such mortgagee or ground lessor so long as there is no uncured Event of Default, and Tenant shall be entitled to receive executed agreements from same to such effect.

Section 10.2 - Prepayment of Rent not to Bind Mortgagee.

No Annual Fixed Rent, Additional Rent, or any other charge payable to the Landlord shall be paid more than thirty (30) days prior to the due date thereof under the terms of this Lease and payments made in violation of this provision shall (except to the extent that such payments are actually received by a mortgagee or ground lessor) be a nullity as against such mortgagee or ground lessor and the Tenant shall be liable for the amount of such payments to such mortgagee or ground lessor.

Section 10.3 - Tenant's Duty to Notify Mortgagee; Mortgagee's Ability to Cure.

No act or failure to act on the part of the Landlord which would entitle the Tenant under the terms of this Lease, or by law, to be relieved of the Tenant's obligations to pay Annual Fixed Rent or Additional Rent hereunder or to terminate this Lease, shall result in a release or termination of such obligations of the Tenant or a termination of this Lease unless (i) the Tenant shall have first given written notice of the Landlord's act or failure to act to the Landlord's mortgagees or ground lessors of record, if any of whose identity and address the Tenant shall have been given notice, specifying the act or failure to act on the part of the Landlord which would give basis to the Tenant's rights; and (ii) such mortgagees or ground lessors, after receipt of such notice, have failed or refused to correct or cure the condition complained of within a reasonable time thereafter, which shall include a reasonable time for such mortgagee or ground lessors, but in no event more than thirty (30) days after receipt of such notice, to obtain possession of the Property if possession is necessary for the mortgagee or ground lessor to correct or cure the condition and if the mortgagee or ground lessor notifies the Tenant of its intention to take possession of the Property and correct or cure such condition.

Section 10.4 - Estoppel Certificates.

The Tenant shall from time to time, upon not less than fifteen (15) days' prior written request by the Landlord, execute, acknowledge and deliver to the Landlord a statement in writing certifying to the Landlord or an independent third party, with a true and correct copy of this Lease attached thereto, to the extent such statements continue to be true and accurate, (i) that this Lease is unmodified and in full force and effect (or, if there have been any modifications, that the same is in full force and effect as modified and stating the modifications); (ii) that the Tenant has

no knowledge of any defenses, offsets or counterclaims against its obligations to pay the Annual Fixed Rent and Additional Rent and to perform its other covenants under this Lease (or if there are any defenses, offsets, or counterclaims, setting them forth in reasonable detail); (iii) that there are no known uncured defaults of the Landlord or the Tenant under this Lease (or if there are known defaults, setting them forth in reasonable detail); (iv) the dates to which the Annual Fixed Rent, Additional Rent and other charges have been paid; (v) that the Tenant has accepted, is satisfied with, and is in full possession of the Premises, including all improvements, additions and alterations thereto required to be made by Landlord under the Lease; (vi) that the Landlord has satisfactorily complied with all of the requirements and conditions precedent to the commencement of the Term of the Lease as specified in the Lease; (vii) that the Tenant has been in occupancy since the Commencement Date and paying rent since the specified dates; (viii) that no monetary or other considerations, including, but not limited to, rental concessions for Landlord, special tenant improvements or Landlord's assumption of prior lease obligations of Tenant have been granted to Tenant by Landlord for entering into Lease, except as specified; (ix) that Tenant has no notice of a prior assignment, hypothecation, or pledge of rents or of the Lease; (x) that the Lease represents the entire agreement between Landlord and Tenant; (xi) that no prepayment or reduction of rent and no modification, termination or acceptance of Lease will be valid as to the party to whom such certificate is addressed without the consent of such party; (xii) that any notice to Tenant may be given it in accordance with Section 12.2 hereof; and (xiii) such other matters with respect to the Tenant and this Lease as the Landlord may reasonably request. On the Commencement Date, the Tenant shall, at the request of the Landlord, promptly execute, acknowledge and deliver to the Landlord a statement in writing that the Commencement Date has occurred, that the Annual Fixed Rent has begun to accrue and that the Tenant has taken occupancy of the Premises. Any statement delivered pursuant to this Section may be relied upon by any prospective purchaser, mortgagee or ground lessor of the Premises and shall be binding on the Tenant.

Landlord shall from time to time, upon not less than fifteen (15) days' prior written request by the Tenant, execute, acknowledge and deliver to the Tenant a statement in writing certifying to the Tenant or an independent third party, with a true and correct copy of this Lease attached thereto, to the extent such statements continue to be true and accurate (i) that this Lease is unmodified and in full force and effect (or, if there have been any modifications, that the same is in full force and effect as modified and stating the modifications); (ii) that the Landlord has no knowledge of any defenses, offsets or counterclaims against its obligations to perform its covenants under this Lease (or if there are any defenses, offsets, or counterclaims, setting them forth in reasonable detail); (iii) that there are no known uncured defaults of the Tenant or the Landlord under this Lease (or if there are known defaults, setting them forth in reasonable detail; (iv) the dates to which the Annual Fixed Rent, Additional Rent and other charges have been paid, and (v) that the Tenant is in full possession of the Premises, including all improvements, additions and alterations thereto required to be made by Landlord under the Lease; (vi) that the Tenant has satisfactorily complied with all of the requirements and conditions precedent to the commencement of the Term of the Lease as specified in the Lease; (vii) that the Tenant has been in occupancy since the Commencement Date and paying rent since the specified dates; (viii) that no monetary or other considerations, including, but not limited to, rental concessions for Landlord, special tenant improvements or Landlord's assumption of prior lease obligations of Tenant have been granted to Tenant by Landlord for entering into the Lease, except as specified; (ix) such other matters with respect to the Tenant and this Lease as the

Tenant may reasonably request. Any statement delivered pursuant to this Section may be relied upon by any prospective lender of Tenant, any prospective assignee or subtenant of Tenant or any prospective purchaser of Tenant or Tenant's assets, and shall be binding on the Landlord.

## ARTICLE XI

## MISCELLANEOUS

Section 11.1 - Notice of Lease.

The Tenant agrees not to record this Lease, but upon request of either party, both parties shall execute and deliver a memorandum of this Lease in form appropriate for recording or registration, an instrument acknowledging the Commencement Date of the Term, and if this Lease is terminated before the Term expires, an instrument in such form acknowledging the date of termination.

Section 11.2 - Notices.

Whenever any notice, approval, consent, request, election, offer or acceptance is given or made pursuant to this Lease, it shall be in writing. Communications and payments shall be addressed, if to the Landlord, at the Landlord's Address for Notices as set forth in Exhibit A or at such other address as may have been specified by prior notice to the Tenant; and if to the Tenant, at the Tenant's Address for Notices or at such other place as may have been specified by prior notice to the Landlord. Any communication so addressed shall be deemed duly given on the earlier of (i) the date received or (ii) on the third business day following the day of mailing if mailed by registered or certified mail, return receipt requested. If the Landlord by notice to the Tenant at any time designates some other person to receive payments or notices, all payments or notices thereafter by the Tenant shall be paid or given to the agent designated until notice to the contrary is received by the Tenant from the Landlord.

Section 11.3 - Authority.

Landlord represents and warrants that the individual executing this Lease on behalf of Landlord is duly authorized to execute and deliver this Lease on behalf of said entity, that said entity is duly authorized to enter into this Lease, and that this Lease is enforceable against said entity in accordance with its terms.

Tenant represents and warrants that the individual executing this Lease on behalf of Tenant is duly authorized to execute and deliver this Lease on behalf of said entity, that said entity is duly authorized to enter into this Lease, and that this Lease is enforceable against said entity in accordance with its terms.

Section 11.4 - Successors and Limitation on Liability on the Landlord.

The obligations of this Lease shall run with the land, and this Lease shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns, except that the original Landlord named herein and each successor Landlord shall be liable only for obligations accruing during the period of its ownership. The obligations of the Landlord shall be

binding upon the assets of the Landlord consisting of an equity ownership of the Property (and including any proceeds realized from the sale of such Property) but not upon other assets of the Landlord and neither the Tenant, nor anyone claiming by, under or through the Tenant, shall be entitled to obtain any judgment creating personal liability on the part of the Landlord or enforcing any obligations of the Landlord against any assets of the Landlord other than an equity ownership of the Property.

Section 11.5 - Waivers by the Landlord.

The failure of the Landlord or the Tenant to seek redress for violation of, or to insist upon strict performance of, any covenant or condition of this Lease, shall not be deemed a waiver of such violation nor prevent a subsequent act, which would have originally constituted a violation, from having all the force and effect of an original violation. The receipt by the Landlord of Annual Fixed Rent or Additional Rent with knowledge of the breach of any covenant of this Lease shall not be deemed a waiver of such breach. In the event of a breach or default of this Agreement by Landlord, any decision not to terminate this Lease shall not be deemed a waiver of such breach by Tenant. No provision of this Lease shall be deemed to have been waived by the Landlord or the Tenant, as the case may be, unless such waiver is in writing signed by the Landlord or the Tenant, as the case may be. No consent or waiver, express or implied, by the Landlord or Tenant to or of any breach of any agreement or duty shall be construed as a waiver or consent to or of any other breach of the same or any other agreement or duty.

Section 11.6 - Acceptance of Partial Payments of Rent.

No acceptance by the Landlord of a lesser sum than the Annual Fixed Rent and Additional Rent then due shall be deemed to be other than a partial installment of such rent due, nor shall any endorsement or statement on any check or any letter accompanying any check or payment as rent be deemed an accord and satisfaction and the Landlord may accept such check or payment without prejudice to the Landlord’s right to recover the balance of such installment or pursue any other remedy in this Lease provided. The delivery of keys to any employee of the Landlord or to the Landlord’s agent or any employee thereof shall not operate as a termination of this Lease or a surrender of the Premises.

Section 11.7 - Interpretation and Partial Invalidity.

If any term of this Lease, or the application thereof to any person or circumstances, shall to any extent be invalid or unenforceable, the remainder of this Lease, or the application of such term to persons or circumstances other than those as to which it is invalid or unenforceable, shall not be affected thereby, and each term of this Lease shall be valid and enforceable to the fullest extent permitted by law. The titles of the Articles are for convenience only and not to be considered in construing this Lease. This Lease contains all of the agreements of the parties with respect to the subject matter thereof and supersedes all prior dealings between them with respect to such subject matter.

Section 11.8 - Quiet Enjoyment.

So long as the Tenant pays Annual Fixed Rent and Additional Rent (subject to Tenant’s right to abate rent as set forth herein), performs all other Tenant covenants of this Lease and observes all conditions hereof, the Tenant shall peaceably and quietly have, hold and enjoy the Premises free of any claims by, through or under the Landlord.

Section 11.9 - Brokerage.

Each party represents and warrants to the other that it has had no dealings with any broker or agent in connection with this Lease other than Colliers Meredith & Grew and CB Richard Ellis ("Acknowledged Brokers") and shall indemnify and hold harmless the other from claims for any brokerage commission to a broker other than the Acknowledged Brokers arising out of the other party's actions.

Section 11.10 - Surrender of Premises and Holding Over.

The Tenant shall surrender possession of the Premises on the last day of the Term and the Tenant waives the right to any notice of termination or notice to quit. The Tenant covenants that upon the expiration or sooner termination of this Lease, it shall, without notice, deliver up and surrender possession of the Premises in the same condition in which the Tenant has agreed to keep the same during the continuance of this Lease and in accordance with the terms hereof, normal wear and tear and damage by fire or other casualty excepted, first removing therefrom all goods and effects of the Tenant and any leasehold improvements Landlord specified for removal pursuant to Section 4.2, and repairing all damage caused by such removal. Upon the expiration of this Lease or if the Premises should be abandoned by the Tenant, or this Lease should terminate for any cause, and at the time of such expiration, vacation, abandonment or termination, the Tenant or Tenant's agents, subtenants or any other person should leave any property of any kind or character on or in the Premises, the fact of such leaving of property on or in the Premises shall be conclusive evidence of intent by the Tenant, and individuals and entities deriving their rights through the Tenant, to abandon such property so left in or upon the Premises, and such leaving shall constitute abandonment of the property. Landlord shall have the right and authority without notice to the Tenant or anyone else, to remove and destroy, or to sell or authorize disposal of such property, or any part thereof, without being in any way liable to the Tenant therefor and the proceeds thereof shall belong to the Landlord as compensation for the removal and disposition of such property.

If the Tenant fails to surrender possession of the Premises upon the expiration or sooner termination of this Lease, the Tenant shall pay to Landlord, as rent for any period after the expiration or sooner termination of this Lease an amount equal to one hundred fifty percent (150%) of the Annual Fixed Rent and the Additional Rent required to be paid under this Lease as applied to any period in which the Tenant shall remain in possession. Acceptance by the Landlord of such payments shall not constitute a consent to a holdover hereunder or result in a renewal or extension of the Tenant's rights of occupancy. Such payments shall be in addition to and shall not affect or limit the Landlord's right of re-entry, Landlord's right to collect such damages as may be available at law, or any other rights of the Landlord under this Lease or as provided by law.

Section 11.11 - Ground Lease.

This Lease is in all respects subject to the ground lease (the "Ground Lease") between the Landlord as lessee and Massachusetts Institute of Technology ("MIT") as lessor dated as of August 20, 1986. If any provision of the Ground Lease shall be inconsistent with the provisions of this Lease, the provisions of the Ground Lease shall be deemed to limit the provisions hereof, except as are expressly otherwise provided in a written agreement signed by MIT, the Landlord and the Tenant.

Section 11.12 - Security Deposit.

(a) Letter of Credit.

Within thirty (30) days of the execution and delivery of this Lease, Tenant has delivered to Landlord as security for the performance of the obligations of Tenant hereunder a cash deposit or a letter of credit in the amount specified in Section 1.3 in accordance with this Section (as renewed, replaced, increased and/or reduced pursuant to this Section, the "Letter of Credit"). The Letter of Credit shall be in the form attached as Exhibit G to this Lease or such other form as Landlord may reasonably approve. If there is more than one Letter of Credit so delivered by Tenant, such Letters of Credit shall be collectively hereinafter referred to as the "Letter of Credit". The Letter of Credit (i) shall be irrevocable and shall be issued by a commercial bank reasonably acceptable to Landlord, (ii) shall require only the presentation to the issuer of a certificate of the holder of the Letter of Credit stating either (a) that a default has occurred under this Lease after the expiration of any applicable notice and cure period (or stating that transmittal of a default notice is barred by applicable bankruptcy or other law if such is the case) or (b) stating that Tenant has not delivered to Landlord a new Letter of Credit having a commencement date immediately following the expiration of the existing Letter of Credit in accordance with the requirements of the Lease, (iii) shall be payable to Landlord and its successors in interest as the Landlord and shall be freely transferable without cost to any such successor or any lender holding a collateral assignment of Landlord's interest in the Lease, (iv) shall be for an initial term of not less than one year and contain a provision that such term shall be automatically renewed for successive one-year periods unless the issuer shall, at least thirty (30) days prior to the scheduled expiration date, give Landlord written notice of such nonrenewal, and (v) shall otherwise be in form and substance reasonably acceptable to Landlord. Notwithstanding the foregoing, the term of the Letter of Credit for the final period of the Term shall be for a term ending not earlier then the date sixty (60) days after the last day of the Term.

If Tenant shall be in default under the Lease, after the expiration of any applicable notice or cure period (or if transmittal of a default or other notice is stayed or barred by applicable bankruptcy or other law), Landlord shall be entitled to draw upon the Letter of Credit to the extent reasonably necessary to cure such default. If, not less than thirty (30) days before the scheduled expiration of the Letter of Credit, Tenant has not delivered to Landlord a new Letter of Credit having a commencement date immediately following the expiration of the existing Letter of Credit in accordance with this Section, Landlord shall also have the right to draw upon the full amount of the Letter of Credit without giving any further notice to Tenant. Landlord may, but shall not be obligated to, apply the amount so drawn to the extent necessary to cure Tenant's default under the Lease. Any funds drawn by Landlord on the Letter of Credit and not applied

against amounts due hereunder shall be held by Landlord as a cash security deposit, provided that Landlord shall have no fiduciary duty with regard to such amounts, shall have the right to commingle such amounts with other funds of Landlord, and shall pay no interest on such amounts. After any application of the Letter of Credit by Landlord in accordance with this paragraph, Tenant shall reinstate the Letter of Credit to the amount then required to be maintained hereunder, within thirty (30) days of demand. Within sixty (60) days after the expiration or earlier termination of the Term the Letter of Credit and any cash security deposit then being held by Landlord, to the extent not applied, shall be returned to the Tenant provided that no Event of Default is then continuing.

(b) Pledge.

The Landlord may pledge its right and interest in and to the cash deposit or Letter of Credit to any mortgagee or ground lessor and, in order to perfect such pledge, have such cash deposit or Letter of Credit held in escrow by such mortgagee or ground lessee or grant such mortgagee or ground lessee a security interest therein. In connection with any such pledge or grant of security interest by the Landlord to a mortgagee or ground lessee ("Pledgee"), Tenant covenants and agrees to cooperate as reasonably requested by the Landlord, in order to permit the Landlord to implement the same on terms and conditions reasonably required by such Pledgee.

(c) Transfer of Security Deposit.

In the event of a sale or other transfer of the Building or transfer of this Lease, Landlord shall transfer the cash deposit or Letter of Credit to the transferee, and Landlord shall thereupon be released by Tenant from all liability for the return of such security. The provisions hereof shall apply to every transfer or assignment made of the security to such a transferee. Tenant further covenants that it will not assign or encumber or attempt to assign or encumber the Letter of Credit or the proceeds thereof, and that neither Landlord nor its successors or assigns shall be bound by any assignment, encumbrance, attempted assignment or attempted encumbrance.

Section 11.13 - Financial Reporting.

Tenant shall from time to time (but at least annually) on the anniversary of the Lease provide Landlord with financial statements of Tenant, together with related statements of Tenant's operations for Tenant's most recent fiscal year then ended, certified by an independent certified public accounting firm.

Section 11.14 - Cambridge Employment Plan.

The Tenant agrees to sign an agreement with the Employment and Training Agency designated by the City Manager of the City of Cambridge as provided in subsections (a)-(g) of Section 24-4 of Ordinance Number 1005 of the City of Cambridge, adopted April 23, 1984.

Section 11.15 - Parking and Transportation Demand Management.

Tenant covenants and agrees to work cooperatively with Landlord to develop a parking and transportation demand management ("PTDM") program that comprises part of a

comprehensive PTDM for University Park, provided that such cooperation shall be at no expense to Tenant. In connection therewith, the use of single occupant vehicle commuting will be discouraged and the use of alternative modes of transportation and/or alternative work hours will be promoted. Without limitation of the foregoing, Tenant agrees that its PTDM program (and Tenant will require in any sublease or occupancy agreement permitting occupancy in the Premises that such occupant's PTDM program) will include offering a subsidized MBTA transit pass, either constituting a full subsidy or a subsidy in an amount equal to the maximum deductible amount therefore allowed under the federal tax code, to any employee working in the Premises requesting one. Tenant agrees to comply with the traffic mitigation measures required by the City of Cambridge, and Tenant shall otherwise comply with all legal requirements of the City of Cambridge pertaining thereto.

Section 11.16 - Cancellation of Existing Lease.

It is hereby acknowledged by the parties hereto that Landlord or its predecessor in interest and Tenant or its predecessor in interest entered into two (2) previous leases in the Building, one on July 30, 2004 and one on September 4, 2008, as the same may have been amended (collectively, "Existing Lease"). As of the date of this Lease, Tenant releases and exculpates Landlord from any liability arising from the Existing Lease, and Landlord releases and exculpates Tenant from any liability arising from the Existing Lease unless such liability is due to Tenant's act of omission. It is hereby acknowledged and agreed that the Existing Lease shall become null and void as of the date of this Lease. Notwithstanding the foregoing, the provisions of this Section 11.16 shall not apply to those provisions of the Existing Lease that by their terms would otherwise survive the expiration or earlier termination thereof (e.g., annual reconciliation of operating expenses and real estate taxes).

IN WITNESS WHEREOF, this Lease has been executed and delivered as of the date first above written as a sealed instrument.

LANDLORD:

THIRTY-EIGHT SIDNEY STREET LIMITED PARTNERSHIP

By: Forest City 38 Sidney Street, Inc.,
a Massachusetts corporation

By: /s/ Michael Farley
Name: Michael Farley
Title: Vice President

TENANT:

AGIOS PHARMACEUTICALS, INC.,
a Delaware corporation

By: /s/ David Schenkein
Name: David Schenkein
Title: CEO

EXHIBIT A
Basic Lease Terms

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| Premises: | The Premises shall be comprised of approximately 38,536 rentable square feet made up of the Existing Premises and the Expansion Premises. |
| Existing Premises: | Approximately 21,608 rentable square feet located on the second floor and currently occupied by Tenant, as shown on Exhibit B. |
| Existing Premises Term Commencement Date: | The date of this Lease. |
| Existing Premises Rent Commencement Date: | The date of this Lease. |
| Existing Premises Annual Fixed Rent for the Term: | Date of Lease through 8/31/2010:<br>$54,00/rentable square foot NNN for 19,093 rentable square feet;<br>$34.00/rentable square foot NNN for 1,729 rentable square feet;<br>$25.00/rentable square foot NNN for 786 rentable square feet.<br><br>9/l/2010 through Expansion Premises Rent Commencement Date for the Third Floor Expansion Premises:<br>$55,00/ rentable square foot NNN for 19,093 rentable square feet;<br>$35/rentable square foot NNN for 1,729 rentable square feet;<br>$25/ rentable square foot NNN for 786 rentable square feet,<br><br>Thereafter: The same Annual Fixed Rent per rentable square foot as the Expansion Premises. |
| Expansion Premises: | Approximately 16,928 rentable square feet, with 3,755 rentable square feet located on the second floor (“Second Floor Expansion Premises”) and 13,173 rentable square feet located on the third floor (“Third Floor Expansion Premises”) as shown on Exhibit B. |
| Expansion Premises Rent Commencement Date: | The date that is five (5) months after the applicable Expansion Premises Term Commencement Date. |
| Expansion Premises Term Commencement: | The Expansion Premises Term Commencement Date commences on the delivery of the applicable Expansion Premises, and the term of this Lease expires on the last day of the sixtieth (60th) month following the Expansion Premises Rent Commencement Date for the Third Floor Expansion Premises (the “Initial Term”). The Landlord will use commercially reasonable efforts to deliver the Third Floor Expansion Premises to the Tenant within ninety (90) days of the full execution of a lease amendment with ETEX. As a |

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| | term of said lease amendment with ETEX, Landlord shall provide for notice to be delivered from ETEX to Landlord in the event that delivery of the Third Floor Expansion Premises will be delayed beyond the ninety (90) day period, and Landlord agrees to provide similar notice to Tenant if Landlord receives a delay notice from ETEX. If the Third Floor Expansion Premises Term Commencement Date has not occurred on or before December 1, 2010, Tenant shall have the right upon written notice to Landlord, to terminate this Lease and Tenant shall be reimbursed for the costs and expenses incurred by or on behalf of Tenant in connection with the Leasehold Improvements eligible for disbursement from the Leasehold Improvements Allowance, which reimbursable amount will not exceed $300,000.00. |
| Expansion Premises Annual Fixed Rent: | Second Floor Expansion Premises: $57.25 per rentable square foot, NNN from the Expansion Premises Rent Commencement Date for the Second Floor Expansion Premises to the Expansion Premises Rent Commencement Date for the Third Floor Expansion Premises.<br><br>Expansion Premises: Commencing with the Expansion Premises Rent Commencement Date for the Third Floor Expansion Premises:<br>Months 1-12: $57.25 per rentable square foot, NNN<br>Months 13-24: $58,25 per rentable square foot, NNN<br>Months 25-36: $59.25.per rentable square foot, NNN<br>Months 37-48: $60.25 per rentable square foot, NNN<br>Months 49-60: $61.25 per rentable square foot, NNN |
| Security Deposit: | $ 570,814.00 |
| Landlord's Address for Notices: | Thirty-Eight Sidney Street Limited Partnership<br>Forest City Commercial Group, Inc.<br>38 Sidney Street<br>Cambridge, Massachusetts 02139<br><br>With a copy to:<br>Forest City Commercial Group, Inc.<br>1360 Terminal Tower<br>50 Public Square<br>Cleveland, Ohio 44113<br>Attention: General Counsel<br><br>Forest City Commercial Management, Inc.<br>38 Sidney Street<br>Cambridge, Massachusetts 02139-4234<br>Attention: Michael Farley |

| | |
|---|---|
| Parking Privileges: | During the Term, Tenant shall be entitled to use and shall pay for parking passes in accordance with (i) the following schedule and (ii) Section 2.4 of the Lease. Upon the date of this Lease, Tenant shall lease a minimum of thirty-two (32) parking passes and may lease up to a maximum of fifty-eight (58) parking passes. Upon the Expansion Premises Rent Commencement Date, Tenant shall be obligated to lease a minimum of fifty-eight (58) parking passes for the term of the Lease. Subject to availability, Tenant shall have the right to lease additional parking spaces from Landlord; such lease for additional parking spaces shall be on a month-to-month basis at the then-prevailing fair market value for such parking spaces. |
| Permitted Uses: | General business and administrative offices, biotechnology research, animal experimentation and customary accessory uses supporting the foregoing, as set forth in Section 6.1 of the Lease. |
| Tenant's Address for Notices: | Agios Pharmaceuticals, Inc.<br>38 Sidney Street<br>Cambridge, Massachusetts 02139<br><br>With a copy to:<br><br>Faber Daeufer & Rosenberg PC<br>950 Winter Street, Suite 4500<br>Waltham, MA 02145<br>ATTN: Joseph L Faber |
| Leasehold Improvements Allowance: | $3,200,000.00 |
| Total Rentable floor Area of Building: | 121,622 rsf |

# EXHIBIT B

## 2nd Floor Premises




The Clark Building
38 Sidney Street
Cambridge, MA 02139

UNIVERSITY PARK AT MIT

# Exhibit B
# 3rd Floor Premises

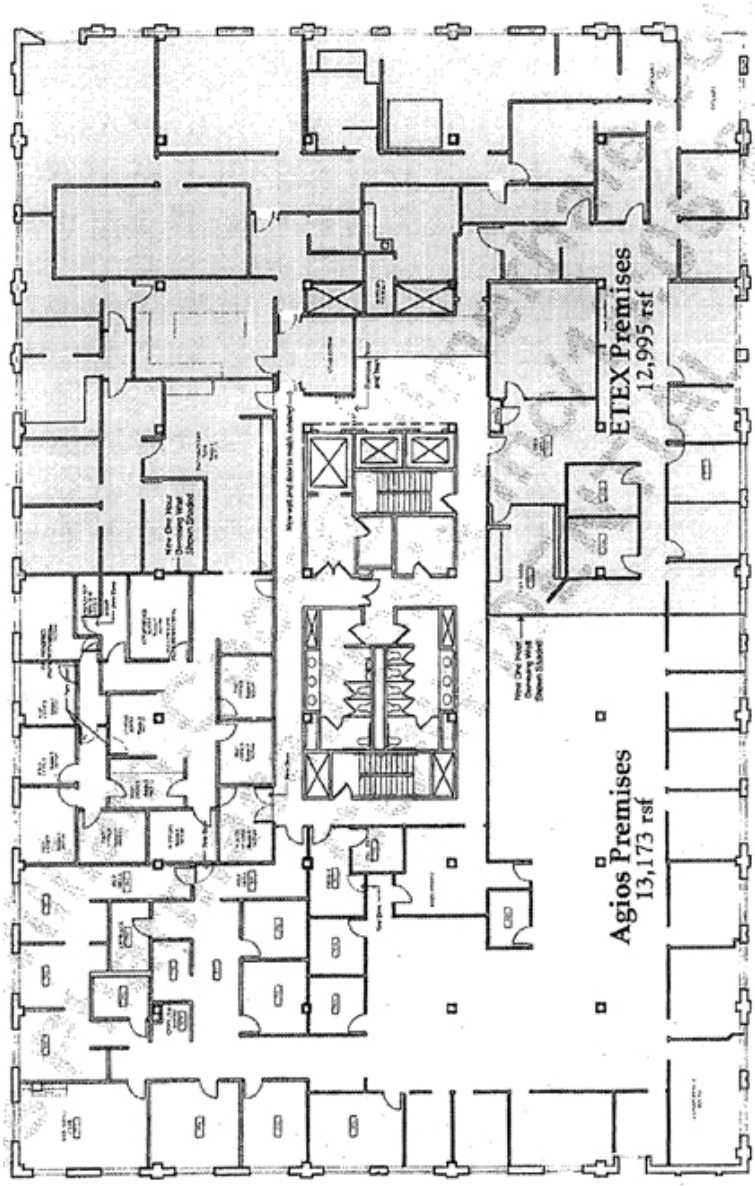

EXHIBIT C

STANDARD SERVICES

The building standard services shall be defined by the Landlord and its Management Agent, A listing of services shall be as promulgated from time to time by the Landlord and shall be further described in the Tenant Handbook.

The following services are provided by the Landlord:

A. Regular maintenance of interior, exterior and parking lot landscaping and University Park common areas.

B. Regular maintenance, sweeping and snow removal of building exterior areas such as roadways, driveways, sidewalks, parking areas and courtyard paving.

C. Complete interior and exterior cleaning of all windows two times per year.

D. Daily, weekday maintenance of hallways, passenger elevators, common area bathrooms, lobby areas and vestibules,

E. Periodic cleaning of stairwells, freight elevators, and back of house areas.

F. Daily, weekday rubbish removal of all tenant trash receptacles.

G. Daily, weekday clearing of Tenant space to building standard.

H. Maintenance and repair of base building surveillance and alarm equipment, mechanical, electrical, plumbing and life safety systems.

I. Building surveillance and alarm system operation and live monitoring service to building standard specifications

J. Conditioned water for HVAC purposes shall be provided to the Premises from central mechanical equipment.

K. Utilities for all interior common areas and exterior building and parking lighting.

EXHIBIT D

RULES AND REGULATIONS

DEFINITIONS

Wherever in these Rules and Regulations the word “Tenant” is used, it shall be taken to apply to and include the Tenant and its agents, employees, invitees, licensees, contractors, any subtenants and is to be deemed of such number and gender as the circumstances require. The word “Premises” is to be taken to include the space covered by the Lease. The word “Landlord” shall be taken to include the employees and agents of Landlord. Other capitalized terms used but not defined herein shall have the meanings set forth in the Lease.

GENERAL USE OF BUILDING

A. Space for admitting natural light into any public area or tenanted space of the Building shall not be covered or obstructed by Tenant except in a manner approved by Landlord.

B. Toilets, showers and other like apparatus shall be used only for the purpose for which they were constructed. Any and all damage from misuse shall be borne by Tenant. These rooms should be locked at all times.

C. Except as otherwise permitted in the Lease, Landlord reserves the right to determine the number of letters allowed Lessee on any directory it maintains.

D. No sign, advertisement, notice or the like, shall be used in the Building by Tenant (other than at its office and then only as approved by Landlord in accordance with building standards). If Tenant violates the foregoing, Landlord may remove the violation without liability and may charge all costs and expenses incurred in so doing to Tenant.

E. Tenant shall not throw or permit to be thrown anything out of windows or doors or down passages or elsewhere in the Building, or bring or keep any pets therein, or commit or make any indecent or improper acts or noises. In addition, Tenant shall not do or permit anything which will obstruct, injure, annoy or interfere with other tenants or those having business with them, or affect any insurance rate on the Building or violate any provision of any insurance policy on the Building.

F. Unless expressly permitted by the Landlord in writing:

(1) No additional locks or similar devices shall be attached to any door or window and no keys other than those provided by the Landlord shall be made for any door; *provided however,* that Tenant may install and manage its own compatible card reader entry system for entry to and within the Premises. If more than two keys for one lock are desired by the Tenant, the Landlord may provide the same upon payment by the Tenant. Upon termination of this lease or of the Tenant’s possession, the Lessee shall surrender all keys to the Premises and shall explain to the Landlord all combination locks on safes, cabinets and vaults.

(2) In order to insure proper use and care of the Premises Tenant shall not install any shades, blinds, or awnings or any interior window treatment without consent of Landlord. Blinds must be building standard.

(3) All doors to the Premises are to be kept closed at all times except when in actual use for entrance to or exit from such Premises. The Tenant shall be responsible for the locking of doors and the closing of any transoms and windows in and to the Premises. Any damage or loss resulting from violation of this rule shall be paid for by the Tenant.

(4) The Tenant shall not install or operate any steam or internal combustion engine, boiler, machinery in or about the Premises, or carry on any mechanical business therein except as currently utilized at the Premises or in accordance with the terms of the Lease. All equipment of any electrical or mechanical nature shall be placed in settings which absorb and prevent any vibration, noise or annoyance.

G. Landlord shall designate the time when and the method whereby freight, small office equipment, furniture, safes and other like articles may be brought into, moved or removed from the Building or Premises, and to designate the location for temporary disposition of such items.

H. In order to insure proper use and care of the Premises Tenant shall not allow anyone other than Landlord’s employees or contractors to clean the Premises without Landlord’s permission, provided, however, that Landlord acknowledges and agrees that Tenant shall clean rooms used for Tenant’s work with animals at the Premises.

I. The Premises shall not be defaced in any way. No changes in the HVAC, electrical fixtures or other appurtenances of said Premises shall be made except in accordance with the Terms of this Lease.

J. For the general welfare of all tenants and the security of the Building, Landlord may require all persons entering and/or leaving the Building on weekends and holidays and between the hours of 6:00 p.m. and 8:00 a.m. to register with the Building attendant or custodian by signing his name and writing his destination in the Building, and the time of entry and actual or anticipated departure, or other procedures deemed necessary by Landlord. Landlord may deny entry during such hours to any person who fails to provide satisfactory identification.

K. No animals, birds, pets, and no bicycles or vehicles of any kind shall be brought into or kept in or about said Premises or the lobby or halls of the Building, excepting those animals used for research purposes, by a disabled person, or otherwise within the scope of the Permitted Uses. Tenant shall not cause or permit any unusual or objectionable odors, noises or vibrations to be produced upon or emanate from said Premises.

L. Unless specifically authorized by Landlord, employees or agents of Landlord shall not perform for nor be asked by Tenant to perform work other than their regularly assigned duties.

M. Canvassing, soliciting and peddling in the Building are prohibited and Tenant shall cooperate to prevent the same from occurring.

N. All parking, Building operation, or construction rules and regulations which may be established from time to time by Landlord on a uniform basis shall be obeyed.

O. Tenant shall not place a load on any floor of said Premises exceeding one hundred (100) pounds per square foot. Landlord reserves the right to prescribe the weight and position of all safes and heavy equipment.

P. Tenant shall not install or use any air conditioning or heating device or system other than in accordance with the terms of the Lease, unless previously approved by Landlord.

Q. Landlord shall have the right to make such other and further reasonable rules and regulations as in the judgment of Landlord, may from time to time be needful for the safety, appearance, care and cleanliness of the Building and for the preservation of good order therein, provided that such other and further reasonable rules and regulations shall not interfere with the Permitted Uses. Landlord shall not be responsible to Tenant for any violation of rules and regulations by other tenants, provided that the Landlord shall use diligent efforts to enforce the rules and regulations and shall do so in a uniform manner with respect to all tenants of the Building.

R. The Blanche Street private way and loading areas, parking areas, sidewalks, entrances, lobbies, halls, walkways, elevators, stairways and other common area provided by Landlord shall not be obstructed by Tenant, or used for other purpose than for ingress and egress.

S. In order to insure proper use and care of the Premises Tenant shall not install any call boxes or communications systems or wiring of any kind except in accordance with the terms of the Lease.

T. In order to insure proper use and care of the Premises Tenant shall not manufacture any commodity, or prepare or dispense for sales any foods or beverages, tobacco, flowers, or other commodities or articles, except vending machines for the benefit of employees and invitees of Tenant, without the written consent of Landlord.

U. In order to insure use and care of the Premises Tenant shall not enter any janitors’ closets, mechanical or electrical areas, telephone closets, loading areas, roof or Building storage areas (except to the extent completely located within the Premises) without reasonable notice to Landlord.

V. In order to insure proper use and care of the Premises Tenant shall not place door mats in public corridors without consent of Landlord.

EXHIBIT E

WORK LETTER

1. Landlord shall provide to Tenant an allowance (the "Leasehold Improvements Allowance") of $3,200,000.00, for application to the costs and expenses, more particularly set forth below, incurred by or on behalf of Tenant. If Tenant incurs costs in excess of the Leasehold Improvements Allowance, then all such excess costs shall be born solely by Tenant. The Tenant must apply to Landlord for reimbursement from the Leasehold Improvements Allowance within one (1) year after the Expansion Premises Term Commencement Date. Any portion of such Leasehold Improvements Allowance for which application for reimbursement has not been made within such one (1) year period shall be cancelled and no longer available.

2, The application of the Leasehold Improvements Allowance by Landlord shall be limited to payment of the following costs and expenses incurred by or on behalf of Tenant in connection with the Improvements: the actual documented and verified cost pursuant to Tenant's design and construction contracts, including without limitation the associated contractor's overhead and profit and general conditions, incurred in the construction of the Improvements to the Premises, except for the making of improvements, installation of fixtures or incorporation of other items which are moveable rather than permanent improvements in the nature of trade fixtures, examples of which may include furniture, telephone communications and security equipment, and bench-top laboratory equipment items such as microscopes.

3. During the construction of any Improvements with respect to which Tenant desires to have the Leasehold Improvements Allowance applied, and in accordance with the commercially reasonable terms and conditions typically imposed upon a landlord pursuant to a construction loan agreement, such as, without limitation, retainage, lien waiver, and other requisition conditions, Tenant shall, on a monthly basis (as the Tenant's contractor submits to Tenant its application for payment), deliver to Landlord a requisition for payment showing the costs of the leasehold improvements in question and the amount of the current payment requested from Landlord for disbursement from the Leasehold Improvements Allowance within thirty (30) days after receipt of Tenant's requisition; provided that any disbursement from the Leasehold Improvements Allowance shall hot occur until the Third Floor Expansion Premises Term Commencement Date or Tenant does not exercise its right to terminate this Lease in writing due to the Third Floor Expansion Premises Term Commencement Date not having occurred on or before December 1, 2010. Payments made on account of Tenant's requisitions shall be made from the Leasehold Improvements Allowance. Following the completion of any such Improvements, Tenant shall deliver to the Landlord, within ninety (90) days of completion, a statement showing the final costs of such Improvements, the amounts paid to date, or on behalf of the Tenant, and any amounts available for release of retainage.

EXHIBIT F

*TENANT CONSTRUCTION WORK AT UNIVERSITY PARK*

The tenant construction work procedure at University Park is designed to provide efficient scheduling of work while protecting other tenants from unnecessary noise and inconvenience. The attached document explains the procedure and has been prepared in keeping with the standard lease at University Park. It contains detailed information to assist you in planning construction projects. Please review it carefully before design begins.

SUMMARY

1. Contact the Property Manager as the first step. The Property Manager will be happy to assist you in completing your project efficiently.
2. Incorporate the provisions of the attached document and the “Indoor Air Quality Guidelines for Tenant Improvement Work” into all of your agreements and contracts. You will need written approval from Forest City Commercial Management before contracting any work.
3. At least four weeks before construction provide four sets of drawings and plans to the Property Manager for approval. The Property Manager must also approve your list of contractors and subcontractors.
4. At least two weeks before construction submit to the Property Manager detailed schedules; addresses and telephone numbers of supervisors contractors and subcontractors; copies of permits; proof of current insurance; Payment, Performance and Lien bonds: and notice of any contractor’s involvement in a labor dispute.
5. We will generally require that you conduct noisy, disruptive or odor and dust producing work, as well as the delivery of construction materials, outside of regular business hours.
6. We expect all contractors to maintain safe and orderly conditions, labor harmony and proper handling of any hazardous materials. We may stop any work that does not meet the conditions outlined in the attached document.
7. Before occupying the completed space, submit the final certificate of occupancy and any other approvals to the Property Manager. We also require an air balancing report signed by a professional engineer. A complete set of “as built” sepia drawings as well as electronic “as-built” drawings in AutoCAD Release 12, DXF format must be hand delivered to the Property Manager.

Please note that this summary highlights key aspects of the attached document (entitled Rules and Regulations for Design and Construction of Tenant Work) for your convenience and does not supersede it in any way.

1. DEFINITIONS

| | | |
|---|---|---|
| 1.1 | Buildings: | University Park a MIT:<br><br>38 Sidney, 45 Sidney, 75 Sidney, 64 Sidney, 88 Sidney, 26 Landsdowne, 35 Landsdowne, 40 Landsdowne, 65 Landsdowne and 350 Mass. Ave |
| 1.2 | Property Manager: | Jay Kiely, or such other individual as Landlord may designate, from time to time. |
| 1.3 | Building Standards Book: | Building Standards at University Park, as amended by Landlord, from time to time. |
| 1.4 | Consultants: | Any architectural, engineering, or design consultant engaged by a Tenant in connection with Tenant Work. |
| 1.5 | Contractor: | Any Contractor engaged by a Tenant of the Building for the performance of any Tenant Work, and any Subcontractor, employed by any such Contractor. |
| 1.6 | Plans: | All architectural, electrical and mechanical construction drawings and specifications required for the proper construction of the Tenant Work. |
| 1.7 | Regular Business Hours: | Monday through Friday, 7:30 A.M. through 5:30 P.M., excluding holidays. |
| 1.8 | Tenant: | Any occupant of the Building. |
| 1.9 | Tenant Work: | Any alternations, improvements, additions, repairs or installations in the Building performed by or on behalf of any Tenant. |
| 1.10 | Tradesperson: | Any employee (including, without limitation, any mechanic, laborer, or Tradesperson) employed by a Contractor performing Tenant Work. |

2.0 GENERAL

2.1 All Tenant Work shall be performed in accordance with these rules and regulations and the applicable provisions of the Lease.

2.2 The provisions of these rules and regulations shall be incorporated in all agreements governing the performance of all Tenant Work, including, without limitation, any agreements governing services to be rendered by each Contractor and Consultant.

2.3 Except as otherwise provided in these Rules and Regulations, all inquiries, submissions and approvals in connection with any Tenant Work shall be processed through the Property Manager.

3. PLANS

3.1 Review and Approval: Any Tenant wishing to perform Tenant Work must first obtain the Landlord's written approval of its plans for such Tenant Work. Landlord will allow the Tenant the right to choose its own space planner (s) and architect for the design of the tenant work, provided, however, Tenant shall be required to retain under separate contract Landlord's mechanical, electrical, plumbing and structural engineers (s) with respect to such Tenant work to ensure operating consistency of the Premises with the building. Under no circumstances will any Tenant Work be permitted prior to such approval. Such approval shall be obtained prior to the execution of any agreement with any Contractor for the performance of such Tenant Work.

3.2 Submission Requirements:

a. Any Tenant performing Tenant Work shall, at the earliest possible time but at least four weeks before any Tenant Work is to begin, furnish to the Property Manager four full sets of plans and specifications describing such Tenant Work.

b. All such Plans shall be drafted in accordance with the Construction Drawing Requirements set out in the Building Standards Book.

c. The design manifested in the Plans will be reviewed by the Landlord and shall comply with his requirements so as to avoid aesthetic or other conflicts with the design and function of the Tenant's premises and of the Building as a whole.

4. PRECONSTRUCTION NOTIFICATION AND APPROVALS

4.1 Approval to Commence Work

a. Tenant shall submit to Property Manager, for the approval of Property Manager, the names of all prospective Contractors prior to issuing any bid packages to such Contractors.

b. No Tenant Work shall be undertaken by any Contractor or Tradesperson unless and until all the matters set forth in Article 4.2 below have been received for the Tenant Work in question and unless Property Manager has approved the matters set forth in Article 4.2 below.

4.2 No Tenant Work shall be performed unless, at least two weeks before any Tenant Work is to begin, all of the following has been provided to the Property Manager and approved. In the event that Tenant proposes to change any of the following, the Property Manager shall be immediately notified of such change and such change shall be subject to the approval of the Property Manager:

a. Schedule for the work, indicating start and completion dates, any phasing and special working hours, and also a list of anticipated shutdowns of building systems.

b. List of all Contractors and Subcontractors, including addresses, telephone numbers, trades employed, and the union affiliation, if any, of each Contractor and Subcontractor.

c. Names and telephone numbers of the supervisors of the work.

d. Copies of all necessary governmental permits, licenses and approvals.

e. Proof of current insurance, to the limits set out in Exhibit A to these Rules and Regulations, naming Landlord as an additional insured party.

f. Notice of the involvement of any Contractor in any ongoing or threatened labor dispute.

g. Payment, Performance and Lien Bonds from sureties acceptable to Landlord, in form acceptable to Landlord, naming Landlord as an additional obligee.

h. Evidence that Tenant has made provision for either written waivers of lien from all Contractors and suppliers of material, or other appropriate protective measures approved by Landlord.

4.3 Reporting Incidents

All accidents, disturbances, labor disputes or threats thereof, and other noteworthy events pertaining to the Building or the Tenant’s property shall be reported immediately to the Property Manager. A written report must follow within 24 hours.

5. CONSTRUCTION SCHEDULE

5.1 Coordination

a. All Tenant Work shall be carried out expeditiously and with minimum disturbance and disruption to the operation of the Building and without causing discomfort, inconvenience, or annoyance to any of the other tenants or occupants of the Building or the public at large.

b. All schedules for the performance of construction, including materials deliveries, must be coordinated through the Property Manager. The Property Manager shall have the right, without incurring any liability to any Tenant, to stop activities and/or to require rescheduling of Tenant Work based upon adverse impact on the tenants or occupants of the Building or on the maintenance or operation of the Building.

c. If any tenant Work requires the shutdown of risers and mains for electrical, mechanical, sprinklers and plumbing work, such work shall be supervised by a representative of Landlord. No Tenant Work will be performed in the Building's mechanical or electrical equipment rooms without both Landlord's prior approval and the supervision of a representative of Landlord, the cost of which shall be reimbursed by the Tenants.

5.2 Time Restrictions

a. Subject to Paragraph 5.1 of these rules and regulations, general construction work will generally be permitted at all times, including during Regular Business Hours.

b. Tenant shall provide the Property Manager with at least twenty-four (24) hours notice before proceeding with Special Work, as hereinafter defined, and such Special Work will be permitted only at times agreed to by the Property Manager during periods outside of Regular Business Hours. "Special Work" shall be defined as the following operations:

(1) All utility disruptions, shutoffs and turnovers;

(2) Activities involving high levels of noise, including demolition, coring, drilling and ramsetting;

(3) Activities resulting in excessive dust or odors, including demolition and spray painting.

c. The delivery of construction materials to the Building, their distribution within the Building, and the removal of waste materials shall also be confined to periods outside Regular Business Hours, unless otherwise specifically permitted in writing by the Property Manager.

d. If coordination, labor disputes or other circumstances require, the Property Manager may change the hours during which regular construction work can be scheduled and/or restrict or refuse entry to and exit from the Building by any Contractor.

6. CONTRACTOR PERSONNEL

6.1 Work in Harmony

a. All Contractors shall be responsible for employing skilled and competent personnel and suppliers who shall abide by the rules and regulations herein set forth as amended from time to time by Landlord.

b. No Tenant shall at any time, either directly or indirectly, employ, permit the employment, or continue the employment of any Contractor if such employment or continued employment will or does interfere or cause any labor disharmony, coordination difficulty, delay or conflict with any other contractors engaged in construction work in or about the Building or the complex in which the Building is located.

c. Should a work stoppage or other action occur anywhere in or about the Building as a result of the presence, anywhere in the Building, of a Contractor engaged directly or indirectly by a Tenant, or should such Contractor be deemed by Landlord to have violated any applicable rules or regulations, then upon twelve hours written notice, Landlord may, without incurring any liability to Tenant or said Contractor, require any such Contractor to vacate the premises demised by such Tenant and the Building, and to cease all further construction work therein.

6.2 Conduct

a. While in or about the Building, all Tradespersons shall perform in a dignified, quiet, courteous, and professional manner at all times. Tradespersons shall wear clothing suitable for their work and shall remain fully attired at all times. All Contractors will be responsible for their Tradespersons' proper behavior and conduct.

b. The Property Manager reserves the right to remove anyone who, or any Contractor which; is causing a disturbance to any tenant or occupant of the Building or any other person using or servicing the Building; is interfering with the work of others; or is in any other way displaying conduct or performance not compatible with the Landlord's standards.

6.3 Access

a. All Contractors and Tradespersons shall contact the Property Manager prior to commencing work, to confirm work location and Building access, including elevator usage and times of operation. Access to the Building before and after Regular Business Hours or any other hours designated from time to time by the Building Manger and all day on weekends and holidays will only be provided when twenty-four (24) hours advanced notice is given to the Property Manager.

b. No Contractor or Tradesperson will be permitted to enter any private or public space in the Building, other than the common areas of the Building necessary to give direct access to the premises of Tenant for which he has been employed, without the prior approval of the Property Manager.

c. All Contractors and Tradespersons must obtain permission from the Property Manager prior to undertaking work in any space outside of the Tenant's premises. This requirement

specifically includes ceiling spaces below the premises where any work required must be undertaken at the convenience of the affected Tenant and outside of Regular Business Hours. Contractors undertaking such work shall ensure that all work, including work required to reinstate removed items and cleaning, be completed prior to opening of the next business day.

d. Contractors shall ensure that all furniture, equipment and accessories in areas potentially affected by any Tenant Work shall be adequately protected by means of drop cloths or other appropriate measures. In addition, all Contractors shall be responsible for maintain security to the extent required by the Property Manager.

e. Temporary access doors for tenant construction areas connecting with a public corridor will be building standards, i.e., door, frame, hardware and lockset. A copy of the key will be furnished to the Property Manager.

6.4 Safety

a. All Contractors shall police ongoing construction operations and activities at all times, keeping the premises orderly, maintaining cleanliness in and about the premises, and ensuring safety and protection of all areas, including truck docks, elevators, lobbies and all other public areas which are used for access to the premises.

b. All Contractors shall appoint a supervisor who shall be responsible for all safety measures, as well as for compliance with all applicable governmental laws, ordinances, rules and regulations such as, for example, “OSHA” and “Right-to-Know” legislation.

c. Any damage caused by Tradespersons or other Contractor employees shall be the responsibility of the Tenant employing the Contractor. Costs for repairing such damage shall be charge directly to such Tenant.

6.5 Parking

a. Parking is not allowed in or near truck docks, in handicapped or fire access lanes, or any private ways in or surrounding the property, vehicles so parked will be towed at the expense of the Tenant who has engaged the Contractor for whom the owner of such vehicle is employed.

b. The availability of parking in any parking areas of the Building is limited. Use of such parking for Contractors and their personnel is restricted and must be arranged with and approved by the Property Manager.

7. BUILDING MATERIALS

7.1 Delivery

All deliveries of construction materials shall be made at the predetermined times approved by the Property Manager and shall be effected safely and expeditiously only at the location determined by the Property Manager.

7.2 Transportation in Building

a. Distribution of materials from delivery point to the work area in the Building shall be accomplished with the least disruption to the operation of the Building possible. Elevators will be assigned for material delivery and will be controlled by the Building management.

b. Contractors shall provide adequate protection to all carpets, wall surfaces, doors and trim in all public areas through which materials are transported. Contractors shall continuously clean all such areas. Protective measures shall include runners over carpet, padding in elevators and any other measures determined by the Property Manager.

c. Any damage caused to the Building through the movement of construction materials or otherwise shall be the responsibility of Tenant who has engaged the Contractor involved. Charges for such damage will be submitted by the Landlord directly to the Tenant.

7.3 Storage and Placement

a. All construction materials shall be stored only in the premises where they are to be installed. No storage of materials will be permitted in any public areas, loading docks or corridors leading to the premises.

b. No flammable, toxic, or otherwise hazardous materials may be brought in or about the Building unless: (i) authorized by the Property Manager, (ii) all applicable laws, ordinances, rules and regulations are complied with, and (iii) all necessary permits have been obtained. All necessary precautions shall be taken by the Contractor handling such materials against damage or injury caused by such materials.

c. All materials required for the construction of the premises must comply with Building standards, must conform with the plans and specifications approved by Landlord, and must be installed in the locations shown on the drawings approved by the Landlord.

d. All work shall be subject to reasonable supervision and inspection by Landlord’s Representative.

e. No alternations to approved plans will be made without prior knowledge and approval of the Property Manager. Such changes shall be documented on the as-built drawings required to be delivered to Landlord pursuant to Paragraph 10 of the rules and regulations.

f. All protective devices (e.g., temporary enclosures and partitions) and materials, as well as their placement, must be approved by the Property Manager.

g. It is the responsibility of Contractors to ensure that the temporary placement of materials does not impose a hazard to the Building or its occupants, either through overloading, or interference with Building systems, access, egress or in any other manner whatsoever.

h. All existing and/or new openings made through the floor slab for piping, cabling, etc. must be packed solid with fiberglass insulation to make openings smoke tight. All holes in the floor slab at abandoned floor outlets, etc. will be filled with solid concrete.

7.4 Salvage and Waste Removal

a. All rubbish, waste and debris shall be neatly and cleanly removed from the Building by Contractors daily unless otherwise approved by the Property Manager. The Building's trash compactor shall not be used for construction or other debris. For any demolition and debris, each Contractor must make arrangements with the Property Manager for the scheduling and location of an additional dumpster to be supplied at the cost of the Tenant engaging such Contractor. Where, in the opinion of the Property Manager, such arrangements are not practical, such Contractors will make alternative arrangements for removal at the cost of the Tenant engaging such Contractors.

b. Toxic or flammable waste is to be properly removed daily and disposed of in full accordance with all applicable laws, ordinances, rules and regulations.

c. Contractors shall, prior to removing any item (including, without limitation, building standard doors, frames and hardware, light fixtures, ceiling diffusers, ceiling exhaust fans, sprinkler heads, fire horns, ceiling speakers and smoke detectors) from the Building, notify the Property Manager that it intends to remove such item. At the election of Property Manager, Contractors shall deliver any such items to the Property Manager. Such items will be delivered, without cost, to an area designated by the Property Manager which area shall be within the Building or the complex in which the Building is located.

8. PAYMENT OF CONTRACTORS

Tenant shall promptly pay the cost of all Tenant Work so that Tenant's premises and the Building shall be free of liens for labor or materials. If any mechanic's lien is filed against the Building or any part thereof which is claimed to be attributable to the Tenant, its agents, employees or contractors, Tenant shall give immediate notice of such lien to the Landlord and shall promptly discharge the same by payment or filing any necessary bond within 10 days after Tenant has first notice of such mechanic's lien.

9. CONTRACTORS INSURANCE

Prior to commencing any Tenant Work, and throughout the performance of the Tenant Work, each Contractor shall obtain and maintain insurance in accordance with Exhibit A attached hereto. Each Contractor shall, prior to making entry into the Building provide Landlord with certificates that such insurance is in full force and effect.

10. SUBMISSIONS UPON COMPLETION

a. Upon completion of any Tenant Work, Tenant shall submit to Landlord a permanent certificate of occupancy and final approval of any other governmental agencies having jurisdiction.

b. A properly executed air balancing report, signed by a professional engineer, shall be submitted to Landlord upon completion of all mechanical work. Such report shall be subject to Landlord's approval.

c. Tenant shall submit to Landlord's Representative a final "as-built" set of sepia drawings as well as electronic "as-built" drawings in AutoCAD Release 12, DXF format.

11. ADJUSTMENT OF REGULATIONS

These Rules and Regulations may be amended from time to time in accordance with the reasonable judgment of Landlord.

12. CONFLICT BETWEEN RULES AND REGULATIONS AND LEASE

In the event of any conflict between the Lease and these rules and regulations, the terms of the Lease shall control.

EXHIBIT A

TO

CONSTRUCTION RULES AND REGULATIONS

INSURANCE REQUIREMENTS FOR CONTRACTORS

When Tenant Work is to be done by Contractors in the Building, the Tenant authorizing such work shall be responsible for including in the contract for such work the following insurance and indemnity requirements to the extent that they are applicable. Insurance certificates must be received prior to construction. Landlord shall be named as an additional insured party on all certificates.

INSURANCE

Each Contractor and each Subcontractor shall, until the completion of the Tenant Work in question, procure and maintain at its expense, the following insurance coverages with companies acceptable to Landlord in the following minimum limits:

Workers' Compensation

(including coverage for Occupational Disease)

| | Limit of Liability |
|---|---|
| Workers' Compensation | Statutory Benefits |
| Employer's Liability | $500,000 |

Comprehensive General Liability

(including Broad Form Comprehensive Liability Enhancement, Contractual Liability assumed by the Contractor and the Tenant under Article 15.3 of the Lease and Completed Operations coverage)

| | Limit of Liability |
|---|---|
| Bodily Injury & Property Damage | $5,000,000 combined single limit |

Comprehensive Automobile Liability

(including coverage for Hired and Non-owned Automobiles)

| | Limit of Liability |
|---|---|
| Bodily Injury & Property Damage | $1,000,000 per occurrence |

SUPPLEMENT TO RULES AND REGULATIONS FOR
DESIGN CONSTRUCTION OF TENANT WORK

FACT SHEET FOR UNIVERSITY PARK

1. PROPERTY MANAGER'S OFFICE

| | |
|---|---|
| CONTACT(S): | Jay Kiely, Property Manager<br>Robyn Arruda, Asst. Property Manager<br>Eddie Arruda, Chief Engineer |
| LOCATION: | Forest City Management<br>38 Sidney Street<br>Cambridge, MA 02139 |
| TELEPHONE NUMBER: | (617) 494-9330 |

2. PERSONNEL, MATERIAL AND EQUIPMENT ACCESS

| | |
|---|---|
| LOCATION OF LOADING BOCK: | |
| NORMAL HOURS OF ACCESS: | 7:30 A.M. TO 5:30 P.M. |
| ENTRANCES NOT AVAILABLE: | All building lobbies. |

3. USE OF ELEVATORS

| | |
|---|---|
| LOCATION OF ELEVATORS: | Specific locations of service elevators will be pointed out by the building staff. |
| NORMAL HOURS OF OPERATION: | 7:30 A.M. to 5:30 P.M. |
| OVERTIME OPERATION CHARGES: | $40.00 per hour |
| ELEVATORS NOT AVAILABLE: | All passenger elevators. |

4. SPECIAL CONDITIONS AND PRECAUTIONS

As University Park consists of multi-use buildings incorporating offices, retail and hotel suites, special care must be taken to control noise at all times.

All window blinds are to be removed prior to construction and replaced without damage immediately after completion of construction by the tenant and/or his contractor.

EXHIBIT G

FORM OF LETTER OF CREDIT

IRREVOCABLE STANDBY LETTER OF CREDIT NO.

DATE: , 200

BENEFICIARY:

_____

_____

_____

APPLICANT:

_____

_____

_____

AMOUNT: US$ ($ and 00/100 U.S. DOLLARS)

EXPIRATION DATE: ,200

LOCATION: AT OUR COUNTERS IN SKOKIE, ILLINOIS

DEAR SIR/MADAM:

WE HEREBY ESTABLISH OUR IRREVOCABLE STANDBY LETTER OF CREDIT NO . IN YOUR FAVOR AVAILABLE BY YOUR DRAFT IN THE FORM OF “ANNEX 1” ATTACHED DRAWN ON US AT SIGHT AND ACCOMPANIED BY THE FOLLOWING DOCUMENTS:

A DATED STATEMENT PURPORTEDLY SIGNED BY AN AUTHORIZED OFFICER OF THE BENEFICIARY ON BENEFICIARY'S LETTERHEAD READING AS FOLLOWS:

(A) THE AMOUNT REPRESENTS FUNDS DUE AND OWING TO US PURSUANT TO THE TERMS OF THAT CERTAIN LEASE BY AND BETWEEN , AS LANDLORD, AND , AS TENANT OR

(B) HEREBY CERTIFIES THAT IT HAS RECEIVED NOTICE FROM THAT THE LETTER OF CREDIT NO. WILL NOT BE RENEWED, AND THAT IT HAS NOT RECEIVED A REPLACEMENT OF THIS LETTER OF CREDIT FROM SATISFACTORY TO AT LEAST THIRTY (30) DAYS PRIOR TO THE EXPIRATION DATE OF THIS LETTER OF CREDIT.

THE LEASE MENTIONED IN THIS LETTER OF CREDIT IS FOR IDENTIFICATION PURPOSES ONLY AND IT IS NOT INTENDED THAT SAID AGREEMENT BE INCORPORATED HEREIN OR FORM PART OF THIS LETTER OF CREDIT.

DRAFT(S) AND DOCUMENTS MUST INDICATE THE NUMBER AND DATE OF THIS LETTER OF CREDIT.

THIS LETTER OF CREDIT SHALL BE AUTOMATICALLY EXTENDED FOR AN ADDITIONAL PERIOD OF ONE YEAR, WITHOUT AMENDMENT OR CONDITION, FROM THE PRESENT OR EACH FUTURE EXPIRATION DATE UNLESS AT LEAST NINETY (90) DAYS PRIOR TO THE THEN CURRENT EXPIRATION DATE WE NOTIFY YOU AND THE APPLICANT BY REGISTERED MAIL/OVERNIGHT COURIER SERVICE AT THE ABOVE ADDRESSES THAT THIS LETTER OF CREDIT WILL NOT BE EXTENDED BEYOND THE CURRENT EXPIRATION DATE.

THIS LETTER OF CREDIT MAY BE TRANSFERRED (AND THE PROCEEDS HEREOF ASSIGNED, WHICH ARE COLLECTIVELY REFERRED TO HEREAFTER AS A TRANSFER), AT THE EXPENSE OF THE APPLICANT (WHICH PAYMENT SHALL NOT BE A CONDITION TO ANY TRANSFER), ONE OR MORE TIMES BUT IN EACH INSTANCE TO A SINGLE BENEFICIARY AND ONLY IN THE FULL AMOUNT AVAILABLE TO BE DRAWN UNDER THE LETTER OF CREDIT. ANY, SUCH TRANSFER MAY BE EFFECTED ONLY UPON PRESENTATION TO US, THE ISSUING BANK, AT THE BELOW SPECIFIED OFFICE, OF THE ATTACHED "EXHIBIT A" DULY COMPLETED AND EXECUTED BY THE BENEFICIARY AND ACCOMPANIED BY THE ORIGINAL LETTER OF CREDIT AND ALL AMENDMENT(S), IF ANY, ANY TRANSFER OF THIS LETTER OF CREDIT MAY NOT CHANGE THE PLACE OF EXPIRATION OF

THE LETTER OF CREDIT FROM OUR BELOW SPECIFIED OFFICE. EACH TRANSFER SHALL BE EVIDENCED BY OUR ENDORSEMENT ON THE REVERSE OF THE ORIGINAL LETTER OF CREDIT AND WE SHALL FORWARD THE ORIGINAL LETTER OF CREDIT TO THE TRANSFEREE.

ALL DEMANDS FOR PAYMENT SHALL BE MADE BY PRESENTATION OF THE DATED CERTIFICATION PRIOR TO A.M. TIME, ON A BUSINESS DAY AT OUR OFFICE (THE "BANK'S OFFICE") AT: , ATTENTION: STANDBY LETTER OF CREDIT SECTION OR BY FACSIMILE TRANSMISSION AT: ( ) ; AND SIMULTANEOUSLY UNDER TELEPHONE ADVICE TO: ( ) , ATTENTION: STANDBY LETTER OF CREDIT NEGOTIATION SECTION WITH ORIGINALS TO FOLLOW BY OVERNIGHT COURIER SERVICE.

PAYMENT AGAINST CONFORMING PRESENTATIONS HEREUNDER SHALL BE MADE BY BANK IN IMMEDIATELY AVAILABLE U.S. FUNDS DURING NORMAL BUSINESS HOURS OF THE BANK'S OFFICE WITHIN TWO (2) BUSINESS DAYS AFTER PRESENTATION NOTWITHSTANDING ANYTHING TO THE CONTRARY IN ARTICLE 13B OR ARTICLE 14(D)(I) OF THE UNIFORM CUSTOMS AND PRACTICE FOR DOCUMENTARY CREDITS (1993 REVISION), INTERNATIONAL CHAMBER OF COMMERCE, PUBLICATION NO. 500

WE HEREBY CERTIFY THAT THIS IS AN UNCONDITIONAL AND IRREVOCABLE CREDIT AND AGREE WITH THE DRAWERS, ENDORSERS AND BONAFIDE HOLDERS THAT THE DRAFTS DRAWN UNDER AND IN ACCORDANCE WITH THE TERMS AND CONDITIONS OF THIS LETTER OF CREDIT SHALL BE DULY HONORED UPON PRESENTATION TO THE DRAWEE, IF NEGOTIATED ON OR BEFORE THE EXPIRATION DATE OF THIS CREDIT.

EXCEPT AS OTHERWISE EXPRESSLY STATED, THIS LETTER OF CREDIT IS SUBJECT TO THE UNIFORM CUSTOMS AND PRACTICE FOR DOCUMENTARY CREDITS (1993 REVISION), INTERNATIONAL CHAMBER OF COMMERCE, PUBLICATION NO. 500.

AUTHORIZED SIGNATURE

AUTHORIZED SIGNATURE

**ANNEX 1**

**BILL OF EXCHANGE**

DATE:

AT SIGHT OF THIS BILL OF EXCHANGE

**P**AY TO THE ORDER OF US DOLLARS (US $ )

**DRAWN UNDER**

**CREDIT NUMBER NO.** **DATED**

**T**O:

**Authorized Signature**

EXHIBIT “A”

DATE:

TO: _____

_____

RE: STANDBY LETTER OF CREDIT
NO. _____
ISSUED BY _____

LADIES AND GENTLEMEN:

FOR VALUE RECEIVED, THE UNDERSIGNED BENEFICIARY HEREBY IRREVOCABLY TRANSFERS TO:

(NAME OF TRANSFEREE) _____

(ADDRESS) _____

_____

ALL RIGHTS OF THE UNDERSIGNED BENEFICIARY TO DRAW UNDER THE ABOVE LETTER OF CREDIT UP TO ITS AVAILABLE AMOUNT AS SHOWN ABOVE AS OF THE DATE OF THIS TRANSFER.

BY THIS TRANSFER, ALL RIGHTS OF THE UNDERSIGNED BENEFICIARY IN SUCH LETTER OF CREDIT ARE TRANSFERRED TO THE TRANSFEREE. TRANSFEREE SHALL HAVE THE SOLE RIGHTS AS BENEFICIARY THEREOF, INCLUDING SOLE RIGHTS RELATING TO ANY AMENDMENTS, WHETHER INCREASES OR EXTENSIONS OR OTHER AMENDMENTS, AND WHETHER NOW EXISTING OR HEREAFTER MADE. ALL AMENDMENTS ARE TO BE ADVISED DIRECT TO THE TRANSFEREE WITHOUT NECESSITY OF ANY CONSENT OF OR NOTICE TO THE UNDERSIGNED BENEFICIARY.

THE ORGINAL OF SUCH LETTER OF CREDIT IS RETURNED HEREWITH, AND WE ASK YOU TO ENDORSE THE TRANSFER ON THE REVERSE THEREOF, AND

FORWARD IT DIRECTLY TO THE TRANSFEREE WITH YOUR CUSTOMARY NOTICE OF TRANSFER.

SINCERELY,

(BENEFICIARY'S NAME)

SIGNATURE OF BENEFICIARY

SIGNATURE AUTHENTICATED

(Name of Bank)

(authorized signature)

**Exhibit 10.13**

EXECUTION COPY

Confidential Materials omitted and filed separately with the
Securities and Exchange Commission. Double asterisks denote omissions.

# DISCOVERY AND DEVELOPMENT COLLABORATION

# AND LICENSE AGREEMENT

by and between

AGIOS PHARMACEUTICALS, INC.

and

CELGENE CORPORATION

TABLE OF CONTENTS

# DISCOVERY AND DEVELOPMENT COLLABORATION AND LICENSE AGREEMENT

This Discovery and Development Collaboration and License Agreement (this "Agreement") is entered into as of April 14, 2010 (the "Effective Date"), by and between Agios Pharmaceuticals, Inc., a corporation organized and existing under the laws of the State of Delaware and having its principal office at 38 Sidney St., 2nd Floor, Cambridge, MA 02139-4169 ("Agios"), and Celgene Corporation, a corporation organized and existing under the laws of the State of Delaware and having its principal office at 86 Morris Avenue, Summit, NJ 07901 ("Celgene").

## INTRODUCTION

1. Agios has expertise and technology relating to the discovery and development of drug candidates that modulate the metabolic functioning of cancer cells.

2. Celgene is engaged in the discovery, development and commercialization of therapeutics in the fields of oncology and immunological diseases.

3. Celgene and Agios desire to establish a collaboration to apply Agios' expertise and technology to the discovery and validation of novel targets, primarily cancer metabolism targets, and the discovery and development of associated therapeutics, primarily in the Oncology Field, and to provide for the development and commercialization of such therapeutics, all on the terms and conditions set forth in this Agreement.

NOW, THEREFORE, in consideration of the respective representations, warranties, covenants and agreements contained herein, and for other valuable consideration, the receipt and adequacy of which are hereby acknowledged, Agios and Celgene hereby agree as follows:

## Article I
## Definitions

When used in this Agreement, each of the following terms shall have the meanings set forth in this Article I:

Section 1.1 "Active" or "Activity" means, with respect to a given compound in relation to a given Collaboration Target, that such compound meets the baseline criteria for activity in modulating such Collaboration Target, the mechanism of action of which is a specific interaction with such Collaboration Target. The general baseline criteria for activity in modulating Collaboration Targets are set forth on Schedule 1.1. The JRC by Mutual Consent may establish more specific baseline criteria for activity in modulating a particular Collaboration Target based on such general baseline criteria.

Section 1.2 "Affiliate" means, as to any Person, any other Person that, directly or indirectly through one or more intermediaries, controls, is controlled by or is under common control with such Person, as the case may be, for so long as such control exists. As used in this Section 1.2, "control" means: (a) to possess, directly or indirectly, the power to direct the management and policies of a Person, whether through ownership of voting securities or by contract relating to voting rights or corporate governance; or (b) direct or indirect beneficial ownership of at least fifty percent (50%) (or such lesser percentage that is the maximum allowed to be owned by a foreign Person in a particular jurisdiction) of the voting share capital in a Person.

Section 1.3 "Agios Collaboration Intellectual Property," "Agios Collaboration Know-How" and "Agios Collaboration Patent Rights" means, respectively, the Collaboration Intellectual Property Controlled by Agios, the Collaboration Know-How Controlled by Agios and the Collaboration Patent Rights Controlled by Agios.

Section 1.4 "Agios Intellectual Property" means Agios Know-How and Agios Patent Rights, collectively.

Section 1.5 "Agios Know-How" means any Know-How that is (a) Controlled by Agios as of the Effective Date or during the Term, and (b) necessary or useful for the Development, Manufacture and/or Commercialization of Collaboration Targets, Celgene Reverted Targets, Collaboration Compounds, Independent Compounds, Celgene Reverted Compounds, Celgene Reverted Products, Licensed Compounds and/or Licensed Products; but excluding (i) Collaboration Know-How, and (ii) Know-How to the extent specifically related to any Target other than a Collaboration Target or Celgene Reverted Target.

Section 1.6 "Agios Patent Rights" means any Patent Rights that (a) are Controlled by Agios as of the Effective Date or during the Term, and (b) Cover, or are otherwise necessary or useful for Development, Manufacture and/or Commercialization of, a Collaboration Target, Celgene Reverted Target, Collaboration Compound, Independent Compound, Celgene Reverted Compound, Celgene Reverted Product, Licensed Compound or Licensed Product (including the composition of matter, manufacture or any use thereof); but excluding (i) Collaboration Patent Rights, and (ii) Patent Rights to the extent specifically related to a Target other than a Collaboration Target or Celgene Reverted Target. Agios Patent Rights as of the Effective Date are as set forth on Schedule 1.6.

Section 1.7 "Agios Reverted Compound(s)" means:

(a) the Picked Compounds with respect to each Picked Validated Program selected by Agios pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii) or Section 15.5);

(b) each Development Candidate with respect to each Optionable Program for which Celgene either rejects the Development Candidate or Celgene does not exercise the Celgene Program Option; provided that, for this purpose and notwithstanding Section 1.47, "Development Candidate" means (i) the one (1) Collaboration Compound that meets the Clinical Candidate Guidelines nominated by Agios, (2) the Back-Up Compound identified by Agios pursuant to Section 3.6(b)(ii), and (3) up to [**] additional Back-Up Compounds identified by the JRC (or the JDC, as applicable) by Mutual Consent at the DC Selection Stage;

(c) notwithstanding Section 1.66, (i) a single Independent Compound under each Independent Program that becomes an Agios Reverted Program that is Developed prior to such Independent Program becoming an Agios Reverted Program, and (ii) [**] Back-Up Compounds identified by the JRC (or the JDC, as applicable) by Mutual Consent at the time of such Independent Program becoming an Agios Reverted Program; and

(d) with respect to any other Program that becomes an Agios Reverted Program in accordance with Section 3.12, (i) one (1) Collaboration Compound that is Active against the Agios Reverted Target and Developed under the applicable Program (but only to the extent Developed prior to such Program becoming an Agios Reverted Program), and (ii) [**] Back-Up Compounds identified by the JRC (or the JDC, as applicable) by Mutual Consent at the time of such Program becoming an Agios Reverted Program.

Section 1.8 "Agios Reverted Product" means a product that contains as an active ingredient any Agios Reverted Compound.

Section 1.9 "Agios Reverted Target" means, with respect to each Discovery Program or Independent Program that becomes an Agios Reverted Program in accordance with Section 3.12, the Target which was the subject of such Discovery Program or Independent Program, as applicable.

Section 1.10 "Agreement Compounds" means Collaboration Compounds, Residual Program Compounds, Development Candidates, Picked Compounds, Picked Products, Back-Up Compounds, Buy-In Compounds, Buy-In Products, Split Compounds, Split Products, Co-Commercialized Products, Licensed Compounds, Licensed Products, Independent Compounds, Agios Reverted Compounds, Agios Reverted Products, Celgene Reverted Compounds and/or Celgene Reverted Products.

Section 1.11 "Analog" means, with respect to a specific Development Candidate, Back-Up Compound, Buy-In Compound, Picked Compound or Celgene Reverted Compound against a specific Target, a molecule (a) that contains the same core structure (meaning [**]) as such specific Development Candidate, Back-Up Compound, Buy-In Compound, Picked Compound, or Celgene Reverted Compound or that contains [**] within the core structure of any of the foregoing; (b) that modulates the Target to which such Development Candidate, Back-Up Compound, Buy-In Compound, Picked Compound, or Celgene Reverted Compound is directed; and (c) that has a level of potency against such Target, expressed as [**], as applicable, for the Development Candidate as defined in Section 1.47(a), the Buy-In Compound as defined in Section 1.14(a)(i), the most advanced Picked Compound as defined in Section 1.98(a)(i), or the most advanced Celgene Reverted Compound as defined in Section 1.23(a), respectively, for such Target, as measured in an [**] assay for such Target designated by the JDC.

Section 1.12 "Back-Up Compound" means, with respect to each Program, Agios Reverted Program or Celgene Reverted Program, as applicable, a Collaboration Compound (a) that meets, [**], the Clinical Candidate Guidelines under such Program, Agios Reverted Program or Celgene Reverted Program, as applicable, and (b) that is directed to the same Collaboration Target, Agios Reverted Target or Celgene Reverted Target, as applicable, as the lead Collaboration Compound in such Program, Agios Reverted Program or Celgene Reverted Program.

Section 1.13 "Business Day" means a day other than a Saturday or Sunday or federal holiday in Cambridge, Massachusetts or Summit, New Jersey.

Section 1.14 "Buy-In Compound" means

(a) with respect to each Independent Program that becomes a Buy-In Program for which Celgene is the Commercializing Party, (i) the Collaboration Compound with respect to which the IND Acceptance is achieved, (ii) Back-Up Compounds identified by the JRC (or the JDC, as applicable) by Mutual Consent at the time of the Buy-In Party's exercise of its Buy-In Right, (iii) any Analogs, Derivatives, [**] of any chemical entity identified in (i) or (ii), and (iv) any compound that contains [**] of any of the foregoing in (i) or (ii) or any series of compounds demonstrating activity against the Target within such Program, in each case as determined by the JRC (or the JDC, as applicable) by Mutual Consent at the time of the Buy-In Party's exercise of its Buy-In Right; and

(b) with respect to each Independent Program that becomes a Buy-In Program for which Agios is the Commercializing Party, (i) the Collaboration Compound with respect to which the IND Acceptance is achieved, and [**] Back-Up Compounds identified by the JRC (or the JDC, as applicable) by Mutual Consent at the time of the Buy-In Party's exercise of its Buy-In Right.

Section 1.15 "Buy-In Product" means any Licensed Product that contains as an active ingredient any Buy-In Compound.

Section 1.16 "Buy-In Program" means any Independent Program for which the Buy-In Party exercises its Buy-In Right pursuant to Section 3.11.

Section 1.17 "Calendar Quarter" means a calendar quarter ending on the last day of March, June, September or December; provided, however, that the first Calendar Quarter shall begin on the Effective Date and end on the last day of June following the Effective Date.

Section 1.18 "Calendar Year" means a period of time commencing on January 1 and ending on the following December 31; provided, however, that the first Calendar Year shall begin on the Effective Date and end on December 31, 2010.

Section 1.19 "Celgene Collaboration Intellectual Property," "Celgene Collaboration Know-How" and "Celgene Collaboration Patent Rights" means, respectively, the Collaboration Intellectual Property Controlled by Celgene, the Collaboration Know-How Controlled by Celgene and the Collaboration Patent Rights Controlled by Celgene.

Section 1.20 "Celgene Intellectual Property" means Celgene Know-How and Celgene Patent Rights, collectively.

Section 1.21 "Celgene Know-How" means any Know-How that is (a) Controlled by Celgene as of the Effective Date or during the Option Term; (b) necessary for the Development, Manufacture and/or Commercialization of Collaboration Targets, Collaboration Compounds, Licensed Compounds and/or Licensed Products; and (c) contributed by Celgene, in Celgene's sole discretion, to the Collaboration, as evidenced by written notice from Celgene to Agios; but excluding (i) Collaboration Know-How, and (ii) Know-How to the extent specifically related to any Target other than a Collaboration Target.

Section 1.22 "Celgene Patent Rights" means any Patent Rights that (a) are Controlled by Celgene as of the Effective Date or during the Option Term; (b) Cover a Collaboration Target, Collaboration Compound, Licensed Compound and/or Licensed Product (including the composition of matter, manufacture or any use thereof); and (c) are contributed by Celgene, in Celgene's sole discretion, to the Collaboration, as evidenced by written notice from Celgene to Agios; but excluding (i) Collaboration Patent Rights, and (ii) Patent Rights to the extent specifically related to a Target other than a Collaboration Target.

Section 1.23 "Celgene Reverted Compound" means, with respect to each Independent Program that becomes a Celgene Reverted Program, (a) the Independent Compound(s) Developed under such Independent Program prior to such Independent Program becoming a Celgene Reverted Program, (b) Back-Up Compounds identified by the JRC (or the JDC) by Mutual Consent at the time of such Independent Program becoming a Celgene Reverted Program, (c) any Analogs, Derivatives, [**] of any chemical entity identified in (a) or (b), and (d) any compound that contains [**] of any of the foregoing in (a) or (b) or any series of compounds demonstrating activity against the Target within such Program, in each case as determined by the JRC (or the JDC, as applicable) by Mutual Consent at the time of such Independent Program becoming a Celgene Reverted Program.

Section 1.24 "Celgene Reverted Product" means any product that contains as an active ingredient a Celgene Reverted Compound.

Section 1.25 "Celgene Reverted Program" means any Independent Program Developed by Celgene and for which Agios does not exercise its Buy-In Right pursuant to Section 3.11.

Section 1.26 "Celgene Reverted Target" means, with respect to any Independent Program Developed by Celgene that becomes a Celgene Reverted Program in accordance with Section 3.11(c)(iii), the Target which was the subject of such Independent Program.

Section 1.27 "Clinical Trial" means a Phase I Study, a Phase II Study, a Phase III Study, a Phase IV Study or a combination of any of the foregoing studies.

Section 1.28 "Co-Commercialized Product" means a Licensed Product under an Optionable Program for which Celgene exercises the Celgene Program Option, excluding (a) any Split Products and (b) any Licensed Product in the US Territory under a Split Program if, after any Agios Opt-Out, Celgene elects not to assume US Territory rights as set forth in Section 3.10(c)(ii).

Section 1.29 "Co-Commercialized Program" means any Licensed Program that relates to a Co-Commercialized Product.

Section 1.30 "Collaboration" means the activities performed or to be performed by a Party or Parties, as the case may be, under or in connection with a Program under this Agreement.

Section 1.31 "Collaboration Compound" means a chemical entity Controlled by Agios (or, if the JRC (or the JDC, as applicable) agree by Mutual Consent in accordance with Section 3.6(a)(i) or Section 3.6(a)(ii), Controlled by Celgene) that is Active against a Collaboration Target as of the date of its inclusion in a Discovery Program, Independent Program or Licensed Program, as applicable, or found to be Active against a Collaboration

Target in the course of conducting a Discovery Program, Independent Program or Licensed Program, as applicable. For purposes of clarity, any Agios Reverted Compound and any Celgene Reverted Compound shall no longer be deemed a "Collaboration Compound" hereunder.

Section 1.32 "Collaboration Intellectual Property" means Collaboration Know-How and Collaboration Patent Rights, collectively.

Section 1.33 "Collaboration Know-How" means any Know-How or interest therein, that is developed or generated, either solely by or on behalf of a Party and/or its Affiliate(s) or jointly by or on behalf of both Parties and/or their Affiliate(s), in the conduct of the Collaboration.

Section 1.34 "Collaboration Patent Rights" means any Patent Rights or interest therein Controlled by either Party or Controlled jointly by the Parties that Cover Collaboration Know-How.

Section 1.35 "Collaboration Target(s)" means the Target(s) on the Target List. For purposes of clarity, any Agios Reverted Target and any Celgene Reverted Target shall no longer be deemed a "Collaboration Target" hereunder.

Section 1.36 "Commercialization" or "Commercialize" means any activities directed to using, marketing, promoting, distributing, importing, offering to sell, and/or selling a product, after or in expectation of receipt of Regulatory Approval for such product (but excluding Development), including carrying out Phase IV Studies commenced after First Commercial Sale of a Licensed Product anywhere in the world.

Section 1.37 "Commercializing Party" means (a) Agios, with respect to a Split Product in the US Territory, unless and until any Agios Opt-Out occurs, (b) Celgene, with respect to a Split Product in the ROW Territory and, upon the occurrence of any Agios Opt-Out and Celgene's assumption of such rights pursuant to Section 3.10(c), the US Territory, (c) Celgene, with respect to any Licensed Product (other than a Split Product or any Buy-In Product) and any Celgene Reverted Product, and (d) the Party that is not the Buy-In Party, with respect to any Buy-In Product.

Section 1.38 "Commercially Reasonable Efforts" means, with respect to the performing Party, the carrying out of obligations of such Party in a diligent, expeditious and sustained manner, including the allocation of a commercially reasonable level of personnel and financial resources, but in no event less than such level of resources that an established biopharmaceutical company [**] typically devotes to products of similar market potential at a similar stage in its development or product life, taking into account scientific and commercial factors, including commercial Manufacturing, issues of safety and efficacy, product profit, difficulty in developing or manufacturing the Collaboration Compound, Licensed Compound or Licensed Product, competitiveness of alternative Third Party products in the marketplace, the patent or other proprietary position of the Collaboration Compound, Licensed Compound or Licensed Product, the regulatory requirements involved and the potential profitability for the performing Party of the Collaboration Compound, Licensed Compound or Licensed Product marketed or to be marketed.

Section 1.39 "Companion Diagnostic" means a biomarker or diagnostic test that may be used with a Licensed Product, or may be developed by the Parties pursuant to Section 3.14, to generate a result for the purposes of diagnosing a disease or condition, or to facilitate the application of the Licensed Product that is used in the cure, mitigation, treatment, or prevention of disease, including a biomarker or diagnostic test used to diagnose the likelihood that a specific patient will contract a certain type of cancer or to predict which patients are suitable candidates for a specific form of chemotherapy.

Section 1.40 "Completion of Phase I MAD" means the completion of the first Phase I MAD Study and the delivery by Agios of a final written report meeting the Phase I Report Criteria, as set forth in Section 3.6(b)(iii)(A)(2). For avoidance of doubt, "Completion of Phase I MAD" does not include the development of a protocol for a Phase II Study.

Section 1.41 "Confidential Information" means (a) all confidential or proprietary information relating to Collaboration Targets, Celgene Reverted Targets, Agios Reverted Targets, Agreement Compounds, and Target Indications, and (b) all other confidential or proprietary documents, technology, Know-How or other information (whether or not patentable) actually disclosed by one Party to the other pursuant to this Agreement or the Prior Confidentiality Agreement, including information regarding a Party's technology, products, business information or objectives and reports and audits under Sections 9.4(a)(ii), 9.4(d), 9.5(e), 9.8 and 9.10, and all proprietary biological materials of a Party. Notwithstanding the foregoing, at such point as a Target is removed from the Target List (whether removed by Mutual Consent of the JRC, upon expiration of the Option Term (or, if applicable, with respect to any Extended Program, following any Post-Option Extension), or otherwise), the identity of such Target shall not be the Confidential Information of either Party, unless added back to the Target List in accordance with Section 3.5.

Section 1.42 "Control" or "Controlled" means, with respect to any (a) Know-How or other information or materials, (b) any compounds, or (c) intellectual property right, the possession (whether by license (other than a license granted under this Agreement) or ownership) by a Party of the ability to grant to the other Party access and/or a license, as provided herein, without violating the terms of any agreement with any Third Party existing as of the Effective Date or thereafter during the Term.

Section 1.43 "Core Patent Rights" means those Patent Rights comprising [**] claims.

Section 1.44 "Cover," "Covering" or "Covered" means that, with respect to a product or technology, but for a license granted to a Person under a Valid Claim included in the Patent Rights under which such license is granted, the Development, Manufacture, Commercialization and/or other use of such product or practice of such technology by such Person would infringe any Valid Claim of any patent included in such Patent Rights or, with respect to a Valid Claim included in any patent application, would infringe such Valid Claim if such patent application were to issue as a patent.

Section 1.45 "Derivative" means, with respect to a specific Development Candidate, Back-Up Compound, Buy-In Compound, Picked Compound or Celgene Reverted Compound against a specific Target, any molecule (a) that is synthesized using a synthetic route that is [**] used for a specific Development Candidate, Back-Up Compound, Buy-In Compound, Picked Compound or Celgene Reverted Compound against a specific Target, respectively, such that such molecule is derived from, by a maximum of [**] synthetic steps (excluding protection/de-protection steps), such a specific Development Candidate, Back-Up Compound, Buy-In Compound, Picked Compound or Celgene Reverted Compound, respectively, and such that any compound modifications (*i.e.*, differences between such molecule and the corresponding Development Candidate, Back-up Compound, Buy-In Compound, Picked Compound or Celgene Reverted Compound) are readily determined to be [**] or [**] the corresponding Development Candidate, Back-Up Compound, Buy-In Compound, Picked Compound, or Celgene Reverted Compound, respectively, and (b) that has a level of potency against such Target, expressed as [**], as applicable, for the Development Candidate as defined in Section 1.47(a), the Buy-In Compound as defined in Section 1.14(a)(i), the most advanced Picked Compound as defined in Section 1.98(a)(i), or the most advanced Celgene Reverted Compound as defined in Section 1.23(a), respectively, for such Target, as measured in an [**] assay for such Target designated by the JDC.

Section 1.46 "Develop" or "Development" means discovery, research, preclinical, non-clinical and clinical development activities, including activities relating to screening, assays, test method development and stability testing, toxicology, pharmacology, formulation, quality assurance/quality control development, Clinical Trials (excluding a Phase IV Study commenced after First Commercial Sale of a product anywhere in the world), technology transfer, statistical analysis, process development and scale-up, pharmacokinetic studies, data collection and management, report writing, and other pre-Regulatory Approval activities.

Section 1.47 "Development Candidate" means, with respect to each Program (excluding any Independent Program), (a) a Collaboration Compound that meets the Clinical Candidate Guidelines, as determined in accordance with Section 3.6(b), (b) the Back-Up Compound identified by Agios pursuant to Section 3.6(b)(ii) and any other Back-Up Compounds identified by the JRC (or the JDC, as applicable) by Mutual Consent at the DC Selection Stage, (c) any [**] of any chemical entity identified in (a) or (b), and (d) any compound that contains [**] of any of the foregoing in (a) or (b) or any series of compounds demonstrating activity against the Target within such Program, in each case as determined by the JRC (or the JDC, as applicable) by Mutual Consent within [**] days of the nomination of the compound described in the foregoing (a) in accordance with Sections 3.6(b) and 3.8(b).

Section 1.48 "Development Cost Initiation Date" means (a) with respect to any Co-Commercialized Program for which Celgene exercises the Celgene Program Option at IND Acceptance, [**]; (b) with respect to any Co-Commercialized Program for which Celgene exercises the Celgene Program Option at Completion of Phase I MAD, [**]; (c) with respect to a Buy-In Program, [**]; (d) with respect to any Picked Validated Program selected by Celgene, [**]; and (e) with respect to any Split Program, [**].

Section 1.49 "Discovery Program" means, for each Collaboration Target, the activities performed or to be performed by Agios (or Celgene, with its prior written consent) in accordance with the Discovery Plan and under the overall direction of the JRC and JSC to discover and Develop Collaboration Compounds directed to such Collaboration Target during the Discovery Term. For purposes of clarity, unless the JRC decides otherwise by Mutual Consent, the Parties intend that activities directed to a distinct method of modulating a Collaboration Target shall not be deemed a distinct Discovery Program (*i.e.*, more than one Discovery Program cannot be directed to the same Collaboration Target). For purposes of clarity, if and when a Discovery Program becomes an Independent Program, Licensed Program, Agios Reverted Program, or Celgene Reverted Program, such Independent Program, Licensed Program, Agios Reverted Program, or Celgene Reverted Program shall no longer be deemed a "Discovery Program" for purposes of this Agreement (unless or until any such Independent Program again becomes a Discovery Program pursuant to Section 3.5(a)(i) or Section 3.5(b)(ii)(B)).

Section 1.50 "Discovery Term" means, with respect to each Discovery Program, the period commencing on the Effective Date and ending upon the earliest of:

(a) rejection or waiver by Celgene at the DC Selection Stage of any confirmed Development Candidate Developed under such Discovery Program pursuant to Section 3.6(b) (or failure to exercise Celgene's right to designate such confirmed Development Candidate for further Development within the exercise period set forth in Section 3.6(b)(iii)), subject to Celgene's right to defer making a DC Commitment pursuant to Section 3.6(d);

(b) if Celgene designates a confirmed Development Candidate for further Development pursuant to Section 3.6(b), the earlier of (i) the Option Exercise Date and (ii) rejection or waiver by Celgene of its right to exercise the Celgene Program Option (or failure to exercise the Celgene Program Option within the applicable Celgene Option Exercise Period), subject to Celgene's right to defer making a DC Commitment pursuant to Section 3.6(d);

(c) such time as such Discovery Program becomes an Independent Program, Agios Reverted Program or a Celgene Reverted Program, as applicable;

(d) such time as the Collaboration Target to which such Discovery Program relates is removed from the Target List pursuant to Section 3.5(b) below, unless such Collaboration Target is added back to the Target List as part of a Discovery Program pursuant to such Section 3.5(a) or 3.5(b), in which event the Discovery Term for such Collaboration Target shall again be in effect; and

(e) the end of the Option Term; provided, however, that, with respect to any Discovery Program directed to [**] that has not yet reached the DC Selection Stage as of the end of the Option Term, the Discovery Term for each such Discovery Program shall not end until the earlier of (i) the [**] year following the end of the Option Term and (ii) IND Acceptance for a Development Candidate in such Discovery Program; provided further that, with respect to any Extended Program, the Discovery Term for each such Extended Program shall not end at the end of the Option Term but shall continue until the expiration of the Post-Option Extension.

Section 1.51 "Executive Officers" means Celgene's Chief Executive Officer (or the officer or employee of Celgene then serving in a substantially equivalent capacity) or his designee and Agios' Chief Executive Officer (or the officer or employee of Agios then serving in a substantially equivalent capacity) or his designee; provided that any such designee must have decision-making authority on behalf of the applicable Party.

Section 1.52 "Exclusivity Period" means, as to each Licensed Program and each Celgene Reverted Program, as applicable, on a Program-by-Program (or Celgene Reverted Program-by-Celgene Reverted Program) and Collaboration Target-by-Collaboration Target (or Celgene Reverted Target-by-Celgene Reverted Target) basis, the period commencing on the earlier of (a) [**] and (b) [**], and ending upon the earlier of (x) [**], and (y) [**] with respect to all Licensed Products in the applicable Licensed Program or all Celgene Reverted Products in the applicable Celgene Reverted Program, as applicable. As to each Independent Program, on a Program-by-Program and Collaboration Target-by-Collaboration Target basis, "Exclusivity Period" means the period commencing upon the expiration of the Option Term and ending upon the earliest of (A) [**] with respect to the applicable Independent Program, (B) [**], and (C) [**]; provided that, if an Independent Program becomes a Buy-In Program or a Celgene Reverted Program, the "Exclusivity Period" set forth in the immediately preceding sentence shall apply.

Section 1.53 "Existing Third Party Agreement" means any agreement listed on Schedule 1.53.

Section 1.54 "FDA" means the United States Food and Drug Administration, or any successor agency thereof.

Section 1.55 "FDCA" means the United States Federal Food, Drug, and Cosmetic Act, and the regulations promulgated thereunder, each as amended from time to time.

Section 1.56 "Field" means the treatment, control, mitigation, prevention or cure or diagnosis of any Indications.

Section 1.57 "First Commercial Sale" means the first commercial sale of a Royalty-Bearing Product by the Commercializing Party, its Affiliates, distributors and/or agents in a country in an arms' length transaction to a Third Party following receipt of applicable Regulatory Approval of such product in such country. Sales for test marketing or clinical trial purposes shall not constitute a First Commercial Sale.

Section 1.58 "FPD" means, with respect to a Clinical Trial, the dosing of the first human subject with any Collaboration Compound, Licensed Compound or Licensed Product, as applicable, in such Clinical Trial.

Section 1.59 "Generic Competition" means, with respect to a Royalty-Bearing Product in a given country in a given Calendar Year, that, during such Calendar Year [**] Generic Products shall be commercially available in such country.

Section 1.60 "Generic Product" means, as to a Royalty-Bearing Product, any product (including a "generic product" approved by way of an Abbreviated New Drug Application by the FDA (or equivalent regulatory mechanism for another Regulatory Authority), "biogeneric," "follow-on biologic," "follow-on biological product," "follow-on protein product," "similar biological medicinal product," or "biosimilar product") that, in each case, (a) is sold by a Third

Party that is not a sublicensee of the Commercializing Party or any of its Affiliates and that has not otherwise been authorized by the Commercializing Party or any of its Affiliates under a Regulatory Approval granted by a Regulatory Authority to such Third Party that is based upon or relies upon the Regulatory Approval granted by such Regulatory Authority for such Royalty-Bearing Product; and (b) in the United States, is "therapeutically equivalent," "comparable," "biosimilar," or "interchangeable," as evaluated by the FDA, applying the definition of "therapeutically equivalent" set forth in the preface to the then-current edition of the FDA publication "Approved Drug Products With Therapeutic Equivalence Evaluations" or any other definitions set forth in the U.S. Code, FDA regulations, or other source of U.S. Law and, outside the United States, meets such equivalent determination by the applicable Regulatory Authorities (including a determination that the product is "comparable," "interchangeable," "bioequivalent," or "biosimilar" with respect to the Royalty-Bearing Product), in each case, as is necessary to permit a pharmacist or other individual authorized to dispense pharmaceuticals under Law to substitute one product for another product in the absence of specific instruction from a physician or other authorized prescriber under Law.

Section 1.61 "IDH1" means (alias PICD, IDPC; UniProt identifier O75874) the persoxisomal/cytosolic form of isocitrate dehydrogenase that catalyzes the NADP+ dependent conversion of isocitrate to alpha-ketoglutarate.

Section 1.62 "IND" means any Investigational New Drug application, filed with the FDA pursuant to Part 312 of Title 21 of the U.S. Code of Federal Regulations, including any supplements or amendments thereto. References herein to IND shall include, to the extent applicable, any comparable filing(s) outside the United States.

Section 1.63 "IND Acceptance" means thirty (30) days following the filing of an IND with the FDA; provided that the FDA has not provided any communication indicating that the conduct of clinical activities described in such IND may not begin within thirty (30) days after such filing. In the event that any such communication is provided by the FDA, "IND Acceptance" means the date that the Parties are permitted by the FDA to begin clinical activities. If the Parties both agree, "IND Acceptance" shall mean the date, following filing of an IND with a Regulatory Authority (other than the FDA), that Agios receives a written communication from such Regulatory Authority pursuant to which the conduct of clinical activities described in the appropriate submissions is permitted to begin.

Section 1.64 "IND-Enabling Studies" means studies that are required to meet the requirements for filing an IND with a Regulatory Authority, including ADME (absorption, distribution, metabolism, and excretion) and GLP (good laboratory practice) toxicology studies, or studies required for the preparation of the CMC (chemistry, manufacturing, and controls) section of such IND, including studies relating to analytical methods and purity analysis, and formulation and Manufacturing development studies, all as necessary to obtain the permission of the Regulatory Authority to begin the human clinical testing proposed to be pursued under the Discovery Plan or Development Plan, as applicable. Unless the Parties mutually agree, all IND-Enabling Studies will be for purposes of filing an IND with the FDA.

Section 1.65 "IND Study Criteria" means the criteria set forth on Schedule 1.65 with respect to IND-Enabling Studies. The IND Study Criteria may not be amended other than by Mutual Consent of the JDC.

Section 1.66 "Independent Compound" means, with respect to each Independent Program, all Collaboration Compounds on the Compound List for such Independent Program immediately prior to it becoming an Independent Program; provided that any Collaboration Compounds that are also on the Compound List of another Program shall not be deemed "Independent Compounds"; provided further that, as the Compound List for such Independent Program becomes narrower, as contemplated by Section 3.6(a)(iii), Collaboration Compounds removed from the Compound List for such Independent Program shall no longer be deemed Independent Compounds but shall become Residual Program Compounds.

Section 1.67 "Independent Program" means a Discovery Program which a Party elects to Develop pursuant to Section 3.5(a) or 3.5(b).

Section 1.68 "Independent Target" means, with respect to each Discovery Program that becomes an Independent Program, the Target that was the subject of such Discovery Program.

Section 1.69 "Indication" means any human disease, condition or syndrome, or sign or symptom of, or associated with, a human disease or condition.

Section 1.70 "Know-How" means any tangible or intangible trade secrets, know-how, expertise, discoveries, inventions, information, data or materials, including ideas, concepts, formulas, methods, procedures, designs, technologies, compositions, plans, applications, technical data, assays, manufacturing information or data, samples, chemical and biological materials and all derivatives, modifications and improvements thereof.

Section 1.71 "Law" means any law, statute, rule, regulation, ordinance or other pronouncement having the effect of law, of any federal, national, multinational, state, provincial, county, city or other political subdivision, as from time to time enacted, repealed or amended, including good clinical practices and adverse event reporting requirements, guidance from the International Conference on Harmonization or other generally accepted conventions, the FDCA and similar laws and regulations in countries outside the United States, and all other rules, regulations and requirements of the FDA and other applicable Regulatory Authorities.

Section 1.72 "Lead Party" means:

(a) With respect to any Discovery Program, Agios until the earlier of the Option Exercise Date and the end of the Discovery Term for such Discovery Program;

(b) With respect to any Co-Commercialized Program, Celgene following the Option Exercise Date;

(c) With respect to any Picked Validated Program selected by Celgene pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii), Section 3.6(c) or Section 15.5), Celgene following Celgene's selection of such Validated Program pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii), Section 3.6(c) or Section 15.5);

(d) With respect to any Split Program in the US Territory, Agios following the Option Exercise Date for such Split Program (unless and until any Agios Opt-Out occurs), except that, if Celgene is the Party responsible for Manufacturing, then Celgene shall be the Lead Party in the US Territory with respect to Manufacturing matters, unless a supply failure occurs under the Supply Agreement, in which event Agios shall be the Lead Party in the US Territory with respect to Manufacturing matters;

(e) With respect to any Split Program in the US Territory after an Agios Opt-Out, Celgene following such Agios Opt-Out if Celgene assumes such US Territory rights pursuant to Section 3.10(c);

(f) With respect to any Split Program in the ROW Territory, Celgene following the Option Exercise Date for such Split Program;

(g) With respect to any Celgene Reverted Program, Celgene at such time as such Program becomes a Celgene Reverted Program;

(h) With respect to any Agios Reverted Program, Agios at such time as such Program becomes an Agios Reverted Program;

(i) With respect to any Buy-In Program, the Commercializing Party; and

(j) With respect to any Independent Program, the Party that elects to undertake the independent Development of such Independent Program pursuant to Section 3.5(a) or Section 3.5(b).

Section 1.73 "Licensed Compound" means (a) any Development Candidate under a Program with respect to which Celgene has exercised the Celgene Program Option pursuant to Section 3.6 (or, as applicable, Section 15.5(a)(iv)), (b) any Picked Compound under a Picked Validated Program selected by Celgene pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii), Section 3.6(c) or Section 15.5), and (c) any Buy-In Compound.

Section 1.74 "Licensed Product" means any product that contains as an active ingredient a Licensed Compound.

Section 1.75 "Licensed Program" means, for each Collaboration Target, the activities performed or to be performed by a Party or Parties, as the case may be, in accordance with the Development Plan and/or the Commercialization Plan, as the case may be, and under the overall direction of the JDC, JCC and JSC, as applicable, to Develop, Manufacture and Commercialize Licensed Compounds and Licensed Products directed to such Collaboration Target following the Discovery Term. For purposes of clarity, a Licensed Program includes a Discovery Program for which Celgene exercises the Celgene Program Option (including a Split Program), a Picked Validated Program selected by Celgene pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii), Section 3.6(c) or Section 15.5), and, upon the Buy-In Party's exercise of its Buy-In Rights with respect to a Buy-In Program, such Buy-In Program, but excludes any Independent Program unless and until the Buy-In Party exercises its Buy-In Rights with respect to such Independent Program.

Section 1.76 "Licensee Partner" means any Third Party to whom a Party or any of its Affiliates grants a sublicense or license with respect to the Development, Manufacture or Commercialization of Licensed Products in the Field under the rights to Agios Intellectual Property, Celgene Intellectual Property or Collaboration Intellectual Property, as the case may

be, granted to such Party or Affiliate hereunder, in each case excluding (a) any Person that is granted a sublicense in accordance with Section 8.4(a), and (b) wholesale distributors or any other Third Party that purchases Licensed Product in an arm's-length transaction, where such Third Party does not have a sublicense to Develop, Manufacture or Commercialize the Licensed Product except for a limited sublicense to the extent required to enable such Third Party to perform final packaging for such Licensed Product for local distribution.

Section 1.77 "Major European Countries" means France, Germany, Italy, Spain and the United Kingdom.

Section 1.78 "Major Market" means each of the United States, Japan, and the Major European Countries.

Section 1.79 "Manufacture" or "Manufacturing" means, as applicable, all activities associated with the production, manufacture, processing, filling, packaging, labeling, shipping, and storage of a drug substance or drug product, and/or any components thereof, including process and formulation development, process validation, stability testing, manufacturing scale-up, preclinical, clinical and commercial manufacture and analytical methods development and validation, product characterization, quality assurance and quality control development, testing and release.

Section 1.80 "Manufacturing Technology" means copies of all Celgene Know-How, Agios Know-How or Collaboration Know-How, as applicable, which are necessary or useful for Manufacturing preclinical, clinical and/or commercial supply, as applicable, of Collaboration Compounds, Licensed Compounds and/or Licensed Products under a Program, including specifications, assays, batch records, quality control data, and transportation and storage requirements.

Section 1.81 "Metabolome" means enzymes, receptors, transporters that are direct exponents of cellular, or biochemical reactions (including redox reactions), in each case, that [**], *e.g.*, amino acids, nucleotides, lipids, carbohydrate monomers and dimers. For the avoidance of doubt, "Metabolome" will exclude, for example, proteins that have activity in signal transduction, epigenetic, protein translation, cellular or sub-cellular structures, gene expression, protein degradation via the ubiquitination pathway as their role in cellular function.

Section 1.82 "Mutual Consent" means a matter requiring the unanimous agreement of both Parties or both Parties' Committee members, as applicable, with each Party, in its sole discretion, being entitled to veto the matter, subject to arbitration pursuant to Section 2.9 in the case of Arbitrable Matters.

Section 1.83 "NDA" means an application submitted to a Regulatory Authority for the marketing approval of a Licensed Product, including (a) a New Drug Application, Product License Application or Biologics License Application filed with FDA or any successor applications or procedures, (b) a foreign equivalent of a U.S. New Drug Application, Product License Application or Biologics License Application or any successor applications or procedures, and (c) all supplements and amendments that may be filed with respect to the foregoing.

Section 1.84 "Oncology Field" means the treatment, control, mitigation, prevention or cure or diagnosis of any oncology Indications or any dysplastic syndromes or states (*e.g.*, MDS).

Section 1.85 "Option Exercise Date" means, on an Optionable Program-by-Optionable Program basis, with respect to each Optionable Program for which Celgene has exercised the Celgene Program Option, the date on which Celgene provides notice of its exercise of the Celgene Program Option pursuant to Section 3.6 (or, as applicable, Section 15.5(a)(iv)).

Section 1.86 "Optionable Program" means (a) a Discovery Program that reaches the DC Selection Stage during the Option Term, (b) a Discovery Program pursuant to which the option set forth in, as applicable, Section 3.6(c) or Section 15.5(a)(iv) is exercisable, or (c) a Discovery Program directed to [**] that does not reach the DC Selection Stage as of the end of the Option Term but reaches the DC Selection Stage during the [**] year period following the end of the Option Term.

Section 1.87 "Party" means Agios or Celgene; "Parties" means Agios and Celgene.

Section 1.88 "Patent Rights" means (a) patents and patent applications anywhere in the world, (b) all divisionals, continuations, continuations in-part thereof or any other patent application claiming priority, or entitled to claim priority, directly or indirectly to (i) any such patents or patent applications or (ii) any patent or patent application from which such patents or patent applications claim, or is entitled to claim, direct or indirect priority, and (c) all patents issuing on any of the foregoing anywhere in the world, together with all registrations, reissues, re-examinations, patents of addition, renewals, supplemental protection certificates, or extensions of any of the foregoing anywhere in the world.

Section 1.89 "Person" means any corporation, limited or general partnership, limited liability company, joint venture, trust, unincorporated association, governmental body, authority, bureau or agency, any other entity or body, or an individual.

Section 1.90 "Pharmacophore" means a [**].

Section 1.91 "Phase I MAD Protocol Criteria" means the criteria for a Phase I MAD Study set forth on Schedule 1.91. The Phase I MAD Protocol Criteria may not be amended other than by Mutual Consent of the JDC.

Section 1.92 "Phase I MAD Study" means a dose-exploratory Phase I Study to determine a recommended Phase II Study dose that is conducted in the US Territory, unless Celgene approves the conduct of such study outside the US Territory.

Section 1.93 "Phase I Report Criteria" means the criteria for the content of a final report on a Phase I MAD Study set forth on Schedule 1.93. The Phase I Report Criteria may not be amended other than by Mutual Consent of the JDC.

Section 1.94 "Phase I Study" means a human clinical trial of a product, the principal purpose of which is a preliminary determination of safety, tolerability and pharmacokinetics in study subjects where potential pharmacological activity may be determined or similar clinical study prescribed by the Regulatory Authorities, from time to time, pursuant to applicable Law or otherwise, including for example the trials referred to in 21 C.F.R. §312.21(a), as amended (or the non-United States equivalent thereof).

Section 1.95 "Phase II Study" means a human clinical trial of a product, the principal purpose of which is a preliminary determination of safety and efficacy or appropriate dosage ranges in the target patient population or a similar clinical study prescribed by the Regulatory Authorities, from time to time, pursuant to applicable Law or otherwise, including for example the trials referred to in 21 C.F.R. §312.21(b), as amended (or the non-United States equivalent thereof).

Section 1.96 "Phase III Study" means a pivotal human clinical trial of a product, the principal purpose of which is to gain evidence with statistical significance of the efficacy of a product in a target population, to obtain expanded evidence of safety for such product that is needed to evaluate the overall benefit-risk relationship of such product, and to provide an adequate basis to determine warnings, precautions, and adverse reactions that are associated with such product in the dosage range to be prescribed, which trial is intended to support or maintain Regulatory Approval for such product, including all tests and studies prescribed by the applicable Regulatory Authority, from time to time, pursuant to applicable Law or otherwise, including for example the trials referred to in 21 C.F.R. §312.21(c), as amended (or the non-United States equivalent thereof).

Section 1.97 "Phase IV Study" means a human clinical trial of a product which is (a) conducted to satisfy a requirement of a Regulatory Authority in order to maintain a Regulatory Approval or (b) conducted voluntarily after Regulatory Approval of the product has been obtained from an appropriate Regulatory Authority for enhancing marketing or scientific knowledge of an approved Indication.

Section 1.98 "Picked Compound" means,

(a) with respect to each Picked Validated Program selected by Celgene pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii), Section 3.6(c) or Section 15.5), (i) any and all Collaboration Compound(s) that are Active against the Collaboration Target that is the subject of such Picked Validated Program and Developed under such Picked Validated Program prior to the expiration of the Option Term, including any Collaboration Compounds on the Compound List for such Picked Validated Program, (ii) Collaboration Compounds (including Back-Up Compounds) identified by the JRC (or the JDC, as applicable) by Mutual Consent following the Option Term as being Active against the Collaboration Target that is the subject of such Picked Validated Program, (iii) any Analogs, Derivatives, [**] of any chemical entity identified in (i) or (ii), (iv) any compound that contains [**] of any of the foregoing in (i) or (ii) or any series of compounds demonstrating activity against the Target within such Program, in each case as determined by the JRC (or the JDC, as applicable) by Mutual Consent following the Option Term, and (v) any compound Controlled by Celgene that is Active against the Collaboration Target that is identified and used by Celgene after Celgene's selection of such Picked Validated Program; and

(b) with respect to each Picked Validated Program selected by Agios pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii) or Section 15.5), (i) one (1) Collaboration Compound that is Active against the Collaboration Target that is the subject of such Picked Validated Program and Developed under such Picked Validated Program prior to the expiration of the Option Term, and (ii) [**] Back-Up Compounds identified by the JRC (or the JDC, as applicable) by Mutual Consent at the time of such Picked Validated Program becoming an Agios Reverted Program.

Section 1.99 "Picked Product" means any Licensed Product that contains as an active ingredient any Picked Compound.

Section 1.100 "[**]" means [**].

Section 1.101 "Prior Confidentiality Agreement" means the Mutual Confidentiality Agreement between Agios and Celgene, dated as of September 9, 2009.

Section 1.102 "Program" means a Discovery Program, Independent Program or a Licensed Program, as the context requires, but excluding any Agios Reverted Program or Celgene Reverted Program. "Programs" means all of the foregoing Discovery Programs, Independent Programs and/or Licensed Programs.

Section 1.103 "Prosecution" or "Prosecute" means the filing, preparation, prosecution (including any interferences, reissue proceedings, reexaminations, and oppositions) and maintenance of Patent Rights.

Section 1.104 "Publication" means any publication in a scientific journal, any abstract to be presented to any scientific audience, any presentation at any scientific conference, including slides and texts of oral or other public presentations, any other scientific presentation and any other oral, written or electronic disclosure directed to a scientific audience that pertains to any Collaboration Targets, Celgene Reverted Targets, Collaboration Compounds, Development Candidates, Independent Compounds, Celgene Reverted Compounds, Celgene Reverted Products, Licensed Compounds, Licensed Products, Target Indications, and Collaboration Know-How, or the use of any of the foregoing, or the data or result from any work under the Validated Programs, Discovery Programs, Licensed Programs, Independent Programs, or Celgene Reverted Programs.

Section 1.105 "Publication Guidelines" means the criteria for Publication set forth on Schedule 1.105. The Publication Guidelines may not be amended other than by Mutual Consent of the JSC.

Section 1.106 "Regulatory Approval" means all approvals of the applicable Regulatory Authority necessary for the commercial marketing and sale of a product for a particular indication in a country.

Section 1.107 "Regulatory Authority" means a federal, national, multinational, state, provincial or local regulatory agency, department, bureau or other governmental entity with authority over the testing, manufacture, use, storage, import, promotion, marketing or sale of a product in a country or territory.

Section 1.108 “Regulatory Documentation” means, with respect to the Collaboration Compounds, Licensed Compounds and Licensed Products, all INDs, NDAs and other regulatory applications submitted to any Regulatory Authority, Regulatory Approvals, pre-clinical and clinical data and information, regulatory materials, drug dossiers, master files (including Drug Master Files, as defined in 21 C.F.R. 314.420 and any non-United States equivalents), and any other data, reports, records, regulatory correspondence and other materials relating to Development or Regulatory Approval of a Collaboration Compound, Licensed Compound or Licensed Product, or required to Manufacture, distribute or sell such Collaboration Compounds, Licensed Compounds and/or Licensed Products, including any information that relates to pharmacology, toxicology, chemistry, Manufacturing and controls data, batch records, safety and efficacy, and any safety database.

Section 1.109 “Regulatory Exclusivity” means, with respect to a Royalty-Bearing Product in a country, that the Royalty-Bearing Product has been granted marketing exclusivity afforded approved drug products, or approved biological products if applicable, pursuant to (a) Sections 505(c), 505(j), and 505A of the FDCA, and the regulations promulgated thereunder, as amended from time to time, or similar laws enacted to apply to biological products, and the regulations promulgated thereunder, as amended from time to time, or their equivalent in a country other than the United States, (b) the orphan drug exclusivity afforded approved drugs designated for rare diseases or conditions under Sections 526 and 527 of the FDCA, and the regulations promulgated thereunder, as amended from time to time, or its equivalent in a country other than the United States, or (c) any future Law.

Section 1.110 “Residual Program Compound” means, subject to Section 3.12(c), any chemical entity (a) included in, or otherwise Developed under a Discovery Program or Independent Program directed to any Collaboration Target that ceases to be a Collaboration Target hereunder (as a result of it being removed from the Target List and/or becoming an Agios Reverted Target or Celgene Reverted Target), excluding any Agios Reverted Compound or Celgene Reverted Compound, or (b) that is removed from a Compound List as set forth in Section 3.6(a)(iii).

Section 1.111 “Right of Reference or Use” means a “Right of Reference or Use” as that term is defined in 21 C.F.R. §314.3(b), and any non-United States equivalents.

Section 1.112 “ROW Territory” means all countries in the world other than the US Territory.

Section 1.113 “Royalty-Bearing Product” means a Co-Commercialized Product, a Split Product, a Buy-In Product, a Picked Product and a Celgene Reverted Product, as applicable.

Section 1.114 “Split Compound” means any Licensed Compound that is Developed under a Split Program.

Section 1.115 “Split Product” means any Licensed Product that contains as an active ingredient any Split Compound.

Section 1.116 "Split Program" means any Licensed Program for which Celgene exercised the Celgene Program Option and under which Agios retains all US Territory rights and Celgene retains all ROW Territory rights pursuant to Section 3.10.

Section 1.117 "Target" means any and all [**] cellular metabolism that is believed to be associated with a disease activity in the Oncology Field when initially included within the Collaboration, all of which shall be collectively regarded as a single target, subject to Section 3.5(c).

Section 1.118 "Target Indication" means, with respect to each Program and the Collaboration Target to which such Program is directed, any Indication that is designated as a target Indication with respect to such Program in accordance with this Agreement.

Section 1.119 "Target List" means the list of Targets attached hereto as Schedule 1.119, as such list may be updated or modified by the JRC pursuant to Section 3.5.

Section 1.120 "Terminated Product" means, with respect to a Terminated Program, any Collaboration Compound, Licensed Compound or Licensed Product Developed in or arising from such Terminated Program.

Section 1.121 "Terminated Program" means (a) with respect to the termination of this Agreement with respect to a Program pursuant to Section 14.2(a) or 14.2(b), the Program subject to such termination; and (b) with respect to the termination of this Agreement in its entirety, all Programs.

Section 1.122 "Territory" means the US Territory and the ROW Territory.

Section 1.123 "Third Party" means any Person other than Agios or Celgene or each Party's respective Affiliates.

Section 1.124 "Third Party Agreement" means (a) any Existing Third Party Agreement and (b) any other Third Party agreements which either Party may enter into, during the Term in accordance with the terms of this Agreement, to acquire or license Third Party Patent Rights or Know-How that are necessary or useful to use a Collaboration Target or for the Development, Manufacture and/or Commercialization of Collaboration Compounds, Licensed Compounds and/or Licensed Products.

Section 1.125 "Third Party Rights" means, with respect to a Party, any rights of, and any limitations, restrictions or obligations imposed by, Third Parties pursuant to any Third Party Agreements.

Section 1.126 "US Territory" means the United States of America, including its territories, possessions and Puerto Rico.

Section 1.127 "Valid Claim" means (a) a claim of any issued, unexpired patent that has not been revoked or held unenforceable or invalid by a decision of a court or governmental agency of competent jurisdiction from which no appeal can be taken, or with respect to which an appeal is not taken within the time allowed for appeal, and that has not been disclaimed or

admitted to be invalid or unenforceable through reissue, disclaimer or otherwise, or (b) a patent application or subject matter of a claim thereof filed by a Person in good faith that has not been cancelled, withdrawn or abandoned, nor been pending for more than [**] years from the earliest filing date to which such patent application or claim is entitled.

Section 1.128 "Validation Criteria" means the criteria for biological validation of the potential efficacy of a Collaboration Target in the Oncology Field, which validation criteria is set forth in Schedule 1.128. The Validation Criteria may not be amended other than by Mutual Consent of the JRC.

Section 1.129 "Validated Program" means a Discovery Program for which the Collaboration Target has met the Validation Criteria and for which a viable starting point for medicinal chemistry, biologics or other treatment modality has been identified.

Section 1.130 Additional Definitions. Each of the following definitions is set forth in the section of this Agreement indicated below:

| DEFINITION | SECTION |
|---|---|
| AAA | 2.9 |
| Accounting Standards | Exhibit A |
| Acquired Party | 15.4(b) |
| Acquired Party Activity | 15.4(c) |
| Acquired Third Party | 15.4(c) |
| Acquirer | 15.4(b) |
| Acquisition | 15.4(b) |
| Agios | Preamble |
| Agios Deferral | 3.10(a)(ii) |
| Agios Indemnified Parties | 13.1(a) |
| Agios Opt-Out | 3.10(c) |
| Agios Opt-Out Date | 3.10(c) |
| Agios Reverted Program | 3.12(a) |
| Agreement | Preamble |
| Alliance Manager | 2.6 |
| Annual Net Sales | Exhibit A |
| Arbitrable Matters | 2.9(e) |
| Audit Team | 9.10(a) |
| Audit Rights Holder | 9.10(f) |
| Auditee | 9.10(f) |
| Bankruptcy Code | 8.11 |
| [**] Agreement | Schedule 1.53 |
| [**] Indemnitees | 13.3(a) |
| Breaching Party | 14.2(b)(i) |
| Buy-In Party | 3.11(a) |
| Buy-In Right | 3.11(b) |
| Buy-In Right Term | 3.11(d)(i) |
| Celgene | Preamble |

| DEFINITION | SECTION |
|---|---|
| Celgene Election Period | 15.5(a)(i) |
| Celgene IND Option Exercise Period | 3.6(b)(iii)(A) |
| Celgene Indemnified Parties | 13.2(a) |
| Celgene MAD Option Exercise Period | 3.6(b)(iii)(A)(2) |
| Celgene Option Exercise Period | 3.6(b)(iii)(A)(2) |
| Celgene Program Option | 3.2 |
| Challenge | 10.8(a) |
| Change of Control | 15.5(c) |
| Clinical Candidate Guidelines | 3.6(b)(i) |
| Combination Product | Exhibit A |
| Commercialization Activities | 6.3(a) |
| Commercialization Plan | 6.2(a)(i) |
| Committee | 2.1 |
| Competitive Infringement | 10.3(b)(i) |
| Compound List | 3.6(a)(iii) |
| CREATE Act Patent | 10.7 |
| DC Commitment | 3.6(b)(iii) |
| DC Selection Stage | 3.6(b)(ii) |
| Delayed Commitment Date | 3.6(d) |
| Development Budget | 3.9(a) |
| Development Costs | Exhibit A |
| Development Plan | 3.9(a) |
| Disclosing Party | 11.1 |
| Discovery Plan | 3.4 |
| Dispute | 15.1 |
| DOJ | 3.6(e)(iv)(A) |
| [**] Agreement | Schedule 1.53 |
| Earlier Patent | 10.7 |
| Effective Date | Preamble |
| Expert | 2.9(a) |
| Extended Initial Phase | 3.3(b)(iii) |
| Extended Program | 3.3(d) |
| Failed Product | 9.6(a)(iv) |
| Field-Based Costs | Exhibit A |
| First Extension Phase | 3.3(b)(i) |
| First Extension Option | 3.3(b)(i) |
| First Picking Party | 3.7(b)(ii) |
| FTC | 3.6(e)(iv)(B) |
| FTE | Exhibit A |
| FTE Rate | Exhibit A |
| Global Development Costs | Exhibit A |
| Global Safety Database | 5.3 |
| Global Study | Exhibit A |
| HHMI | 15.12 |
| HSR Act | 3.6(e)(iii)(C) |

| DEFINITION | SECTION |
|---|---|
| IND Amount | 9.3(a)(i) |
| Initial Phase | 3.3(a) |
| Invalidity Claim | 10.4(b) |
| JCC | 2.1 |
| JDC | 2.1 |
| Joint Inventions | 10.1(c) |
| Joint Patents | 10.1(c) |
| JRC | 2.1 |
| JSC | 2.1 |
| Licensing Opportunity | 3.10(d) |
| Major Pharmaceutical Company | 11.3(b)(ii)(E) |
| Manufacturing Costs | Exhibit A |
| Manufacturing Scale-Up Costs | Exhibit A |
| Net Sales | Exhibit A |
| Non-Breaching Party | 14.2(b)(i) |
| Option Term | 3.3(d) |
| Out-of-Pocket Costs | Exhibit A |
| Partnered Programs | 8.8(a)(C) |
| Payments | 9.11(a) |
| Pharmacovigilance Agreement | 5.3 |
| Pick or Picked Validated Program | 3.7(b) |
| Phase I Amount | 9.3(a)(ii) |
| Post-Option Extension | 3.3(d) |
| Receiving Party | 11.1 |
| Redacted Version | 11.3(b)(i) |
| Regulatory Interactions | 5.1(h) |
| Regulatory Expenses | Exhibit A |
| Released Target | 3.5(b) |
| Responsible Party | 10.3(c) |
| Royalty Term | 9.7(f)(i) |
| Second Extension Option | 3.3(c) |
| Second Extension Option Trigger Event | 3.3(b)(i)(A) |
| Second Extension Phase | 3.3(c) |
| Second Generation Product | 9.6(a)(iv) |
| SPA | 3.10(e) |
| Supply Agreement | 4.1(c)(i) |
| Term | 14.1(a) |
| Territory-Specific Development Costs | Exhibit A |
| Third Party Activity | 15.4(b) |
| Third Party Contractors | 8.4(a)(ii) |
| Third-Party Infringement | 10.3(a) |
| [**] Agreement | Schedule 1.53 |
| Unilateral In-License | 9.7(g)(ii)(E) |
| Validated Program Discovery Costs | 3.7(a) |

## Article II
## Governance

Section 2.1 General. The Parties shall establish (a) a Joint Steering Committee ("JSC") to oversee and coordinate the overall conduct of all Programs hereunder; (b) a Joint Research Committee ("JRC") to oversee and coordinate discovery, research and pre-clinical Development activities with respect to each Discovery Program during the applicable Discovery Term; (c) a Joint Development Committee ("JDC") for each Licensed Program to oversee and coordinate clinical Development (including Manufacturing of clinical supply) of Licensed Compounds under such Licensed Program; and (d) a Joint Commercialization Committee ("JCC") to oversee the Commercialization (including Manufacturing of commercial supply) of Licensed Products (the JSC, the JRC, the JDC and the JCC shall each be referred to as a "Committee"). Each Committee may from time to time establish subcommittees or project teams to handle matters within the scope of its authority.

Section 2.2 Joint Steering Committee.

(a) Establishment. Within forty-five (45) days following the Effective Date, Agios and Celgene shall establish the JSC. The JSC shall have oversight over each Discovery Program and each Licensed Compound (and the related Program).

(b) Duties. The JSC shall:

(i) oversee and coordinate the conduct of all Programs and related matters within the responsibilities of the Committees hereunder;

(ii) by Mutual Consent provide strategic guidance, and coordinate efforts between the Parties, with respect to any Publications and by Mutual Consent approve requests for Publication, from either Party, according to the Publication Guidelines and Section 11.4 hereof;

(iii) serve as a forum for dispute resolution in accordance with Section 2.8 with respect to matters that are not resolved at the JRC, JDC or JCC; and

(iv) perform such other duties as are specifically assigned to the JSC under this Agreement.

Section 2.3 Joint Research Committee.

(a) Establishment. Within forty-five (45) days following the Effective Date, Agios and Celgene shall establish the JRC. The JRC shall have oversight over each Discovery Program during the applicable Discovery Term.

(b) Duties. The JRC shall:

(i) approve the initial Discovery Plan and review and approve any proposed updates or amendments to the Discovery Plan;

(ii) approve the addition and removal of Collaboration Targets from the Target List by Mutual Consent or at the request of Celgene in accordance with Section 3.5;

(iii) establish and update a prioritization of Collaboration Targets for validation work;

(iv) oversee, review, coordinate and provide strategic guidance to the Parties with respect to the conduct of each Discovery Program, including assigning activities to be performed by each Party under such Discovery Program (except that Celgene shall not be assigned any such activities without its prior written consent);

(v) review proposed modifications to the Clinical Candidate Guidelines, baseline criteria for determining whether a compound is Active, and Validation Criteria for each Discovery Program, and approve modifications to such guidelines and criteria by Mutual Consent;

(vi) review existing prioritization and allocation of resources among Validated Programs;

(vii) evaluate validation work conducted with respect to a Collaboration Target against the Validation Criteria for each Discovery Program and by Mutual Consent determine whether such Discovery Program is a Validated Program;

(viii) evaluate discovery research work conducted with respect to a Collaboration Target against the Clinical Candidate Guidelines for each Validated Program and determine whether progress is sufficient to advance to a short list of potential Development Candidates;

(ix) review each Development Candidate nomination package, determine whether a nomination meets the Clinical Candidate Criteria and by Mutual Consent confirm nominations for Development Candidates;

(x) manage the initial Development of any biomarkers;

(xi) in conjunction with the JDC and JCC, approve for which Target Indication(s) in the Oncology Field the first IND should be filed for Collaboration Compounds (with Celgene having the right to decide any unresolved matter, except with respect to Independent Compounds);

(xii) in conjunction with the JDC and JCC, discuss additional Indications for Development;

(xiii) oversee and coordinate the Parties' activities with respect to the Manufacture of pre-clinical and clinical supply of Collaboration Compounds, Licensed Compounds and/or Licensed Products (to the extent the JDC has not yet been formed);

(xiv) provide a forum for the Parties (A) to discuss the objectives of each Discovery Program; and (B) to exchange and review scientific information and data relating to the activities being conducted under each Discovery Program, including the exchange and review of data, Collaboration Compound structures and the results of each Discovery Program; and

(xv) perform such other duties as are specifically assigned to the JRC under this Agreement.

(c) JRC Project Teams. Within [**] days following a determination that a Collaboration Target has met the Validation Criteria, the JRC shall establish a project team for such Validated Program associated with such Collaboration Target. At Celgene's election, each project team shall have at least two representatives from Celgene, which representatives may be members of more than one project team. At Agios' election, each project team shall have at least two representatives from Agios, which representatives may be members of more than one project team.

Section 2.4 Joint Development Committee.

(a) Establishment. Within [**] days following the delivery to the JRC of the first data package for a potential Development Candidate to be selected at the DC Selection Stage pursuant to Section 3.6(b), Agios and Celgene shall establish the JDC. The JDC shall have oversight over each Split Compound (and the related Split Program), Licensed Compound in a Co-Commercialized Program (and the related Co-Commercialized Program), and Buy-In Compound (and the related Buy-In Program).

(b) Duties. The JDC shall:

(i) review and approve the applicable Development Plan (and applicable Development Budget) for each Licensed Program and any proposed updates or amendments thereto, and propose revisions to each Development Plan (and applicable Development Budget) as needed;

(ii) after the JRC's approval of the Target Indication for the first IND and after the Option Exercise Date with respect to a particular Program, in conjunction with the JCC, approve for which Target Indication(s) in the Field INDs should be filed for Collaboration Compounds (with Celgene having the right to decide any unresolved matter, except with respect to Independent Compounds, Buy-In Compounds for which Agios is the Lead Party or with respect to Split Compounds);

(iii) manage the Development of any Companion Diagnostics, including, following the initial oversight by the JRC, the Development of any biomarkers;

(iv) review proposed modifications to the Phase I MAD Protocol Criteria and the Phase I Report Criteria and approve modifications to such Phase I MAD Protocol Criteria and the Phase I Report Criteria by Mutual Consent;

(v) oversee, review, coordinate and provide strategic guidance to the Parties on the worldwide Development of each Licensed Compound and Licensed Product, including assigning activities to be performed by each Party under a Licensed Program (except that Celgene shall not be assigned any such activities without its prior written consent);

(vi) subject to and within the parameters of each Development Plan (A) oversee and approve the implementation of the Development Plan (including evaluation of clinical trial protocols and review of the conduct of clinical trials conducted pursuant to the Development Plan); and (B) oversee and approve the overall strategy and positioning of all material submissions and filings with the applicable Regulatory Authorities;

(vii) oversee, as applicable, the transfer of Development responsibility and activities from Agios to Celgene hereunder;

(viii) oversee, review and coordinate the studies required for the preparation of the CMC section of an IND for filing with Regulatory Authorities for each Licensed Compound, including studies relating to analytical methods and purity analysis, and (in conjunction with the JCC) formulation and Manufacturing development studies, together with associated regulatory activities;

(ix) oversee, review and coordinate process research and development activities (including, in conjunction with the JCC, Manufacturing and formulation development activities);

(x) in conjunction with the JCC, oversee and coordinate the Parties' activities with respect to the Manufacture of pre-clinical and clinical supply of Collaboration Compounds, Licensed Compounds and/or Licensed Products; and

(xi) perform such other duties as are specifically assigned to the JDC under this Agreement.

Section 2.5 Joint Commercialization Committee. Upon initiation of the [**] Study with respect to a Split Program, Co-Commercialized Program or Buy-In Program, Agios and Celgene shall establish the JCC. The JCC shall have oversight over (x) each Split Product (and the related Program), (y) each Co-Commercialized Product (and the related Program), to the extent set forth in clauses (a)(v) through (a)(xi) below, and (z) each Buy-In Product (and the related Program), to the extent set forth in clauses (a)(vii) through (a)(xi) below.

(a) Duties: The JCC shall:

(i) oversee, review and coordinate the Commercialization of Split Products between the Parties in their respective territories;

(ii) develop and oversee a brand strategy for Split Products;

(iii) set overall strategic objectives and plans related to Commercialization of Split Products on a global basis;

(iv) review and approve the annual global Commercialization Plan for each Split Product, and any updates or amendments thereto, and propose revisions to each Commercialization Plan as needed;

(v) review and approve the annual Commercialization Plan for the US Territory for each Co-Commercialized Product with respect to Commercialization Activities assigned to each Party pursuant to Article VI, and oversee, review and coordinate such activities;

(vi) review and approve all sales, promotional and communication materials for Co-Commercialized Products in the US Territory and for Split Products worldwide;

(vii) provide a forum for the Parties to share information with respect to the Commercialization of Licensed Products worldwide;

(viii) review and provide strategic guidance on all Commercialization activities and plans with respect to Licensed Products worldwide;

(ix) subject to and within the parameters of the Commercialization Plan, oversee the implementation of such plan;

(x) oversee and coordinate the Parties' activities with respect to the Manufacture of commercial supply of Licensed Compounds and/or Licensed Products; and

(xi) perform such other duties as are specifically assigned to the JCC under this Agreement.

Section 2.6 Alliance Managers. Each Party shall appoint one designated representative to serve as an alliance manager ("Alliance Manager") with responsibility for being the primary point of contact between the Parties with respect to the Collaboration. The Alliance Managers shall attend JSC, JRC, JDC and JCC meetings, as necessary, as non-voting observers. Nothing herein shall prohibit a Party from appointing its Alliance Manager as a member of one or more Committees.

Section 2.7 General Committee Membership and Procedures.

(a) Committee Membership. Each Committee shall each be composed of three (3) representatives from each of Celgene and Agios, each of which representatives shall be of the seniority and experience appropriate for service on the applicable Committee in light of the functions, responsibilities and authority of such Committee and the status of Development and Commercialization of the Licensed Products being pursued hereunder from time to time. Each Party may replace any of its representatives on any Committee at any time with prior written notice to the other Party; provided that such replacement meets this standard. Each Committee shall appoint a chairperson from among its members, with the chairperson for the JRC being a representative from [**], the chairperson for the JDC and JCC being a representative from [**], and the chairperson for the JSC being a representative from [**] until such time as [**]. Within 15 days following each Committee meeting, the chairperson of each Committee shall circulate to all Committee members a draft of the minutes of such meeting. The Committee shall then approve, by Mutual Consent, such minutes within 15 days following circulation.

(b) Committee Meetings.

(i) The JSC and JRC shall hold an initial joint meeting within [**] days of the Effective Date or as otherwise agreed by the Parties. The JDC and the JCC shall meet at the time such Committees are formed in accordance with Section 2.4 and Section 2.5, respectively. Thereafter, each Committee shall meet at least once every Calendar Quarter, unless the respective Committee members otherwise agree. All Committee meetings shall be conducted in person, unless otherwise determined by the applicable Committee by Mutual Consent.

(ii) Each project team of the JRC formed pursuant to Section 2.3(c) shall meet [**], unless the applicable project team agrees otherwise. Such meetings shall be conducted by telephone, video conference or in person, as determined by the applicable project team.

(iii) Unless otherwise agreed by the Parties, all in-person meetings for each Committee shall be held on an alternating basis between Agios' facilities in Cambridge, Massachusetts (or such future location as Agios' facilities may move to) and Celgene's facilities in Summit, New Jersey or San Diego, California, as determined by Celgene, (or such future location as Celgene's facilities may move to). A reasonable number of other representatives of a Party may attend any Committee meeting as non-voting observers; provided that such additional representatives are under obligations of confidentiality and non-use applicable to the Confidential Information of the other Party that are at least as stringent as those set forth in Article XI; and provided further that the Parties, reasonably in advance of the applicable Committee meeting approve the list of non-voting observers to attend such meeting. Each Party shall be responsible for all of its own personnel and travel costs and expenses relating to participation in Committee meetings.

(c) Dissolution. The JSC, JRC, JDC and JCC, as applicable, shall be dissolved and its activities and authority terminated upon the earliest of (i) with respect to the JRC, the end of the Option Term (or, if applicable, with respect to any Extended Program, the end of the Post-Option Extension), (ii) with respect to the JDC, when no Licensed Compounds that are subject to JDC oversight are being Developed under any Licensed Program, (iii) with respect to the JCC, until the end of the Royalty Term for all Split Products and Co-Commercialized Products in the US Territory, (iv) a Change of Control to the extent provided in Section 15.5, and (v) the termination or expiration of this Agreement in its entirety.

Section 2.8 Decision-Making.

(a) Committee; Referral to JSC and to Executive Officers. All decisions of a Committee shall be made by unanimous vote, with each Party's Representatives collectively having one (1) vote, and shall be set forth in minutes approved by both Parties. Upon [**] Business Days prior written notice, either Party may convene a special meeting of a Committee for the purpose of resolving any failure to reach agreement on a matter within the scope of the authority and responsibility of such Committee. No Committee shall have the authority to

resolve any dispute involving the breach or alleged breach of this Agreement or to amend or modify this Agreement or the Parties' respective rights and obligations hereunder. If the JRC, JDC or JCC is unable to reach agreement on any matter so referred to it for resolution by one or both Parties within [**] Business Days after the matter is so referred to it, such matter shall be referred to the JSC for resolution. If the JSC is unable to reach agreement on any matter within [**] Business Days after the matter is referred to it or first considered by it, such matter shall be referred to the Executive Officers for resolution.

(b) Decision-Making Authority. If the matter is not resolved by the Executive Officers after in-person discussions between such Executive Officers within [**] Business Days after referral to the Executive Officers, then, on a Program-by-Program basis, subject to Sections 2.8(c), 2.9, 3.10(e), 15.5(a)(iv)(B), and 15.5(a)(v)(D)(1) and except as otherwise provided herein, [**] at such time for such Program shall have the right to decide the unresolved matter; provided that [**] shall give due consideration to any comments or preferences expressed by the other Party with respect to such matter.

(c) Exceptions. Notwithstanding the foregoing, neither Party shall have the right to finally resolve a dispute pursuant to Section 2.8(b):

(i) in a manner that excuses such Party from any of its obligations specifically enumerated under this Agreement;

(ii) in a manner that negates any consent rights or other rights specifically allocated to the other Party under this Agreement;

(iii) to resolve any dispute involving the breach or alleged breach of this Agreement;

(iv) to amend or modify any Development Plan or the Development Budget with respect to a Buy-In Program or a Split Program (or the Commercialization Plan and related budget to the extent described in Section 6.1(c)(i)), without the other Party's consent if it would require the other Party to expend additional resources, whether internal or external, including capital expenditures; provided that such consent shall not be required for amendments or modifications that are part of the annual updates for a Development Plan or Development Budget (or such Commercialization Plan and related budget);

(v) to resolve any dispute regarding whether a milestone event set forth in Section 9.6 has been achieved;

(vi) to resolve a matter if the provisions of this Agreement specify that unanimous or mutual agreement of the Parties, including Mutual Consent, is required for such matter; or

(vii) in a manner that would require the other Party to perform any act that is inconsistent with any Law.

Section 2.9 Dispute Resolution for Certain Decisions by Mutual Consent. If a Committee cannot agree by Mutual Consent with respect to any Arbitrable Matter, after referring such matter to the Executive Officers pursuant to Sections 2.8(a) and 2.8(b), then either Party may request that such disputes be resolved by binding arbitration in accordance with the expedited procedures applicable to the Commercial Arbitration Rules of the American Arbitration Association (the "AAA") and the provisions of this Section 2.9.

(a) The Party desiring to initiate an arbitration proceeding with respect to an Arbitrable Matter will send a written notice to the other Party requesting the commencement of the arbitration proceeding and specifying the issue to be resolved. Within [**] days from the date such notice is sent, the Parties shall negotiate in good faith to appoint a mutually acceptable independent person, with scientific, technical, and regulatory experience with respect to the development of pharmaceutical products in the Field necessary to resolve such dispute and with availability to comply with the time periods in this Section 2.9 (an "Expert"). If the Parties fail to choose an Expert within the foregoing time period, the AAA shall choose an Expert (with such experience and availability) on behalf of the Parties within [**] days of receipt of written request by a Party to the AAA. Disputes about arbitration procedure will be resolved by the Expert or, failing agreement, by the AAA in New York, New York. Unless otherwise agreed by the Parties, the arbitration proceedings will be conducted in New York, New York. The fees and costs of the Expert and the AAA, if applicable, shall be shared equally by the Parties.

(b) Within [**] days of the selection of the Expert, each Party shall simultaneously deliver to the Expert and the other Party a written statement: (i) stating each of the issues that is the subject of the Arbitrable Matter dispute, (ii) setting forth such Party's position on each issue in dispute, and (iii) setting forth such Party's final position with respect to each such issue. With such statement, each Party may also submit supporting documentation, if any, for such Party's final position. Each Party shall have [**] days from receipt of the other Party's submission to submit to the Expert and the other Party a written response thereto, which may include any scientific and technical information in support thereof. The Expert shall have the right to meet with the Parties, either alone or together, as necessary to make a determination.

(c) In resolving the dispute, the Expert will have no authority to make a decision on any issue other than by selecting the final position of one of the Parties. An arbitration decision with respect to the Arbitrable Matter will be rendered in writing within [**] days of the designation of the Expert, which award will be final and binding on the Parties and will be deemed enforceable in any court having concurrent jurisdiction of the subject matter hereof and the Parties. In selecting the final position of one of the Parties, the arbitrator will have the authority to grant specific performance; provided that the Expert will have no authority to award damages, and each Party irrevocably waives any claim to recover such damages.

(d) For all purposes under this Agreement, any decision made pursuant to this Section 2.9 shall be deemed to be the decision of the Parties, or the applicable Committee, by Mutual Consent.

(e) The dispute resolution in this Section 2.9 shall apply only to the following matters if the Parties or the applicable Committee cannot agree by Mutual Consent ("Arbitrable Matters"): (i) whether [**] and, therefore, whether the nomination thereof as a Development Candidate is confirmed; (ii) whether [**]; and (iii) whether [**].

Section 2.10 Scope of Governance. Notwithstanding the creation of each of the Committees, each Party shall retain the rights, powers and discretion granted to it under this Agreement, and no Committee shall be delegated or vested with rights, powers or discretion unless such delegation or vesting is expressly provided herein, or the Parties expressly so agree in writing. It is understood and agreed that issues to be formally decided by a particular Committee are only those specific issues that are expressly provided in this Agreement to be decided by such Committee, as applicable.

Section 2.11 Agios Right to Discontinue Participation. Notwithstanding anything in this Article II to the contrary, at any time after the end of the Option Term (or, if applicable, with respect to any Extended Program, after the end of any Post-Option Extension) hereunder, Agios shall have the right to discontinue its participation in, and to not appoint members to, any Committee or any subcommittee or project team other than to the JRC or any subcommittee or project team of the JRC. If Agios discontinues participation in, or does not appoint members to, any Committee or any subcommittee or project team, (a) it shall not be a breach of this Agreement; (b) no consideration shall be required to be returned; (c) unless and until such members are appointed, Celgene may unilaterally discharge the roles of such Committee, subcommittee or project team, as applicable, for which members were not appointed, including making in Celgene's sole discretion all decisions of such Committee, subcommittee, or project team, including decisions requiring Mutual Consent; provided that Celgene shall not unilaterally discharge the roles of such Committee, subcommittee or project team, as applicable, as permitted under this Article II unless Agios has not appointed any members within [**] days after Celgene has completed its appointment of its members; and (d) Agios shall abide by all decisions made by Celgene on behalf of the applicable Committee, subcommittee, or project team and shall continue to perform its obligations hereunder. If Agios thereafter appoints members to a Committee, subcommittee or project team, Celgene shall no longer have the unilateral right to discharge the role of such Committee, subcommittee or project team, as applicable; provided that such Committee, subcommittee or project team shall not thereafter repeal prior decisions made by Celgene when Celgene was unilaterally discharging such role.

## Article III
## Discovery and Development Collaboration

Section 3.1 Primary Goals and General Responsibilities of Discovery Program.

(a) Discovery Program. During the Option Term, Agios shall be responsible for conducting discovery research activities with the principal goals of (i) identifying and validating Collaboration Targets in accordance with the Validation Criteria, (ii) identifying and discovering Collaboration Compounds that either activate or inhibit through direct binding to a Collaboration Target, (iii) nominating Development Candidates, and (iv) characterizing, optimizing and supporting the pre-clinical Development of Development Candidates, including IND-Enabling Studies; provided that, if Celgene and Agios both consent, Celgene may also be assigned responsibility for some of the foregoing discovery research activities at Agios' sole expense.

(b) Updates. During the Discovery Term, each Party shall provide the other Party with regular quarterly written reports on such Party's activities relating to the Discovery Program, including a summary of results, information, and data generated, any activities planned with respect to Development going forward (including, for example, updates regarding regulatory matters and Development activities for the next Calendar Quarter), challenges anticipated and updates regarding intellectual property issues (including a disclosure of Collaboration Intellectual Property developed or generated since the last written report) relating to each Discovery Program. Such written reports may be discussed by telephone or video-conference, or may be provided at each JRC, JDC or JCC meeting, as applicable; provided that, reasonably in advance of the meeting of such Committee, the Party providing the written report will deliver to the other Party an agenda for the meeting setting forth what will be discussed during the meeting. The Party receiving such written report shall have the right to reasonably request, and to receive in a timely manner clarifications and answers to, questions with respect to such reports.

Section 3.2 Option. Subject to the terms and conditions of this Agreement, Agios hereby grants to Celgene the exclusive right, exercisable, at Celgene's sole discretion, in accordance with Section 3.6, to elect, with respect to any Optionable Program, on an Optionable Program-by-Optionable Program basis, to obtain an exclusive license under Section 8.2 to Develop, Commercialize, and Manufacture the applicable Licensed Compounds and Licensed Products under such Optionable Program under the terms and conditions set forth in this Agreement (each such right to elect, a "Celgene Program Option").

Section 3.3 Option Term.

(a) Initial Phase. Except as otherwise set forth in Section 3.3(b)(iii) below, the initial phase of the Collaboration shall commence on the Effective Date and end three (3) years following the Effective Date (the "Initial Phase").

(b) First Extension Phase.

(i) Celgene shall have the right to elect to extend the Option Term following the Initial Phase ("First Extension Option") for a period (the "First Extension Phase") ending upon the earlier of:

(A) the date following the Effective Date on which (1) FPD of [**] Collaboration Compounds has occurred and (2) the JRC has confirmed the nomination of [**] Development Candidate (the "Second Extension Option Trigger Event"); and

(B) two (2) years following the end of the Initial Phase.

(ii) Celgene may exercise the First Extension Option by (x) providing written notice to Agios of such election; and (y) paying to Agios [**] Dollars (US$[**]). If Celgene elects to exercise such option, such notice and payment shall be made as follows:

(A) Unless Section 3.3(b)(ii)(B) or 3.3(b)(ii)(C) below applies, if Celgene elects the First Extension Option, Celgene must provide such exercise notice [**]months prior to the end of the Initial Phase and must pay such $[**] within [**] days following the end of the Initial Phase; provided that such notice shall not have to be given prior to [**] or such payment made prior to [**] days following [**].

(B) If Agios has not nominated [**] Development Candidates that are confirmed by the JRC at least [**] months prior to the end of the Initial Phase but [**] Development Candidates are so confirmed prior to the end of the Initial Phase, then, if Celgene elects the First Extension Option, Celgene must provide such exercise notice within [**] months following such confirmation of both Development Candidates and must pay such $[**] within [**] days following the later of (1) delivery of such notice and (2) the end of the Initial Phase.

(C) If Celgene elects to have Agios continue Development of the Development Candidates into the Extended Initial Phase in accordance with Section 3.3(b)(iii), then, if Celgene elects the First Extension Option, Celgene must provide such exercise notice on or prior to the date that is [**] days following the end of the Extended Initial Phase and must pay such $[**] days following delivery of such notice.

(iii) Notwithstanding anything in this Section 3.3 to the contrary, if Agios believes that Agios will not be able to nominate at least [**] Development Candidates that meet the Clinical Candidate Guidelines by the end of the Initial Phase, Agios shall notify Celgene thereof (to the extent practicable, by no later than [**] months prior to the end of the Initial Phase). If the JRC has not confirmed at least [**] Development Candidates nominated by Agios that meet the Clinical Candidate Criteria within the Initial Phase, then Celgene shall have the right to either exercise its First Extension Option as provided in Section 3.3(b)(ii)(A) or to have Agios continue Development following the end of the Initial Phase. If Celgene elects to have Agios continue Development, the Initial Phase shall be extended until the earlier of (x) [**] following the end of the original three (3)-year Initial Phase and (y) such time as the JRC has confirmed the nomination of at least [**] Development Candidates that meet the Clinical Candidate Guidelines following the Effective Date (the "Extended Initial Phase").

(A) If Celgene elected to have Agios continue Development through the Extended Initial Phase and the JRC confirms [**] Development Candidates nominated by Agios that meet the Clinical Candidate Guidelines by the end of the Extended Initial Phase, Celgene shall have the right to elect, in its sole discretion (to be exercised in accordance with Section 3.3(b)(ii)(C)), to extend the Option Term following such Extended Initial Phase for the remainder of the First Extension Phase. If Celgene does not elect to extend the Option Term through such remainder of the First Extension Phase, the Option Term shall expire at the end of such Extended Initial Phase and the picking mechanism set forth in Section 3.7 shall apply with respect to Validated Programs at such time.

(B) If the JRC confirms [**] nominated by Agios that meets the Clinical Candidate Guidelines by the end of the Extended Initial Phase, but fails to confirm the nomination of a [**] Development Candidate by the end of the Extended Initial Phase, Celgene shall have the right, in its sole discretion (to be exercised in accordance with Section 3.3(b)(ii)(C)), to extend the Option Term following such Extended Initial Phase for the remainder of the First Extension Phase. If Celgene does not elect to extend the Option Term through such remainder of the First Extension Phase, the Option Term shall expire at the end of such Extended Initial Phase and the picking mechanism set forth in Section 3.7 shall apply with respect to Validated Programs at such time; provided, however, that, notwithstanding anything in Section 3.7, 9.3(b) or 9.6(a) to the contrary, (1) Celgene shall be entitled to the first [**] Picks (including, if such Program has not reached the DC Selection Stage, [**]), and the Parties shall

then alternate turns (with [**] having the first turn) selecting [**] until all Validated Programs have been selected; (2) Celgene shall not be obligated to pay any Validated Program Discovery Costs with respect to Celgene's Picked Validated Program(s); and (3) Celgene shall be obligated to pay to Agios royalties as set forth in Section 9.7(d) but shall not be obligated to pay to Agios any of the milestone payments set forth in Section 9.6(a), in each case, with respect to Licensed Compounds and Licensed Products under Celgene's Picked Validated Program(s).

(C) If the JRC fails to confirm the nomination of any Development Candidate by the end of the Extended Initial Phase, Celgene shall have the right, in its sole discretion (to be exercised in accordance with Section 3.3(b)(ii)(C)), to extend the Option Term following such Extended Initial Phase for the remainder of the First Extension Phase. If Celgene does not elect to extend the Option Term through such remainder of the First Extension Phase, the Option Term shall expire at the end of such Extended Initial Phase and the picking mechanism set forth in Section 3.7 shall apply with respect to Validated Programs at such time; provided, however, that, notwithstanding anything in Section 3.7, 9.3(b) or 9.6(a) to the contrary, (1) Celgene shall have the right to select all Validated Programs remaining in the Collaboration at such time (including, if such Program has not reached the DC Selection Stage, [**]); (2) Celgene shall not be obligated to pay any Validated Program Discovery Costs with respect to Celgene's Picked Validated Program(s); and (3) Celgene shall be obligated to pay to Agios royalties as set forth in Section 9.7(d) but shall not be obligated to pay to Agios any of the milestone payments set forth in Section 9.6(a), in each case, with respect to Licensed Compounds and Licensed Products under such Picked Validated Program(s).

(D) For clarity, if Celgene elects to extend the Option Term following such Extended Initial Phase for the remainder of the First Extension Phase, such First Extension Phase shall extend until the earlier of (1) the Second Extension Option Trigger Event and (2) two (2) years following the end of the original three (3)-year Initial Phase.

(E) For purposes of clarity, if the JRC confirms [**] Development Candidates nominated by Agios in the same Calendar Year prior to the end of the Extended Initial Phase, Agios shall be deemed to have met its obligation under this Section 3.3(b)(iii) to nominate at least [**] Development Candidates that the JRC confirms meet the Clinical Candidate Guidelines by the end of the Extended Initial Phase irrespective of whether Celgene defers (or has the right to defer) making the DC Commitment with respect to either such Development Candidate pursuant to Section 3.6(d) below. In addition, if, during the Initial Phase (or, if applicable, the Extended Initial Phase):

(1) Celgene elects to unilaterally remove a Target from the Target List pursuant to Section 3.5(b) after a Development Candidate directed to such Target had been nominated by Agios and the JRC has not determined that such Development Candidate does not meet the Clinical Candidate Guidelines (as described in Section 3.6(b)(v)),

(2) Celgene elects to unilaterally remove a Target from the Target List within the [**]-year period prior to when a Development Candidate directed to such Target would have been nominated by Agios (as contemplated under the Discovery Plan); provided that the lead optimization chemical series in the Discovery Program related to such Target has demonstrated [**],

(3) Celgene decides to exercise its Celgene Program Option or to take a license early pursuant to Section 3.6(c) or Section 15.5, as applicable, to a Discovery Program under which a Development Candidate had been nominated by Agios prior to such early exercise,

(4) Celgene exercises its right pursuant to Section 14.2(a) to terminate for convenience any Discovery Program under which a Development Candidate had been nominated by Agios prior to such termination and the JRC has not determined that such Development Candidate does not meet the Clinical Candidate Guidelines (as described in Section 3.6(b)(v)), or

(5) Celgene terminates a Discovery Program for convenience within the [**]-year period prior to when a Development Candidate would have been nominated by Agios under such Discovery Program (as contemplated under the Discovery Plan); provided that the lead optimization chemical series in the Discovery Program related to such Target has demonstrated [**],

then, in each of the foregoing cases, such nominated (or would-be nominated, as applicable) Development Candidate shall be counted as a Development Candidate that has been confirmed by the JRC as meeting the Clinical Candidate Guidelines for purposes of determining whether Agios has met its obligation under this Section 3.3(b) to nominate at least [**] Development Candidates that the JRC confirms meet the Clinical Candidate Guidelines.

(c) Second Extension Option. Celgene shall have the right to elect to extend the Option Term beyond the First Extension Phase ("Second Extension Option") for an additional [**] months following the end of the First Extension Phase ("Second Extension Phase"). Celgene may exercise the Second Extension Option by (i) providing written notice to Agios of such election, and (ii) paying to Agios [**] Dollars (US$[**]) within [**] days following the end of the First Extension Phase. Such written notice shall be provided at least [**] months prior to the end of the First Extension Phase (or within [**] days following the Second Extension Option Trigger Event, as applicable); provided that, if the Parties enter into the Extended Initial Phase and such Extended Initial Phase continues until [**] following the end of the original Initial Phase, then such notice need not be provided until at least [**] months prior to the end of the First Extension Phase.

(d) Option Term. The "Option Term" shall refer to the period commencing on the Effective Date and ending upon the earliest of (i) the expiration of the Initial Phase (or Extended Initial Phase, if applicable), if Celgene does not exercise the First Extension Option; (ii) the expiration of the First Extension Phase, if Celgene exercises the First Extension Option but does not exercise the Second Extension Option; and (iii) the expiration of the Second Extension Phase, if Celgene exercises the Second Extension Option; provided that, notwithstanding the foregoing, if on the date of the events described in the foregoing clauses (i), (ii), and (iii), DC Selection Stage for a Development Candidate has been reached pursuant to Section 3.6(b)(ii) during the Option Term and the Celgene Program Option for such Development Candidate has not expired or been rejected, waived or not exercised within the applicable exercise period, then Celgene's right to exercise such Celgene Program Option will continue for such Development Candidate (and associated Discovery Program) beyond the end

of the Option Term as set forth in Section 3.6 until such Celgene Program Option has been exercised or been rejected or waived (such extended period, the "Post-Option Extension," and the Discovery Program associated with such Development Candidate, the "Extended Program"). For purposes of clarity, except as provided in the proviso in the prior sentence or in Section 3.3(b)(iii), if Celgene does not provide written notice of election to Agios in a timely manner, the Option Term shall expire as of the end of the then-current Initial Phase (or Extended Initial Phase, if applicable), First Extension Phase or Second Extension Phase, as the case may be.

Section 3.4 Discovery Plan. Within thirty (30) days following the Effective Date, Agios shall prepare and deliver to Celgene and, within fifteen (15) days after the establishment of the JRC, the JRC shall approve, a Discovery Plan (the "Discovery Plan") which shall set forth the prioritization of Collaboration Targets, initial validation work to be conducted with respect to Collaboration Targets, anticipated post-validation discovery research activities to be conducted under a Discovery Program, and the Party responsible for performance of an activity (which shall be Agios unless both Agios and Celgene otherwise agree). Thereafter, the JRC shall approve updates to the Discovery Plan on a quarterly basis during the Option Term (or, if applicable, with respect to any Extended Program, during any Post-Option Extension).

Section 3.5 Determination of Collaboration Targets During Option Term. As of the Effective Date, the Parties have selected the initial Collaboration Targets (as set forth on Schedule 1.119) with respect to which the Parties shall conduct Discovery Programs under this Agreement. During the Discovery Term for each Collaboration Target and the Discovery Program that is directed to such Collaboration Target, the Discovery Plan shall specify that the primary Target Indication for such Collaboration Target, and the Discovery Program shall be in the Oncology Field (it being understood that after the Discovery Term, the Development Plan for any Licensed Program may specify other Target Indications outside of the Oncology Field). The Parties intend that the Target List be dynamic and that Collaboration Targets will be prioritized on, added to, or removed from the Target List from time to time during the Option Term as available data and literature warrant to reflect the priorities of the Parties. At each JRC meeting, the JRC shall review, manage and determine the prioritization of Collaboration Targets on the Target List, and of the corresponding Discovery Programs that are directed to such Collaboration Targets. Targets shall be added to the Target List at any time in accordance with Section 3.5(a) below and shall be removed from the Target List at any time in accordance with Section 3.5(b). In furtherance of the foregoing, the following provisions shall apply:

(a) Targets shall be added to the Target List pursuant to this Section 3.5(a).

(i) During each [**] month period during the Option Term (with the first such period commencing on the Effective Date, the second such period commencing on [**], and so forth), Agios will nominate, for inclusion on the Target List, at least [**] new Targets that meet the criteria set forth on Schedule 3.5(a). Such Target(s) shall be added to the Target List, unless Celgene provides Agios written notice within [**] Business Days of Agios' nomination that such Target is already subject to an ongoing and active discovery program at Celgene (or such program is being initiated and a Celgene project team has already been formed) or under a collaboration with a Third Party, or is the subject of ongoing negotiations for a collaboration with a Third Party as evidenced by a bona fide term sheet (which may be redacted, including the identity of the Third Party), in which case either (x) if such Target was nominated

during the Initial Phase, such Target shall not be included on the Target List, but the restriction set forth in Section 8.8(a)(ii) shall apply to Agios with respect to such Target (as if such Target were on the Target List) until the end of the Initial Phase (at which point, Agios may again propose to include such Target on the Target List pursuant to this Section 3.5(a)(i)), or (y) if such Target was nominated after the Initial Phase, Agios may elect to undertake an Independent Program for such Target, in which event the effects set forth in clauses (A) and (B) of Section 3.5(b)(i) below shall apply; provided that, within [**] following such Independent Program being undertaken, Celgene may elect, by written notice to Agios, to treat such Independent Program as a Discovery Program hereunder, in which event such Independent Program shall become a Discovery Program.

(ii) In addition, at any time during the Option Term, Celgene may nominate, for inclusion on the Target List, any Target that meets the criteria set forth on Schedule 3.5(a); and such Target shall be added to the Target List unless Agios provides Celgene written notice within [**] Business Days of Celgene's nomination that such Target is already subject to a Partnered Program between Agios and a for-profit Third Party.

(b) The JRC (with [**] having the final say in the case of any dispute) may also agree at any time to discontinue Collaboration activities with respect to a Collaboration Target and either remove such Collaboration Target from the Target List (including as a result of criteria such as those set forth on Schedule 3.5(b)) (a "Released Target") or designate such Collaboration Target as an Independent Target with one Party continuing to independently Develop such Independent Target, and the associated Independent Program, in the Oncology Field. A Released Target may later be added back onto the Target List in accordance with Section 3.5(a), at which time it shall no longer be deemed a "Released Target."

(i) If the JRC's decision to remove a Collaboration Target from the Target List is not made by Mutual Consent but is made by [**] having the final say, upon [**] written election to [**] within [**] days of the removal of such Collaboration Target, Agios may elect to undertake an Independent Program for such Target, in which event (A) such Collaboration Target shall remain on the Target List for purposes of Agios' Independent Program, and Agios' Independent Program shall be subject to the terms of this Agreement, including this Section 3.5(b) and Section 3.11; and (B) such Target shall not remain on the Target List for purposes of Celgene's obligations hereunder, and notwithstanding Section 3.5(b)(ii), 8.8(b), or 8.8(c), Celgene shall not be restricted with respect to its activities on such Target unless and until Celgene exercises its Buy-In Right with respect to Agios' Independent Program on such Collaboration Target.

(ii) If the JRC agrees by Mutual Consent to designate a Collaboration Target as an Independent Target, such Independent Target shall remain on the Target List, the Discovery Program directed to such Independent Target shall be referred to as an "Independent Program," the JRC by Mutual Consent shall determine which Party shall undertake the independent Development of such Independent Program, and the terms set forth in Section 3.11, and in this Section 3.5(b)(ii) shall apply with respect to such Independent Program. In connection with designating a Discovery Program as an Independent Program, the JRC shall confirm which Collaboration Compounds shall be allocated to such Independent Program as "Independent Compounds" in accordance with Sections 1.66 and 3.6(a)(i).

(A) Unless and until the Buy-In Party's Buy-In Right with respect to such Independent Target has expired without the Buy-In Party exercising such right pursuant to Section 3.11, neither Party shall have any right (1) to enter into a collaboration or licensing agreement with a Third Party with respect to such Independent Target or (2) to Develop, Manufacture, or Commercialize such Independent Target for any Indications outside the Oncology Field.

(B) Notwithstanding anything in Section 3.11 or this Section 3.5 to the contrary, if, prior to the Buy-In Party's exercise of any applicable Buy-In Right with respect to an Independent Program, the Party that is independently Developing such Independent Program no longer desires to pursue Development of such Independent Program in the Oncology Field, (1) such Party may discontinue such Independent Program, (2) all Independent Compounds associated with such Independent Program shall be deemed Residual Program Compounds unless the Parties continue the Independent Program as a Discovery Program, and (3) except with respect to an Independent Program of Agios' described in Section 3.5(a)(i) or Section 3.5(b)(i), such Independent Target shall remain on the Target List unless the JRC (with Celgene having the final say in the case of any dispute) agrees to remove such Collaboration Target from the Target List pursuant to this Section 3.5.

(iii) All Collaboration Compounds for any Discovery Program or Independent Program directed to a Released Target shall remain in the Collaboration and shall become Residual Program Compounds, unless such Released Target is added back onto the Target List as set forth in this Section 3.5(b) (either in whole with respect to both Parties or partially with respect to Agios), in which event the original Collaboration Compounds for the applicable Discovery Program or Independent Program shall go back on the Compound List for such Discovery Program or Independent Program, to the extent not already allocated to another Program hereunder.

(c) The JRC by Mutual Consent (or the JDC by Mutual Consent, to the extent that the JRC is no longer in effect) may elect to (i) limit a Collaboration Target to [**], or (ii) pursue separate Programs with respect to the same Collaboration Target.

(d) For the avoidance of doubt, Targets subject to a Licensed Program shall remain on the Target List at the end of the Option Term unless such Licensed Program is terminated pursuant to Article XIV.

Section 3.6 Discovery and Nomination of Compounds for Licensed Program.

(a) Collaboration Compounds; Validation.

(i) Agios shall propose, for approval by the JRC, the initial compounds for which initial discovery and other Development activities shall be conducted hereunder. Unless the JRC (or the JDC, as applicable) agree by Mutual Consent that Celgene should contribute compounds, the compounds included in the Collaboration as Collaboration Compounds shall be compounds Controlled by Agios. In addition, if the JRC (or the JDC, as applicable) agrees by Mutual Consent, the same Collaboration Compounds contained within the Pharmacophore assigned to one Program may be used as a "Development Candidate" or Back-

Up Compound assigned to another Program; provided that, if Celgene's rights with respect to one Program terminate for any reason, including as a result of such Program becoming an Agios Reverted Program, Celgene's rights to such Collaboration Compound with respect to the second Program shall not terminate solely as a result of such first Program termination. Programs that are further along in Development shall have priority to Collaboration Compounds (*i.e.*, Licensed Programs shall have priority over Discovery Programs or Independent Programs), and Licensed Compounds and Discovery Programs shall have priority to Collaboration Compounds over Independent Programs.

(ii) Subject to JRC Mutual Consent, either Party may propose additional compounds Controlled by such Party for study in a Discovery Program, Independent Program or Licensed Program and, if such compounds are demonstrated to be Active against a Collaboration Target, such compounds shall be included in a Discovery Program, Independent Program or Licensed Program, as applicable, directed to such Collaboration Target. The Discovery Plan or Development Plan, as applicable, shall be updated as necessary to reflect such work on such additional compounds.

(iii) The JRC shall determine by Mutual Consent and maintain a list (the "Compound List") (accessible to both Parties) of those compounds identified in each Discovery Program or each Independent Program as meeting the criteria established by the JRC for designation as Collaboration Compounds, including identifying which compounds meet such criteria with respect to more than one Program, and shall update such list from time to time by Mutual Consent by adding or removing compounds based on the results of the Parties' Development activities relating thereto. The Parties intend that as compounds are progressed towards achievement of the Clinical Candidate Guidelines under a Program, the Compound List shall become a narrower, more focused list in regards to such Program, with Collaboration Compounds removed from the Compound List becoming Residual Program Compounds.

(iv) For each of the Validated Programs, prior to nomination in the course of lead optimization toward a Development Candidate under Section 3.6(b), Agios shall conduct a freedom to operate analysis on both the applicable Collaboration Target and associated chemical matter, with a defined strategy on how that chemical matter will be Developed with respect to chemical structure and intellectual property. Agios shall provide a summary of the analysis for review and approval of the JRC.

(b) Clinical Candidate Guidelines; Selection of Development Candidates at DC Selection Stage; Exercise of Celgene Program Option.

(i) As of the Effective Date, the Parties have established clinical candidate guidelines, attached hereto as Schedule 3.6(b) (the "Clinical Candidate Guidelines"), which Clinical Candidate Guidelines, if met, would indicate the suitability of a Collaboration Compound for advancement into IND-Enabling Studies under a Discovery Program, including demonstration of mechanism-based cell growth inhibition, chemical properties as defined in the Clinical Candidate Guidelines and non-clinical pharmacokinetic, pharmacodynamic, safety and efficacy criteria. Such Clinical Candidate Guidelines may be amended upon mutual written agreement of the Parties or subsequent Clinical Candidate Guidelines may be agreed in writing by the Parties and attached to this Agreement from time to time as appropriate.

(ii) Based upon the Clinical Candidate Guidelines and the results of Development activities with respect to a Discovery Program, Agios may nominate a Collaboration Compound directed to the Collaboration Target that is the subject of such Discovery Program as a Development Candidate, by providing written notice thereof to Celgene and the JRC. Such notice shall be accompanied by a package of all relevant data with respect to such Collaboration Compound, including relevant chemistry, biology, in vitro and in vivo pharmacology, drug metabolism and pharmacokinetics (DMPK) and pilot toxicology, and an initial Development Plan (with Development Budget) for such Discovery Program separated by the US Territory and the ROW Territory and including proposed Global Studies and other global Development activities. As part of the Development Candidate nomination, the package must also set forth at least one Back-Up Compound associated with such Development Candidate (which is not already allocated to another Program under this Agreement), which Back-Up Compound(s) shall have been tested for purposes of comparison with the proposed Development Candidate. The JRC by Mutual Consent shall have [**] days following such nomination by Agios to confirm such nomination (the stage of Development characterized by JRC's confirmation of such nomination shall be referred to as the "DC Selection Stage"); provided that, within [**] days following such nomination, Celgene or the JRC may reasonably request that Agios provide additional information and access to records (to the extent available to Agios at such time and not yet disclosed to the JRC as part of the regular updates under Section 3.1(b)) with respect to such Collaboration Compound and with respect to other Collaboration Compounds directed against other Collaboration Targets under Validated Programs that have not yet reached the DC Selection Stage, or are in preclinical Development, in which event the JRC's [**]-day period for confirming such nomination shall not begin to run until such information and access have been provided; provided further that, on a Development Candidate-by-Development Candidate basis, Celgene may waive the application of the Clinical Candidate Guidelines, in whole or in part, to a nominated Development Candidate in order to enable the JRC to confirm such Development Candidate hereunder. For clarity, in connection with the nomination and confirmation of a Development Candidate, all references to the "Development Candidate" nominated and confirmed as a Development Candidate pursuant to this Section 3.6(b) shall refer to the [**] that meets the Clinical Candidate Guidelines nominated by Agios, together with at least [**], and, after Celgene's exercise of the Celgene Program Option, all references to the "Development Candidate" so nominated and confirmed shall include all compounds set forth in clauses (a), (b), (c) and (d) of Section 1.47 unless the context requires otherwise.

(iii) If the JRC confirms the nomination of a Collaboration Compound as a Development Candidate, Celgene shall have [**] days following such confirmation to designate such nominated Development Candidate (and the associated Discovery Program) for further Development (on a Discovery Program-by-Discovery Program basis, a "DC Commitment"), as follows:

(A) If Celgene makes such DC Commitment, such nominated Development Candidate shall be deemed a "Development Candidate" for purposes of this Agreement, and Agios shall be responsible for conducting IND-Enabling Studies with respect to such Development Candidate. Upon completion of the IND-Enabling Studies, Agios shall provide written notice thereof to the JRC, JDC and Celgene. Such notice shall be accompanied by a package of all relevant data with respect to such IND-Enabling Studies. The JRC by Mutual Consent (with review and input from the JDC) shall have [**] days following such notice by

Agios to confirm that the IND Study Criteria have been met with respect to such IND-Enabling Studies for such Development Candidate; provided that, within [**] days following such notice, Celgene, the JDC or the JRC may reasonably request that Agios provide additional information and access to records (to the extent available and not yet disclosed to the JRC or the JDC as part of the regular updates under Section 3.1(b) or Section 3.8(c)) with respect to such Development Candidate, in which event the [**]-day period for confirming that the IND Study Criteria have been met shall not begin to run until such information and access have been provided. If the JRC determines the IND Study Criteria have not been met, Agios shall perform additional IND-Enabling Studies. If the JRC confirms that the IND Study Criteria have been met, Agios shall file the applicable IND with respect to such IND-Enabling Studies, and Celgene shall be obligated to pay the IND Amount(s) upon IND Acceptance pursuant to Section 9.3(a)(i). In addition, Celgene shall have [**] days following written notice from Agios of such IND Acceptance to take the actions described in Section 3.6(b)(iii)(A)(1) or (2) below; provided that, within [**] days following such notice from Agios, Celgene may reasonably request that Agios provide additional information and access to records (to the extent available to Agios at such time and not yet disclosed to the JRC or the JDC as part of the regular updates under Section 3.1(b) or 3.8(c) or under Section 3.6(b)(ii) or this Section 3.6(b)(iii)) with respect to other Collaboration Compounds directed against other Collaboration Targets under Validated Programs that have not yet reached the DC Selection Stage, or are in preclinical Development, in which event Celgene's [**]-day period for undertaking the actions described in Section 3.6(b)(iii)(A)(1) or (2) below shall not begin to run until such information and access have been provided (such period, as may be so extended, the "Celgene IND Option Exercise Period"):

(1) Celgene, within such Celgene IND Option Exercise Period, may provide Agios written notice of Celgene's election to exercise the Celgene Program Option with respect to such Development Candidate (and the associated Discovery Program), in which event the provisions of Section 3.6(b)(iv) shall apply; or

(2) Celgene, within such Celgene IND Option Exercise Period, may provide Agios written notice that Celgene elects that Agios conduct the first Phase I MAD Study for the Development Candidate. In such event, Agios shall be responsible for conducting the first Phase I MAD Study with respect to such Development Candidate under a protocol approved by the JRC by Mutual Consent that meets the Phase I MAD Protocol Criteria, and, unless the Program becomes a Split Program, Celgene shall be obligated to pay the Phase I Amount pursuant to Section 9.3(a)(ii). Upon Agios' completion of such first Phase I MAD Study, Agios shall deliver to Celgene a final written report that meets the Phase I Report Criteria. Within [**] days of Celgene's receipt of such written report, Celgene may reasonably request that Agios provide additional information and access to records (to the extent available to Agios at such time and not yet disclosed to the JRC or JDC as part of the regular updates under Section 3.1(b) or 3.8(c), or under Section 3.6(b)(ii) or this Section 3.6(b)(iii)) with respect to such Phase I MAD Study and with respect to other Development Candidates that are undergoing IND-Enabling Studies or are at a later stage of Development under a different Program. Within [**] days following the Completion of Phase I MAD (and such any additional information or access) (such period, as may be so extended, the "Celgene MAD Option Exercise Period"; either the "Celgene IND Option Exercise Period" or the "Celgene MAD Option Exercise Period" may be referred to as a "Celgene Option Exercise Period"), Celgene may provide Agios written notice of its election to exercise the Celgene Program Option, in which event the provisions of Section 3.6(b)(iv) shall apply;

(B) If Celgene (x) rejects the nominated Development Candidate pursuant to Section 3.6(b)(iii), or does not make a DC Commitment with respect to such nominated Development Candidate during the exercise period set forth in Section 3.6(b)(iii) above, (y) makes the DC Commitment but does not, within the Celgene IND Option Exercise Period, exercise the Celgene Program Option pursuant to Section 3.6(b)(iii)(A)(1) above or request that Agios conduct a first Phase I MAD Study pursuant to Section 3.6(b)(iii)(A)(2) above, or (z) after requesting that Agios conduct the first Phase I MAD Study under Section 3.6(b)(iii)(A)(2) above within the Celgene IND Option Exercise Period, does not exercise the Celgene Program Option within the Celgene MAD Option Exercise Period pursuant to Section 3.6(b)(iii)(A)(2) above, then the following shall occur:

(1) The Celgene Program Option with respect to such Discovery Program shall terminate,

(2) The Discovery Program under which the Development Candidate was Developed shall terminate hereunder (with the Collaboration Target subject to such Discovery Program being automatically removed from the Target List), and

(3) Except as provided in Section 8.9, all rights related to such Discovery Program granted by Agios to Celgene hereunder shall terminate, and such Discovery Program shall be deemed an Agios Reverted Program in accordance with Section 3.12.

(C) For clarity, a DC Commitment by Celgene pursuant to this Section 3.6(b)(iii) shall not be deemed a commitment to exercise a Celgene Program Option but shall require payment of the IND Amount if the requirements for such payment are met.

(iv) If Celgene exercises a Celgene Program Option with respect to a Discovery Program within the applicable Celgene Option Exercise Period pursuant to Section 3.6(b)(iii) above, upon such exercise:

(A) such Discovery Program shall become a Licensed Program;

(B) Agios shall be responsible for continuing Development activities and Clinical Trials with respect to such Development Candidate through Completion of Phase I MAD for the applicable Licensed Program, subject to the JRC or the JDC, as applicable, assigning any such Development activities to Celgene (based upon Celgene's agreement and as set forth in the applicable Development Plan and Development Budget) or as otherwise may be mutually agreed by the Parties. In addition, Agios shall conduct additional Development activities with respect to such Development Candidate as requested by Celgene and agreed to by Agios, subject to Section 3.6(b)(iv)(D) below;

(C) following Completion of Phase I MAD for each such Licensed Program (except as otherwise set forth in Section 3.10 with respect to any Split Program), Celgene shall undertake all further Development activities, subject to the JRC or the JDC, as applicable, assigning any such Development activities to Agios (based upon Agios' agreement and as set forth in the applicable Development Plan and Development Budget) or as otherwise may be mutually agreed by the Parties;

(D) Celgene shall also be responsible, pursuant to Section 9.4(a), for the Development Costs of Agios conducting any additional Development activities under such Licensed Program (except as otherwise set forth in Section 3.10 with respect to any Split Program) that are pursuant to a Development Budget under the Development Plan for such Licensed Program and that are incurred after the Development Cost Initiation Date for such Licensed Program; and

(E) Celgene shall be obligated to pay to Agios any other milestone payments or royalties which may become payable to Agios with respect to Licensed Compounds and Licensed Products arising from such Licensed Program pursuant to Section 9.6 or Section 9.7, respectively (it being understood that if such Licensed Program becomes a Split Program pursuant to Section 3.10, then Section 3.10(a)(iii) shall apply).

(v) If the JRC does not confirm the nomination of a Collaboration Compound as a Development Candidate, the Parties shall continue Development of the Collaboration Compound as contemplated in this Agreement pursuant to the applicable Discovery Plan for it.

(c) Early Exercise of Option. Notwithstanding anything herein to the contrary, Celgene shall have the following rights, as applicable, to exercise its Celgene Program Option early, in accordance with the terms set forth below:

(i) Celgene may exercise, upon written notice to Agios at any time prior to the expiration of the Option Term (or, if applicable, with respect to any Extended Program, expiration of any Post-Option Extension), any Celgene Program Option early with respect to each Development Candidate (and the applicable Discovery Program) that has been nominated by Agios pursuant to Section 3.6(b)(ii) (and, in the event of such early election, the JRC shall be deemed to have confirmed such nomination and Celgene shall be deemed to have made the DC Commitment); provided that, with respect to each such Discovery Program, notwithstanding Celgene's early exercise of such Celgene Program Option pursuant to this Section 3.6(c)(i), Section 3.6(b) and Section 3.10 shall apply in the same manner as though the Celgene Program Option had been exercised pursuant to Section 3.6(b), including the following (to the extent applicable depending on the stage of Development of such Discovery Program); provided that Celgene's license under Section 8.2 with respect to such Program shall be effective immediately:

(A) unless Celgene requests and Agios agrees otherwise, Agios shall complete all IND-Enabling Studies and obtain IND Acceptance with respect to such Discovery Program for which the Celgene Program Option has been exercised;

(B) regardless of which Party completes such IND-Enabling Studies and obtains IND Acceptance, Agios shall be entitled to the IND Amount pursuant to Section 9.3(a)(i) in the same manner as if a DC Commitment had been made (and as if the Celgene Program Option had not yet been exercised) in accordance with Section 3.6(b);

(C) Agios shall continue to have a right to retain its US Territory rights with respect to any such Discovery Program in accordance with Section 3.10 (including, as applicable, the right to make an Agios Deferral); and

(D) Celgene shall still remain obligated to make the milestone payments due pursuant to Section 9.6 and royalty payments due pursuant to Section 9.7 in the same manner as though Celgene had exercised the Celgene Program Option pursuant to Section 3.6(b) and subject to Section 3.10.

(ii) Prior to the earlier of (x) the expiration of the Option Term (or if, applicable, with respect to any Extended Program, expiration of any Post-Option Extension) and (y) the date of [**], Celgene may exercise its Celgene Program Option for any Discovery Program with respect to which Agios has nominated a Development Candidate pursuant to Section 3.6(b) (and, in the event of such early election, the JRC shall be deemed to have confirmed such nomination and Celgene shall be deemed to have made the DC Commitment) or take an exclusive license under Section 8.2 with respect to any other applicable Validated Program as a Picked Validated Program, upon written notice to Agios upon (A) Agios' failure to provide any financial statement in accordance with Section 3.6(c)(iii), which failure is not corrected within [**] days after written notice of Celgene; or (B) the occurrence of any event described in Section 3.6(c)(iv). The consequence of any such early exercise of a Celgene Program Option pursuant to this Section 3.6(c)(ii) shall be the same as an early exercise under Section 3.6(c)(i), and the consequence of any such early exercise of a license for a Picked Validated Program shall be the same as though such Picked Validated Program were selected by Celgene pursuant to Section 3.7; provided that, with respect to any Discovery Program for which Celgene exercises its Celgene Program Option, Celgene may assume all such Development responsibilities or, at Celgene's election, permit Agios to continue such Development in accordance with Section 3.6(b), but, if Celgene assumes such Development responsibilities, (1) Celgene shall be responsible for all its Development Costs in connection with such Development, (2) Agios shall not be entitled to a Phase I Amount, and (3) Agios shall be entitled to the IND Amount pursuant to Section 9.3(a)(i) in the same manner as if a DC Commitment had been made (and as if the Celgene Program Option had not yet been exercised) in accordance with Section 3.6(b), except that Celgene may deduct from any such IND Amount all Development Costs incurred by Celgene or its Affiliates through IND Acceptance; provided further that, with respect to any Discovery Program for which Celgene exercises its Celgene Program Option or takes an exclusive license early under this Section 3.6(c)(ii), Celgene shall no longer remain obligated to make any of the milestone payments due pursuant to Section 9.6, except for paying the milestone payments upon the occurrence of the events set forth in Section 9.6(a)(3) and Section 9.6(a)(4).

(iii) Prior to the earlier of (x) the expiration of the Option Term (or if, applicable, with respect to any Extended Program, expiration of any Post-Option Extension) and (y) the date of [**], Agios will furnish to Celgene (A) within [**] days after the end of each month, an unaudited balance sheet of Agios as of the end of such month (or as of the end of the fiscal quarter, if applicable) and unaudited statements of income and of cash flows of Agios for

such month (or such quarter) and for the current fiscal year to the end of such month (or such quarter), setting forth in comparative form Agios' projected financial statements for the corresponding periods for the current fiscal year, and (B) within [**] days after the end of each fiscal year of Agios, an audited balance sheet of Agios as at the end of such year and audited statements of income and of cash flows of Agios for such year, certified by certified public accountants of established regional or national reputation selected by Agios, and prepared in accordance with generally accepted accounting principles consistently applied. Agios will notify Celgene prior to Agios entering into discussions with potential lenders or equity investors in order to avoid having any event described in Section 3.6(c)(iv) occur.

(iv) Prior to the earlier of (x) the expiration of the Option Term (or if, applicable, with respect to any Extended Program, expiration of any Post-Option Extension) and (y) the date of [**], Agios covenants to provide Celgene with written notice no later than [**] after the occurrence of any of the following events: (A) the sum of all of Agios' liabilities exceed the sum of all of Agios' assets; (B) Agios is unable to pay its debts as they become due; (C) Agios admits its inability to pay its debts as they fall due; (D) there is an occurrence and continuance (for a period in excess of any applicable cure period) of a default by Agios with respect to any of its debt or payment obligations in excess of $[**] or any agreement having a materially adverse effect on Agios' business or Agios' ability to perform under this Agreement; (E) Agios suspends, closes, or otherwise ceases to operate a portion of its business having a materially adverse effect on this Agreement; (F) Agios initiates any action to undertake restructuring of its assets or business in a manner that would have a materially adverse effect on this Agreement, including hiring counsel or financial advisors with respect to such restructuring; (G) Agios fails to have sufficient available cash to fund at least [**] of its budgeted operating expenses, based on the budget approved by Agios pursuant to Section 4.3(d) of the Amended and Restated Investor Rights Agreement among Agios and certain stockholders, dated as of the Effective Date; (H) Agios plans to take any action that would give Celgene a termination right under Section 14.2(b)(ii); (I) Agios retains counsel or financial advisors to assist Agios in connection with any potential bankruptcy or insolvency proceeding; (J) one or more creditors of Agios notify Agios in writing that such creditors have organized for the purpose of commencing negotiations with regard to a possible bankruptcy filing of Agios, or Agios has commenced negotiations with one or more creditors with regard to a possible bankruptcy filing of Agios; or (K) any corporate or other action is taken by Agios for the purpose of effecting any of the foregoing. Celgene will treat all notices and financial reports (and the information contained therein) as Confidential Information of Agios, subject to the terms of Article XI.

(d) Limitation on Development Candidates. Notwithstanding anything herein to the contrary, the Parties agree that (x) Celgene shall not be required to exercise or waive its right to make a DC Commitment with respect to more than [**] in any Calendar Year, and (y) if Agios has already nominated [**] Development Candidates with respect to [**] which Celgene has made a DC Commitment, as provided in Section 3.6(b), then Celgene shall not be required to exercise or waive its right to make a DC Commitment with respect to a [**] proposed Development Candidate prior to [**]. If Agios nominates a Development Candidate that is confirmed by the JRC and that would exceed either of the thresholds in the prior sentence, then Celgene may make the DC Commitment for such Development Candidate at such time or may defer making the DC Commitment until [**] days following the earlier of (i) the expiration of the Option Term and (ii)(A) with respect to clause (x) above, [**] of the following Calendar

Year, or (B) with respect to clause (y) above, [**] (the earlier such date, the "Delayed Commitment Date"). Failure of Celgene to take any action during the original applicable DC Commitment exercise period set forth in Section 3.6(b)(iii) if the conditions in clauses (x) or (y) above are met shall be deemed an election to defer the decision to make the DC Commitment pursuant to this Section 3.6(d). If the decision to make the DC Commitment is so deferred, Agios may either, in its sole discretion:

(i) hold such Collaboration Compound in the Discovery Program and nominate it again as a Development Candidate following the Delayed Commitment Date, at which point the JRC shall automatically confirm such nominated Development Candidate unless the Development Candidate no longer meets the Clinical Candidate Guidelines, and Celgene shall have [**] days from the JRC's confirmation of such Development Candidate to make the DC Commitment in accordance with Section 3.6(b)(iii); or

(ii) pursue Development of such Collaboration Compound until IND Acceptance at Agios' own cost but under the oversight of the JRC or JDC, as applicable, in which event the following shall apply:

(A) Agios shall provide [**] updates to the JRC or JDC, as applicable, and Celgene on the progress of such Development activities since the prior update and on the general scope of proposed activities, including anticipated timelines and budgets, through at least IND Acceptance;

(B) Agios shall not have the right to file any IND, unless the JRC or JDC, as applicable, determines by Mutual Consent that the IND Study Criteria have been met as described in Section 3.6(b)(iii)(A). In addition, at least [**] days prior to any proposed IND Acceptance, Agios shall provide to Celgene the proposed materials to be submitted as part of the IND Acceptance;

(C) if Agios achieves an IND Acceptance with respect to such Collaboration Compound, Agios shall provide written notice to Celgene and all relevant information and access to records with respect to such Collaboration Compound (and with respect to other Collaboration Compounds directed against other Collaboration Targets under Validated Programs that have not yet reached the DC Selection Stage or are in preclinical Development) as may be reasonably requested by Celgene within [**] days of such notice (to the extent such information and access are available to Agios at such time and not yet disclosed to the JRC or JDC); and

(D) Celgene shall have [**] days from the delivery of the information and access described in Section 3.6(d)(ii)(C) to make the DC Commitment (in which event the provisions of Section 3.6(b)(iii) shall apply) or exercise the Celgene Program Option (in which event the provisions of Section 3.6(b)(iv) shall apply); provided that, if the condition in Section 3.6(d)(y) has been met, such [**]-day period shall run from [**]. If Celgene does make the DC Commitment or exercise the Celgene Program Option, Celgene shall pay Agios the IND Amount pursuant to Section 9.3(a)(i) within [**] days following delivery of its exercise notice.

(e) HSR Clearance; Cooperation.

(i) Notwithstanding anything in this Section 3.6 to the contrary, if the exercise of any Celgene Program Option requires clearance under the HSR Act, the Parties shall use Commercially Reasonable Efforts to promptly obtain any necessary clearance under the HSR Act for the exercise by Celgene of any Celgene Program Option, including the prompt filing of a copy of this Agreement and each Party's respective premerger notification and report forms with the FTC and the DOJ pursuant to the HSR Act, and shall keep each other apprised of the status of any communications with, and any inquiries or requests for additional information from, the FTC and the DOJ and shall comply with any such inquiry or request; provided, however, that neither Party shall be required to consent to the divestiture or other disposition of any of its assets or assets of its Affiliates or to consent to any other structural or conduct remedy, and each Party and its Affiliates shall have no obligation to consent, administratively or in court, any ruling, order or other action of the FTC or DOJ or any Third Party respecting the transactions contemplated by this Agreement.

(ii) The Parties commit to instruct their respective counsel to cooperate with each other and use Commercially Reasonable Efforts to facilitate and expedite the identification and resolution of any such issues and, consequently, the expiration of the applicable HSR Act waiting period. Each Party's counsel will undertake (A) to keep each other appropriately informed of communications from and to personnel of the reviewing antitrust authority, and (B) to confer with each other regarding appropriate contacts with and response to personnel of the FTC or DOJ. Celgene shall be responsible for the filing fee in connection with any HSR Act filing relating to the transactions contemplated in this Agreement.

(iii) Celgene may exercise the Celgene Program Option subject to receipt of required clearances under the HSR Act. For clarity, if clearance under the HSR Act is required with respect to any Celgene Program Option, as described above, exercise of such Celgene Program Option shall not be effective until after the expiration or termination of all applicable waiting periods under the HSR Act; provided that, as long as Celgene has provided notice of its intention to exercise such Celgene Program Option during the time periods set forth in this Section 3.6, then the Post-Option Extension with respect to the applicable Program shall remain in effect until the expiration or termination of such waiting periods.

(iv) For purposes of this Section 3.6(e), the following definitions shall apply:

(A) "DOJ" means the United States Department of Justice.

(B) "FTC" means the United States Federal Trade Commission.

(C) "HSR Act" means the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended (15 U.S.C. §18a), and the rules and regulations promulgated thereunder.

(D) In addition, notwithstanding anything herein to the contrary, if the grant of an exclusive license under Section 8.2 to Celgene with respect to Celgene's Picks, a Buy-In Program with respect to which Celgene is the Commercializing Party, or a Celgene Reverted Program requires clearance under the HSR Act, the provisions of this Section 3.6(e) shall apply and the grant of such exclusive license to Celgene shall not be effective until after the expiration or termination of all applicable waiting periods under the HSR Act.

Section 3.7 Selection of Validated Programs Upon Expiration of Option Term. Upon expiration of the Option Term, the Parties will begin the process set forth below for selecting Validated Programs from the Discovery Programs remaining in the Collaboration that have not yet reached the DC Selection Stage.

(a) Within [**] days after the expiration of the Option Term, Agios shall provide to the JRC and Celgene an update to the Compound List with respect to each Discovery Program remaining in the Collaboration as of the expiration of the Option Term. Within [**] days following delivery of such updated list, the JRC, by Mutual Consent, shall confirm which of those Discovery Programs are Validated Programs that have not yet reached the DC Selection Stage, and establish a list of such Validated Programs; provided that, within [**] days following such delivery of such list, Celgene or the JRC may reasonably request that Agios provide additional information and access to records (to the extent available to Agios at such time and not yet disclosed to the JRC or JDC) with respect to such Discovery Programs, in which event the JRC's [**]-day period for confirming such Discovery Programs as Validated Programs shall not begin to run until such information and access have been provided. Promptly following the JRC's confirmation of Validated Programs, Agios shall provide to Celgene and to the JRC an accounting of all FTE costs and Out-of-Pocket Costs incurred by Agios to conduct discovery and other Development activities under each Validated Program prior to the expiration of the Option Term (the "Validated Program Discovery Costs"). For purposes of clarity, if any such Discovery Program remaining in the Collaboration is not determined to be a Validated Program by the JRC, except as provided in Section 8.9, all rights related to such Discovery Program granted by Agios to Celgene hereunder shall terminate, and such Discovery Program shall be deemed an Agios Reverted Program in accordance with Section 3.12.

(b) Except as otherwise provided in Section 3.3(b)(iii) or 15.5, the Parties will select the Validated Programs for potential future Development by a Party by taking turns picking (each Party's pick of a Validated Program or Validated Programs, as applicable, shall be referred to as a "Pick" or "Picked Validated Program") until all Validated Programs have been picked, as follows:

(i) Within [**] days following Agios' delivery to Celgene and the JRC of the Validated Program Discovery Cost information for all confirmed Validated Programs, Agios shall propose in writing to Celgene [**] potential in-person meeting dates on Business Days, such potential dates to be within [**] days after such proposal is made, and Celgene shall respond by accepting one proposed meeting date within [**] Business Days after such proposal is made. The meeting shall be held at a location to be mutually agreed by the Parties.

(ii) At such meeting, the Parties shall begin the picking process by undertaking a coin toss conducted by a mutually-agreed Third Party. The Party that wins the coin toss shall select the Party that has the right to make the first Pick (the "First Picking Party"). At the meeting, the First Picking Party may select as its Pick, in the first turn, [**]. The Party

that is not the First Picking Party may then select as its Pick, in the second turn, up to [**]. For each turn after the second turn, starting with the First Picking Party, the Parties shall take alternating turns selecting [**] after the other Party's Pick until all Validated Programs have been selected by a Party. If neither Party exercises its right to select the last remaining Validated Program(s), such Validated Program(s) shall terminate, and, except as provided in Section 8.9, all rights related to such Validated Program(s) granted by Agios to Celgene hereunder shall terminate, and such Validated Program shall be deemed an Agios Reverted Program in accordance with Section 3.12, unless otherwise mutually agreed by the Parties.

(c) Any Picked Validated Program selected by Celgene shall be deemed a Licensed Program hereunder and the Picked Compounds under such Picked Validated Program shall include any and all Collaboration Compounds on the Compound List associated with the Collaboration Target in the Picked Validated Program (unless such compounds are already associated with a Picked Validated Program selected earlier in the picking process), data on any compounds that meet the "Screening Hits" criteria under the baseline Activity criteria set forth on Schedule 1.1 under such Picked Validated Program up to the date of expiration of the Option Term, and any in vivo and in vitro data with respect to such Picked Validated Program; and the licenses granted to a Party pursuant to Section 8.2(b) with respect to such Validated Program shall become effective upon such Validated Program becoming a Pick of Celgene. Each Party's Development obligations under any Picked Validated Program selected by Celgene shall be as set forth in Section 3.8(a)(iv) below, and Celgene shall be obligated to pay to Agios Validated Program Discovery Costs as set forth in Section 9.3(b), milestone payments as set forth in Section 9.6(a), and royalties as set forth in Section 9.7(d). For clarity, no IND Amount or Phase I Amount shall be due with respect to Celgene's Picks.

(d) Any Picked Validated Program selected by Agios (or not selected by either Party pursuant to Section 3.7(b)(ii) above) shall be deemed an Agios Reverted Program for all purposes hereunder in accordance with Section 3.12.

(e) Notwithstanding any of the foregoing, except as provided in Section 3.3(b)(iii), any Discovery Program remaining in the Collaboration as of the end of the Option Term that has not reached the DC Selection Stage and is directed to [**] (each such Discovery Program shall be deemed an "Extended Program") shall not be subject to the picking mechanism set forth in this Section 3.7, but shall remain in the Collaboration as a Discovery Program until the end of its Discovery Term for all purposes hereunder (such extended period shall be deemed a "Post-Option Extension") and shall remain subject to the Celgene Program Option until the end of its Discovery Term. With respect to such [**] Discovery Programs:

(i) such Discovery Program shall be subject to the same process for DC Selection Stage, DC Commitment and Celgene Option Exercise as described in Section 3.6(b) as other Discovery Programs were subject to during the Option Term, including making any payments as set forth in Section 9.3(a), if applicable;

(ii) the licenses granted to a Party pursuant to Section 8.2 with respect to such Discovery Program shall become effective only upon the Option Exercise Date for such Discovery Program;

(iii) each Party's Development obligations shall be as set forth in Section 3.8(a)(ii); and

(iv) if Celgene exercises the Celgene Program Option for such Discovery Program, Celgene shall be obligated to pay to Agios Development Costs as set forth in Section 9.4, milestone payments as set forth in Section 9.6, and royalties as set forth in Section 9.7. The Discovery Programs directed to [**] shall be subject to the provisions of Section 3.6 and Section 3.10 in the same way as other Discovery Programs that reach the DC Selection Stage during the Option Term (*i.e.*, if such [**] Discovery Program is the [**] if an Agios Deferral is made) Optionable Program).

Section 3.8 Primary Goals and General Responsibilities of Licensed Program.

(a) Licensed Program.

(i) With respect to each Split Program or Co-Commercialized Program, following the end of the Discovery Term for such Licensed Program, except as otherwise expressly set forth in this Agreement or mutually agreed by the Parties:

(A) Agios shall be responsible for (1) if Celgene has requested Agios to conduct the first Phase I MAD Study pursuant to Section 3.6(b)(iii)(A)(2), conducting all Clinical Trials through Completion of Phase I MAD with respect to Licensed Compounds Developed under such Licensed Program, and (2) conducting other Development activities as may be contemplated under the Development Plan (but only such activities that Agios has consented to conduct); and

(B) Except as set forth in Section 3.10 with respect to any Split Program, Celgene shall be responsible for (1) conducting all Clinical Trials with respect to Licensed Compounds Developed under such Licensed Program following Completion of Phase I MAD, and (2) conducting other Development activities as may be contemplated under the Development Plan (but only such activities prior to Completion of Phase I MAD that Celgene has consented to conduct).

(ii) With respect to each (if any) Discovery Program directed to [**] that has not yet reached the DC Selection Stage as of the end of the Option Term, Agios shall be responsible for Development activities under the Discovery Plan for such Program until the earlier of (A) [**] years following the end of the Option Term and (B) IND Acceptance (or, if the DC Commitment is made, Completion of Phase I MAD) for a Development Candidate in such Program. If IND Acceptance is not achieved by [**] years following the end of the Option Term or, if IND Acceptance is achieved by such time but Celgene does not exercise the Celgene Program Option within the Celgene Option Exercise Period, except as provided in Section 8.9, all rights related to such Program(s) granted by Agios to Celgene hereunder shall terminate, and such Program(s) shall be deemed an Agios Reverted Program in accordance with Section 3.12.

(iii) With respect to each Buy-In Program, following the end of the Discovery Term for such Buy-In Program, except as otherwise expressly set forth in this Agreement or mutually agreed by the Parties, the Commercializing Party with respect to such Buy-In Program shall be responsible for all Development activities under such Buy-In Program.

(iv) With respect to each Picked Validated Program selected by Celgene, following the end of the Discovery Term for such Program, except as otherwise expressly set forth in this Agreement or mutually agreed by the Parties, Celgene shall be responsible for all Development activities under such Program.

(b) Back-Up Compounds.

(i) It is understood that the JRC (or the JDC, as applicable) will identify Back-Up Compounds as contemplated by Sections 1.7, 1.14, 1.23, 1.47, and 1.98 and the compounds that contain the [**] or any series of compounds demonstrating activity against a Target as contemplated by Sections 1.14(a)(iv), 1.23(d), 1.47(d), and 1.98(a)(iv). When the JRC (or the JDC, as applicable) identifies a Collaboration Compound to be designated as a Back-Up Compound in a Program, such Collaboration Compound can only be so designated if it has not previously been allocated to another Program or if the Committee by Mutual Consent (after disclosure of the previous allocation of such Collaboration Compound to another Program) determines to designate such Collaboration Compound as a Back-Up Compound to such second Program.

(ii) As part of Agios' Development responsibilities, upon Celgene's written request at any time following IND Acceptance for a Development Candidate under a Licensed Program, Agios will advance the Development of [**] related to such Development Candidate through IND-Enabling Studies; provided that, regardless of the results of the IND-Enabling Studies, Agios shall not be required to pursue additional IND-Enabling Studies for such [**] under such Licensed Compound. All costs associated with Development of such [**] through such IND-Enabling Studies shall be at Agios' sole cost and shall not be Development Costs to be reimbursed by Celgene hereunder; and Agios shall not be entitled to an IND Amount with respect to any Back-Up Compounds. Subject to the foregoing, if none of the [**] Developed by Agios and included within a Licensed Program meet the Clinical Candidate Guidelines, upon Celgene's written request, Agios will use Commercially Reasonable Efforts to identify another [**] that will meet such guidelines and that is not already allocated to another Program. Any original [**] that is replaced as provided in this section shall become a Residual Program Compound.

(c) Updates. Following the Discovery Term for a Licensed Program and thereafter with respect to each Licensed Program, each Party shall provide the other Party with regular quarterly written reports on such Party's activities relating to the Development, Commercialization, or other Collaboration activities following the Discovery Term, including a summary of results, information, and data generated, any activities planned with respect to Development going forward (including, for example, updates regarding regulatory matters and Development activities for the next [**]), challenges anticipated and updates regarding intellectual property issues (including a disclosure of Collaboration Intellectual Property developed or generated since the last written report) relating to each Licensed Program. Such written reports may be discussed by telephone or video-conference, or may be provided at each JRC, JDC or JCC meeting, as applicable; provided that, reasonably in advance of the meeting of such Committee, the Party providing the written report will deliver to the other Party an agenda setting forth what will be discussed during the meeting. The Party receiving such written report shall have the right to reasonably request, and to receive in a timely manner clarifications and

answers to, questions with respect to such reports. During the Term, with respect to each Licensed Program, each Party shall coordinate with, and keep the other Party and the JDC informed with respect to, activities assigned to such Party under the applicable Development Plan, including the conduct of any applicable Clinical Trials. Notwithstanding the foregoing, with respect to any Picked Validated Program selected by Celgene or with respect to any Buy-In Program, each Party shall only have an obligation to provide such written reports [**].

Section 3.9 Development Plans.

(a) The Development under each Co-Commercialized Program, Split Program, or Buy-In Program shall be governed by a Development Plan (the "Development Plan") that describes the proposed overall objectives of such Licensed Program, as well as the activities to be performed, the Party responsible for performance of an activity (which shall be as provided in Section 3.8), [**] budget of Development Costs ("Development Budget"), and anticipated timelines for performance; provided that the Development Budget will only be applicable for periods following the Development Cost Initiation Date for such Licensed Program. In addition, if Celgene requests that Agios perform any Development activities for a Celgene Picked Validated Program and Agios consents to perform such activities, such activities shall also be governed by a Development Plan, with Development Budget.

(b) With respect to each Co-Commercialized Program, Agios will prepare and deliver to the JDC the initial Development Plan as set forth in Section 3.6(b)(ii). Within [**] days following the Option Exercise Date with respect to such Co-Commercialized Program, the JDC shall review and approve such initial Development Plan, with such modifications as determined by the JDC. The Development Plan for a Co-Commercialized Program shall not include a Development Budget, except for such Development activities as are to be conducted by Agios pursuant to Section 3.8.

(c) With respect to each Buy-In Program, the Commercializing Party will prepare and deliver to the JDC the initial Development Plan as set forth in Section 3.11(a). Within [**] days following the Buy-In Party's exercise of the Buy-In Right with respect to such Buy-In Program, the JDC shall approve such plan, with such modifications as determined by the JDC.

(d) With respect to each Split Program, Agios will prepare and deliver to the JDC the initial Development Plan as set forth in Section 3.6(b)(ii). Within [**] days following the Option Exercise Date for such Split Program, the JDC shall review and approve such initial Development Plan, with such modifications as determined by the JDC.

(e) The Commercializing Party shall prepare [**] updates to each Development Plan for each Co-Commercialized Program, Buy-In Program, and Split Program in the Field in the Commercializing Party's Territory, which [**] updates shall be submitted for approval by the JDC. Subject to Section 2.8, the Development Plan may be amended during the [**] by the JDC.

Section 3.10 Split Programs; Agios Deferral Right; Development Activities; Agios Opt-Out.

(a) Split Programs; Agios Deferral.

(i) Within [**] days of the IND Acceptance for an Optionable Program, Agios shall have the right to elect to retain all US Territory rights with respect to the [**] Optionable Programs or, if Agios makes an Agios Deferral, with respect to the [**] such Optionable Programs, by providing written notice to Celgene within such [**]-day period. For clarity, Agios shall have no US Territory rights pursuant to this Section 3.10, or a right to make an Agios Deferral, with respect to the [**] Optionable Programs and shall only have the US Territory rights pursuant to this Section 3.10 with respect the [**] Optionable Program or, if Agios makes the Agios Deferral, the [**] Optionable Program (but, with respect to the [**] Optionable Programs with respect to which Agios does not retain the US Territory rights, Agios shall retain the rights specified in Article VI with respect to Co-Commercialized Products). Agios may exercise its rights to retain US Territory rights by providing written notice to Celgene within such [**]-day period; provided that, if Agios fails to take any action within such [**]-day period, Agios shall be deemed to have waived its right to retain all US Territory rights with respect to the [**] (or if Agios has made an Agios Deferral, the [**]) Optionable Program out of every [**] Optionable Programs. The [**] if an Agios Deferral is made) Optionable Program with respect to which Agios retains the US Territory rights under this Section 3.10 shall be deemed a Split Program.

(ii) Instead of exercising its US Territory rights on the [**]Optionable Programs pursuant to Section 3.10(a)(i) above, Agios shall have the right to defer its US Territory rights to the [**] Optionable Program ("Agios Deferral"), by providing Celgene written notice thereof within [**] days of the IND Acceptance for such Optionable Program, in which event Agios' right to elect to retain the US Territory rights pursuant to Section 3.10(a)(i) above shall apply to such [**] Optionable Program.

(iii) Upon the Option Exercise Date for a Split Program, (A) Agios shall have the exclusive right to pursue the Development and Commercialization of Licensed Compounds and Licensed Products under such Split Program in the US Territory; (B) Celgene shall have the exclusive right to pursue the Development and Commercialization of Licensed Compounds and Licensed Products under such Split Program in the ROW Territory; (C) the licenses granted to a Party under Section 8.2(c) with respect to such Split Program shall become effective; (D) the Parties shall share in the Global Development Costs of Licensed Compounds and Licensed Products Developed under such Split Program as set forth in Section 9.4; (E) Celgene shall be responsible for paying to Agios specified royalties on Net Sales in the ROW Territory as set forth in Section 9.7(b)(i); (F) Celgene shall be responsible for paying to Agios specified milestone payments upon achievement of specific milestone events associated with the ROW Territory as set forth in Section 9.6; and (G) Agios shall be responsible for paying to Celgene specified royalties on Net Sales in the US Territory as set forth in Section 9.7(b)(ii). Celgene shall have no obligation to pay any IND Amount on any Split Program.

(iv) The [**] Optionable Program out of every [**] Optionable Programs (or, if Agios makes an Agios Deferral, the [**] Optionable Program), upon the Option Exercise Date, shall be deemed Co-Commercialized Programs hereunder; provided that, if Agios elects not to exercise its right to retain US Territory rights under Section 3.10(a)(i) with respect to the [**] (or if Agios makes an Agios Deferral, the [**]) such Optionable Program, then such Optionable Program shall also be deemed a Co-Commercialized Program hereunder.

(v) For purposes of clarity, (A) Agios' US Territory rights, and right to make an Agios Deferral, shall apply to the [**], as applicable) out of the first [**] Optionable Programs for which Celgene exercises the Celgene Program Option, then shall apply to the [**], as applicable) out of the next [**] such Optionable Programs, and shall continue with respect to each set of [**] Optionable Programs for which Celgene exercises the Celgene Program Option; and (B) if Celgene does not exercise the Celgene Program Option for an Optionable Program, such Optionable Program shall not count as [**] Optionable Programs for purposes of this Section 3.10, and, to the extent Agios exercised its rights to retain US Territory rights or made an Agios Deferral with respect to such Optionable Program, such election shall not count as Agios' exercise of rights or an Agios Deferral, which shall then transfer to the next Optionable Program.

(b) Development Activities.

(i) The Commercializing Party shall be responsible for conducting all Development activities as may be contemplated under the Development Plan for each Split Program with respect to such Commercializing Party's portion of the Territory (*i.e.*, the US Territory for Agios and the ROW Territory for Celgene). Neither Commercializing Party shall conduct any Development activities for any Split Program outside such Party's portion of the Territory (even if such Development activities are for purposes of Development in such Party's portion of the Territory), unless the JDC by Mutual Consent approves of such activities, including any protocol associated with a Clinical Trial, and such activities are reflected in the applicable Development Plan.

(ii) The Parties will share all Global Development Costs in accordance with Section 9.4(b); provided that Celgene shall not be responsible for any of Agios' Global Development Costs prior to the Development Cost Initiation Date. For clarity, Celgene's obligation to share Global Development Costs shall not include any Development Costs incurred prior to the Development Cost Initiation Date or any Development Costs related to any Clinical Trial for which the FPD occurred prior to the Development Cost Initiation Date even if completed following the Development Cost Initiation Date; instead, Celgene's obligations will be limited to Development activities related to any company-sponsored Phase II Studies or later stages of Development.

(iii) If either Party proposes to undertake any Development activities for a Split Program in such Party's portion of the Territory that the other Party reasonably determines are reasonably likely to have a material adverse impact on the Development or Commercialization of Split Compounds or Split Products in the other Party's portion of the Territory, such proposing Party shall not proceed with such Development activities unless approved by the JDC (with any disputes resolved in accordance with the dispute resolution procedure of Section 2.8, including the Lead Party having the final decision-making authority to the extent provided in Section 2.8(b)).

(iv) With respect to each Split Program, each Party shall be entitled to use the data and results (including clinical data) from all Development activities conducted by the other Party; provided that a Party shall not interpret such data or results in a different manner than the Party who performed the Development activity giving rise to the data or results without the performing Party's prior written consent (which may be given through the Party's representatives on the JDC). In furtherance thereof, each Commercializing Party shall update the other Party pursuant to Section 3.8(c) on the status of all Development activities for Split Programs, including a summary of relevant data. Each Commercializing Party will use Commercially Reasonable Efforts to ensure the other Party has access to such data and results, including, if appropriate, providing for such access in any agreement with a Third Party Contractor.

(c) Agios Opt-Out. Notwithstanding any of the foregoing in this Section 3.10 and without it being a breach of Section 7.2(a)(ii), following the [**] of the Option Exercise Date for a Split Program, Agios shall have the right, effective upon [**] prior written notice, to elect to opt-out of its US Territory rights under such Split Program (the "Agios Opt-Out" and the effective date of such Agios Opt-Out being the expiration of such [**] period, the "Agios Opt-Out Date") (which notice shall may not be given prior to the [**] of the Option Exercise Date). Upon receipt of such Agios Opt-Out notice:

(i) Celgene may elect to assume all US Territory rights under such Split Program (effective on the Agios Opt-Out Date) by providing Agios with written notice, in which event, (A) Agios shall provide to Celgene a reasonably detailed accounting of all Development Costs incurred by Agios under such Split Program prior to the Agios Opt-Out Date; (B) Agios and Celgene shall continue to share Global Development Costs through the Agios Opt-Out Date under Section 9.4; (C) Agios shall provide to Celgene a reasonably detailed summary of Development activities, including Global Studies and other global Development activities, undertaken by Agios under such Split Program, including any Clinical Trials committed but not yet completed as of such date; (D) Agios shall undertake, and coordinate with Celgene with respect to, any wind-down or transitional activities reasonably necessary to transfer to Celgene Development, Manufacturing and Commercialization responsibility in the US Territory for such Split Program, at Agios' sole expense; provided that the Parties shall reasonably cooperate in seeking to minimize the costs of such wind-down or transitional activities; provided further that, (1) if Celgene requests that any contracts or agreements that extend beyond the Agios Opt-Out Date be terminated, Agios shall be responsible for all costs associated with such termination, and, (2) if Celgene requests that any such contract or agreement remain in effect, Celgene shall be responsible for all Territory-Specific Development Costs under such contract or agreement following the Agios Opt-Out Date or, if Celgene requests assignment of such contract or agreement prior to the Agios Opt-Out Date, following such assignment (whichever is earlier); (E) upon the Agios Opt-Out Date, each Licensed Product under such Split Program shall become a Co-Commercialized Product both with respect to the US Territory and the ROW Territory, and such Split Program shall become a Co-Commercialized Program in both the US Territory and ROW Territory, and shall thereafter be subject to the milestone payment and royalty provisions of Section 9.6 and 9.7 applicable to other Co-Commercialized Products, without any retroactive application of such provisions; provided that Agios shall not be entitled to perform Commercialization Activities for such Co-Commercialized Product pursuant to Section 6.3; and (F) the licenses granted to each Party with respect to such Split Program under Section 8.2(c) shall convert to the licenses granted to each Party with respect to a Co-Commercialized Program under Section 8.2(a). For clarity, upon the Agios Opt-Out Date, if Celgene elects to assume all US Territory rights, Celgene shall be responsible for all Development Costs for such Co-Commercialized Program, except as provided in clause (D) above.

(ii) If Celgene elects not to assume all US Territory rights under such Split Program, then upon the Agios Opt-Out Date, (A) Celgene shall retain its ROW Territory rights and obligations hereunder and shall have no obligation to pay Agios for Global Development Costs incurred by Agios under such Split Program (other than paying for Celgene's share of Global Development Costs incurred prior to the Agios Opt-Out Date); (B) each Split Product in the ROW Territory shall become a Co-Commercialized Product and the applicable Split Program shall become a Co-Commercialized Program, in each case, with respect to the ROW Territory, except that the licenses for such Program shall continue to be as described in Section 8.2(c)(i); (C) Celgene's license to Agios under Section 8.2(c)(ii) shall terminate; (D) each Party shall be prohibited from pursuing the Development, Manufacture or Commercialization of Split Compounds and Split Products under such Split Program in the US Territory; (E) Agios, at Celgene's election, either transfer all INDs with respect to such Split Program to Celgene or close such INDs; and (F) Agios shall not license Agios Intellectual Property and Agios Collaboration Intellectual Property to a Third Party in connection with the Development, Manufacture or Commercialization of Split Compounds or Split Products under such Split Program in the US Territory, and Celgene shall not license the Celgene Intellectual Property or Celgene Collaboration Intellectual Property previously exclusively licensed to Agios pursuant to Section 8.2(c) to a Third Party in connection with the Development, Manufacture or Commercialization of Split Compounds or Split Products under such Split Program in the US Territory.

(d) Celgene Right of First Negotiation. If Agios intends to begin negotiations with any Third Party(ies) to grant a license to such Third Party to the US Territory rights for a Split Program (excluding licenses to Third Party Contractors or solely for purposes of promotion, distribution or other marketing and sales activities with or on behalf of Agios) (the "Licensing Opportunity"), Agios shall provide written notice of such intent to Celgene, and Celgene shall have [**] days to notify Agios in writing that Celgene desires to negotiate with respect to such Licensing Opportunity. If Celgene provides such notice in such [**]-day period, Agios shall exclusively negotiate in good faith with Celgene with respect to such Licensing Opportunity. If the Parties are unable to enter into a definitive agreement with respect to such Licensing Opportunity within [**] days (or such longer period agreed to by the Parties) following written notice from Celgene of its interest in entering into negotiations, then Agios shall be free during the next [**] months after the expiration of the foregoing [**]-day (or, if applicable, longer) negotiation period to enter into a transaction relating to such Licensing Opportunity with any Thirty Party(ies); provided that, if Agios does not enter a Licensing Opportunity prior to the expiration of such [**]-month period, such Licensing Opportunity shall again be subject to the provisions of this Section 3.10(d); provided further that, if Agios offers terms to any Third Party with respect to the Licensing Opportunity that are the same or more favorable to such Third Party than the terms last offered by Celgene, taken as a whole, with respect to the Licensing Opportunity, then (i) Agios shall first offer such terms or more favorable terms to Celgene and Celgene shall have the right to enter into an agreement with Agios with respect to the Licensing Opportunity on such terms or more favorable terms; and (ii) if Celgene does not exercise such right to enter into an agreement with Agios with respect to the Licensing Opportunity on such

terms or more favorable terms by providing written notice to Agios within [**] days following Agios' notice to Celgene of such terms or more favorable terms, Celgene's right to negotiate the terms of, or enter into an agreement with respect to, the Licensing Opportunity with Agios under this Section 3.10(d) shall terminate, and Agios shall be free to enter into a transaction relating to the Licensing Opportunity with any Third Party(ies) on such terms or such more favorable terms, as applicable, within such [**]-month period. Celgene's rights with respect to a Licensing Opportunity shall be on a Split Program-by-Split Program basis, and the expiration of such rights for one Split Program shall not affect Celgene's rights to negotiate a Licensing Opportunity with a different Split Program pursuant to the provisions of this Section 3.10(d).

(e) Agios Licensing of US Territory Rights. If Agios grants a license to a Third Party to Develop or Commercialize Split Products in the US Territory under the first Split Program only (excluding licenses to Third Party Contractors or solely for purposes of promotion, distribution or other marketing and sales activities with or on behalf of Agios), then, notwithstanding anything herein to the contrary (including Section 2.8(c)(iv)), if any dispute arises at the JDC with respect to any changes to the Development Plan (including the Development Budget) or any Development activities conducted by a Party under such Split Program (including clinical Manufacturing activities), and such dispute is not resolved at the JDC or JSC level or by the Executive Officers pursuant to Section 2.8, [**] shall have final decision-making authority with respect to such dispute, [**], until (i) FDA approval of the first special protocol assessment ("SPA") for the first pivotal trial for such first Split Program, if the JDC decides to pursue a SPA, or (ii) JDC approval of the protocol design for the first pivotal trial for such first Split Program, if the JDC decides not to pursue a SPA; provided that [**] shall exercise any such final decision-making authority in a manner consistent with a commitment of Commercially Reasonable Efforts to the Development and Commercialization of Split Product under such Split Program in the US Territory.

Section 3.11 Independent Programs; Buy-In Right at IND Acceptance.

(a) Buy-In Right. Either Party (but not both Parties) may Develop an Independent Program pursuant to Section 3.5(b)(ii); provided that (i) such Party shall provide quarterly updates to the JRC (or the JDC, as applicable) and the other Party on the progress of such Development activities since the prior update and the general scope of proposed activities, including anticipated timelines and budgets, through at least IND Acceptance, (ii) at least [**] days prior to any proposed IND Acceptance in the Oncology Field, such Party shall provide to the JRC and the other Party the proposed materials to be submitted as part of the IND Acceptance, and (iii) in the event that such Party achieves an IND Acceptance with respect to any such Independent Program, such Party shall provide written notice to the other Party thereof (the "Buy-In Party") and all relevant information and data with respect to such Independent Program as may be reasonably requested by the Buy-In Party, including pre-clinical data, proposed Development Plans, budgets and timelines.

(b) Exercise of Buy-In Right. The Buy-In Party shall have [**] days from the delivery of the information and data described in Section 3.11(a)(iii) above to exercise its right to buy into such Independent Program ("Buy-In Right") by:

(i) providing written notice to the other Party of such exercise; and

(ii) paying the other Party a one-time, non-refundable payment of [**] Dollars (US$[**]) within [**] days following such notice as a Buy-In Right exercise fee.

(c) Effects of Exercising or Waiving Buy-In Right.

(i) If the Buy-In Party exercises its Buy-In Right with respect to an Independent Program, such Independent Program shall thereafter be deemed a Buy-In Program and each Party's rights and obligations under this Agreement with respect to such Buy-In Program shall become effective, including the licenses granted pursuant to Section 8.2(d), the Parties' obligations to share in Development Costs as set forth in Section 9.4(c), and the obligation of the Commercializing Party to pay the Buy-In Party specified royalties on worldwide Net Sales as set forth in Section 9.7(c). Notwithstanding anything herein to the contrary, Celgene shall not owe any IND Amount or Phase I Amount for any Buy-In Product, regardless of who is the Buy-In Party.

(ii) If Celgene declines to exercise its Buy-In Right (or does not provide any notice within such [**]-day period) with respect to an Independent Program being independently Developed by Agios, except as provided in Section 8.9, all rights related to such Independent Program granted by Agios to Celgene hereunder shall terminate, and such Independent Program shall become an Agios Reverted Program in accordance with Section 3.12.

(iii) If Agios declines to exercise its Buy-In Right (or does not provide any notice within such [**]-day period) with respect to an Independent Program being independently Developed by Celgene, such Independent Program shall thereafter be deemed a Celgene Reverted Program, and the licenses granted to Celgene pursuant to Section 8.2(e) with respect to such Celgene Reverted Program shall become effective. Celgene shall have no further financial obligations, and Agios shall have no further rights, with respect to such Celgene Reverted Program, except that (A) Celgene shall be obligated to pay Agios royalties on Net Sales of Celgene Reverted Products Commercialized under such Celgene Reverted Program in accordance with Section 9.7(e), (B) any Celgene Reverted Program and any Celgene Reverted Products shall be considered a "Program" and "Licensed Product," respectively, solely for purposes of Article XIV, and (C) in the event that Celgene breaches Section 9.7(e), and subject to Section 14.2(b)(i), Agios shall have the right to terminate this Agreement and the licenses granted to Celgene pursuant to Section 8.2(e) with respect to such Celgene Reverted Program, in which case the effects of termination set forth in Section 14.3(a) shall apply with respect to such Celgene Reverted Program as if it were a Terminated Program.

(d) Term.

(i) With respect to each Independent Program, the Buy-In Rights described in this Section 3.11 shall terminate upon the later of (A) the end of the Option Term and (B) [**] years following such time as such Independent Program became an Independent Program hereunder, unless the IND Acceptance has been achieved prior to such time (in which event, the Buy-In Party shall be entitled to exercise or waive the Buy-In Right in accordance with this Section 3.11(b)) (the "Buy-In Right Term").

(ii) For purposes of clarity, if IND Acceptance has not been achieved under an Independent Program during the Buy-In Right Term for such Independent Program, then (A) the Buy-In Party's Buy-In Right with respect to such Independent Program shall terminate as of the end of such Buy-In Right Term, (B) such Independent Program shall be deemed an Agios Reverted Program (if Agios was the Party independently Developing such Independent Program prior to the end of the Buy-In Right Term) or a Celgene Reverted Program (if Celgene was the Party independently Developing such Independent Program prior to the end of the Buy-In Right Term), (C) the Independent Target shall be deemed an Agios Reverted Target or Celgene Reverted Target, as applicable, and (D) the licenses set forth in Sections 8.2(f) and 8.2(e), respectively, shall apply with respect to such Agios Reverted Program or Celgene Reverted Program, as applicable.

Section 3.12 Agios Reverted Programs.

(a) With respect to (i) each Discovery Program for a Development Candidate with respect to which (A) Celgene does not make a DC Commitment within the period required (including any deferral period as described in Section 3.6(d)) or (B) if Celgene makes a DC Commitment, Celgene does not exercise the Celgene Program Option, (ii) each Picked Validated Program that is selected by Agios, or not selected as a Pick by either Party, at the end of the Option Term, (iii) each Discovery Program that is not confirmed as a Validated Program at the end of the Option Term pursuant to Section 3.7, (iv) each Independent Program Developed by Agios for which Celgene does not exercise its Buy-In Right at IND Acceptance or for which the Buy-In Right expires at the end of the Buy-In Right Term, and (v) each Discovery Program or Independent Program related to a Collaboration Target that is removed from the Target List pursuant to Section 3.5(b) above and not added back to the Target List (either as a whole with respect to both Parties or partially with respect to Agios) pursuant to Section 3.5(a) or Section 3.5(b) (but, as provided in Section 3.5(b)(iii), all Collaboration Compounds associated with such Discovery Program or Independent Program shall be deemed Residual Program Compounds) (each, an "Agios Reverted Program"), except as provided in this Section 3.12 or Section 8.9, (x) all rights granted hereunder by Agios to Celgene with respect to such Agios Reverted Program shall terminate as further set forth below; and (y) all rights granted by Celgene to Agios with respect to such Program (prior to it becoming an Agios Reverted Program) shall terminate but any licenses granted by Celgene to Agios pursuant to Section 8.2(f) shall apply with respect to such Agios Reverted Program.

(b) Subject to Section 3.5 (to the extent a Collaboration Target is added back onto the Target List) and Section 8.8, Agios shall have no further obligations to Celgene, and Celgene shall have no further rights from Agios, with respect to any Agios Reverted Program, including related Agios Reverted Compounds, Agios Reverted Targets or Agios Reverted Products.

(c) The Parties agree that Programs within the Collaboration will have priority to all chemistry Developed in the Collaboration and that, as such, Residual Program Compounds shall remain in the Collaboration until the end of the Option Term (or, if applicable, with respect to any Residual Program Compounds that have application to any Extended Program, at the end of any Post-Option Extension).

(i) During the Option Term, the Parties may test the Residual Program Compounds against the Collaboration Targets that are the subject of Programs in the Collaboration. If any Residual Program Compound is determined by the JRC (or the JDC, as applicable) to be Active against a Collaboration Target remaining in the Collaboration, such Residual Program Compound shall become a Collaboration Compound under the applicable Program.

(ii) In addition, at the end of the Option Term, Agios shall use Commercially Reasonable Efforts to test a reasonable number of representative and available Residual Program Compounds against each Collaboration Target under a Validated Program that has not yet reached the DC Selection Stage as of the end of the Option Term. Based on such test results, the JRC (or the JDC, if the JRC no longer remains in effect) by Mutual Consent shall determine whether such Residual Program Compounds are Active against any Collaboration Target under any such Validated Program. If any such Residual Program Compound is found to be Active against a Collaboration Target under a Validated Program, such Residual Program Compound shall become a Collaboration Compound under such Validated Program. Thereafter, with respect to all other Residual Program Compounds remaining on the Compound List, all rights related to such chemical entity(ies) granted by Agios to Celgene hereunder shall terminate and such chemical entity(ies) shall thereafter no longer be deemed a Collaboration Compound(s) or Residual Program Compound(s) hereunder.

(d) With respect to any Agios Reverted Program or Buy-In Program for which Agios is the Commercializing Party, if at any time after the Initial Phase (or the Extended Initial Phase, if applicable), Agios determines that any Back-Up Compound included in such Agios Reverted Program or Buy-In Program does not meet the Clinical Candidate Guidelines, Agios shall be entitled to substitute, in place of such original Back-Up Compound, another Back-Up Compound that (i) is identified by the JRC (or the JDC, as applicable) following Agios' notification to such Committee of such failure, and (ii) is not already allocated to another Program under this Agreement. Any original Back-Up Compound that is replaced as provided in this section shall become a Residual Program Compound.

(e) In determining which Collaboration Compounds are to be deemed Agios Reverted Compounds at the time a Program becomes an Agios Reverted Program, no Collaboration Compounds shall be deemed Agios Reverted Compounds if they are already a Collaboration Compound for another Program within the Collaboration, but instead such Collaboration Compound shall remain part of such other Program.

Section 3.13 Initial Target Indication in Oncology Field. The Parties acknowledge and agree that each Program shall initially be directed towards Target Indications in the Oncology Field. Unless otherwise mutually agreed by the Parties, the first Clinical Trial in patients conducted by or on behalf of Celgene under a Licensed Program shall be for a Target Indication in the Oncology Field. It is understood by the Parties that, subject to compliance with the prior sentence, either Party may identify other Indications outside of the Oncology Field for such Collaboration Compound, Licensed Compound or Licensed Product.

Section 3.14 Companion Diagnostics.

(a) Development of Companion Diagnostic. The Parties may mutually agree to Develop and/or Commercialize a Companion Diagnostic for use with a Collaboration Compound, Licensed Compound or Licensed Product; provided that, unless the JRC (or the JDC, as applicable) agrees by Mutual Consent otherwise, the Commercializing Party (or, with respect to a Split Program, the Party designated by the JDC) will use a Third Party Contractor reasonably acceptable to both Parties to perform all Development and Commercialization for the Companion Diagnostic. In such event:

(i) the definition of such "Collaboration Compound," "Licensed Compound" or "Licensed Product" shall and hereby does include the Companion Diagnostic for purposes of defining Agios Patent Rights, Celgene Patent Rights and Collaboration Patent Rights, and each of the licenses granted to a Party under Section 8.1 or 8.2, as applicable, with respect to such Collaboration Compound, Licensed Compound or Licensed Product; and

(ii) All profits of the Commercializing Party (or the Party designated by the JDC for a Split Program) with respect to such Companion Diagnostic shall be [**] by the Parties pursuant to a mechanism agreed to by the Parties at the time the Third Party Contractor is appointed.

(b) Separate Obligations. No separate milestones shall be owed by Celgene to Agios pursuant to Section 9.6 with respect to a Companion Diagnostic. Upon termination of the Program or reversion of rights to a Party with respect to a Program hereunder in association with which the Companion Diagnostic was Developed or Commercialized, in addition to the effects of such termination or reversion set forth in Section 14.3, separate transitional activities shall be undertaken with respect to the Companion Diagnostic to ensure that the appropriate Regulatory Approvals, Manufacturing Technology or other Know-How or Patent Rights necessary for the Development, Manufacture and/or Commercialization of such Companion Diagnostic shall be transferred to the Party to whom the rights to the underlying Program are transferred to the same extent as Regulatory Approvals, Manufacturing Technology or other Know-How or Patent Rights otherwise associated with such Program are transferred.

(c) No Other Diagnostics. For purposes of clarity, unless otherwise mutually agreed by the Parties, neither Party shall have any right, under the licenses granted to such Party pursuant to Section 8.1 or 8.2 and notwithstanding the definition of "Field" hereunder, to Develop, Manufacture and/or Commercialize any biomarker or diagnostic product for use with a Collaboration Compound, Licensed Compound or Licensed Product, other than a Companion Diagnostic pursuant to this Section 3.14.

Section 3.15 Records; Tech Transfer.

(a) Agios shall maintain in all material respects, and shall require its Third Party Contractors to maintain in all material respects, complete and accurate records in segregated books of all work conducted in furtherance of any Program and all results, data and developments made in conducting such activities. Such records shall be complete and accurate and shall fully and properly reflect all such work done and results achieved in sufficient detail and in good scientific manner appropriate for patent and regulatory purposes. Agios shall require the applicable study sites to maintain original source documents from Clinical Trials of

Collaboration Compounds and Licensed Compounds, until either (i) the end of the Discovery Term for such Program, if Celgene does not exercise any applicable Celgene Program Option or obtain an exclusive license under Section 8.2 to such Program, and (ii) for at least [**] years (or such longer period as is commercially reasonable under the circumstances, taking into account maintenance requirements under applicable Law) following completion of the Development activities undertaken by Agios or its Third Party Contractors under the Licensed Program, if Celgene does exercise such option or take an exclusive license under Section 8.2 to such Program; provided that Celgene or Agios shall be entitled to obtain copies of such source documents at the end of such [**]-year period.

(b) Celgene shall have the right, during normal business hours and upon reasonable notice, to inspect and copy (or request Agios to copy) all records of Agios or its Third Party Contractors, as applicable, maintained in connection with the work done and results achieved in the performance of activities under a Program, but solely to the extent access to such records is necessary for Celgene to exercise its rights under this Agreement with respect to the applicable Program.

(c) As soon as reasonably practical after Celgene exercises the Celgene Program Option for a Program or obtains an exclusive license under Section 8.2 to a Program and thereafter upon Celgene's reasonable request during the Term, Agios shall transfer to Celgene[**] copies of all Agios Know-How and Agios Collaboration Know-How related to such Program. In addition, Agios shall provide reasonable assistance, including making its personnel reasonably available for meetings or teleconferences to answer questions and provide technical support to Celgene with respect to the use of such Agios Know-How and Agios Collaboration Know-How in the Development, Manufacture and Commercialization of the applicable Licensed Compounds or Licensed Products. The costs and expense incurred by Agios in connection with such assistance shall be provided [**].

Section 3.16 Third Parties.

(a) Use of Third Party Contractors. If Agios desires to use any Third Party Contractors to conduct any of its Development, Commercialization or other Collaboration activities hereunder, or if Celgene desires to use any Third Party Contractors to conduct any of its Development, Commercialization or other Collaboration activities hereunder, such Party must comply with the obligations of Section 8.4(a)(ii)(A) through (D), even to the extent no sublicense of rights is granted to such Third Party.

(b) Third Party Collaborators. If Agios desires to enter into any collaboration with Third Parties involving the Metabolome, Agios shall implement guidelines to (i) limit or prohibit its employees or consultants from working on activities under the Collaboration hereunder and under Agios' Third Party collaboration where the knowledge gained from one project may be inappropriately used in the other (whether intentionally or unintentionally); and (ii) use separate laboratories, or separate parts of a lab, to perform Agios' obligations hereunder.

Article IV
Manufacture and Supply

Section 4.1 Pre-Clinical, Clinical and Commercial Supply. Except as set forth below in this Section 4.1 or Section 4.2, unless otherwise determined by the JSC, JRC, JDC or JCC, as applicable, or as otherwise mutually agreed by the Parties:

(a) Discovery Term. Agios shall be solely responsible for Manufacturing, or having Manufactured by its designee, all pre-clinical and clinical supply of any Collaboration Compounds, Licensed Compounds and/or Licensed Products under a Discovery Program, including any necessary raw materials or other components, necessary for use by both Parties to conduct each Discovery Program through the Discovery Term for such Discovery Program and, solely with respect to Licensed Programs for which Celgene exercises the Celgene Program Option, through Completion of Phase I MAD. Agios shall be solely responsible for all Manufacturing Costs associated with the activities described in this Section 4.1(a).

(b) Picked Products and Co-Commercialized Products. After the Discovery Term, Celgene shall be solely responsible for all Manufacturing activities with respect to each Picked Validated Program selected by Celgene. After the Discovery Term or after Completion of Phase I MAD, if applicable, Celgene shall be solely responsible for all Manufacturing activities with respect to each Co-Commercialized Program. Celgene shall be solely responsible for all Manufacturing Costs associated with the activities described in this Section 4.1(b).

(c) Split Products.

(i) After the Discovery Term or after Completion of Phase I MAD, if applicable, with respect to each Split Program, (A) Celgene shall be solely responsible for all Manufacturing activities for supply of Split Compounds and Split Product in the ROW Territory (or Celgene's activities in the US Territory in accordance with the license under Section 8.2(c)(i)(B)), and (B) Celgene shall Manufacture Agios' supply of Split Compounds and Split Products in the US Territory (or Agios' activities in the ROW Territory in accordance with the license under Section 8.2(c)(ii)(B)), pursuant to the terms and conditions of a supply agreement (including customary terms such as forecasting procedures and allocation of supply) to be negotiated in good faith and mutually agreed upon by the Parties (the "Supply Agreement"), and Celgene shall establish and engage a Third Party manufacturer as a secondary source of clinical and commercial supply of Split Compounds and/or Split Products for the US Territory; provided that in the event of a supply failure under the Supply Agreement (to be further defined in the Supply Agreement in terms of failure to provide adequate and/or timely supply), the Supply Agreement shall permit Agios to, at Agios' election, (A) if Celgene fails to supply, directly purchase supply of Split Compounds and Split Products from the applicable manufacturer, or (B) if Celgene and its Third Party Manufacturer(s) fail to supply, engage and obtain supply from Third Party suppliers designated by Agios; provided further that with respect to Agios' right under the Supply Agreement to purchase any supply of Split Compounds and Split Products from Third Parties, Celgene shall reasonably cooperate with Agios and transfer to such Third Party supplier all Manufacturing Technology Controlled by Celgene used to, and reasonably necessary for such Third Party to, Manufacture such Split Compound or Split Product, as more specifically set forth in the Supply Agreement.

(ii) Celgene shall be solely responsible for all Manufacturing Costs associated with the commercial supply of Split Compounds and Split Product in the ROW Territory. Agios shall be solely responsible for all Manufacturing Costs associated with the commercial supply of Split Compounds and Split Products in the US Territory, including any costs incurred by Celgene for such Manufacturing that are specifically related to the US Territory; provided that any supply provided by Celgene to a sublicensee of Agios shall be provided at Celgene's Manufacturing Cost plus [**]%. Manufacturing Costs associated with clinical supply of Split Compounds and Split Products (including pre-clinical and clinical scale-up costs) shall be shared in accordance with Section 9.4(b) if deemed Global Development Costs or paid by the Commercializing Party if deemed Territory-Specific Development Costs. Notwithstanding the foregoing, Manufacturing Scale-Up Costs for Split Compounds and Split Products for the Territory shall be deemed Global Development Costs and shared pursuant to Section 9.4.

(d) Buy-In Products. The Commercializing Party shall be solely responsible for all Manufacturing activities for supply of Buy-In Compounds and Buy-In Products necessary for use by both Parties to conduct any Buy-In Program. The Commercializing Party's Manufacturing Costs associated with the activities described in this Section 4.1(d) following the Development Cost Initiation Date to the extent associated with clinical supply of Buy-In Compounds and Buy-In Products (including pre-clinical and clinical scale-up costs) shall constitute Development Costs that will be shared by the Parties pursuant to Section 9.4(c); and the Commercializing Party shall be solely responsible for all other Manufacturing Costs associated with the activities described in this Section 4.1(d), including all Manufacturing Costs for commercial supply of Buy-In Compounds and Buy-In Products and all Manufacturing Scale-Up Costs.

(e) Independent Compounds. The Party conducting an Independent Program shall be solely responsible for all Manufacturing activities for supply of Independent Compounds necessary for use by such Party in the Independent Program. The Party conducting such Independent Program shall be solely responsible for all Manufacturing Costs associated with the activities described in this Section 4.1(e).

(f) Celgene Reverted Products. Celgene shall be solely responsible for all Manufacturing activities for supply of Celgene Reverted Compounds and Celgene Reverted Products necessary for use by Celgene in a Celgene Reverted Program. Celgene shall be solely responsible for all Manufacturing Costs associated with the activities described in this Section 4.1(f).

(g) Third Party Manufacturers. If Agios uses any Third Party to fulfill its Manufacturing obligations under Section 4.1(a) with respect to any supply to be used in any Development or Commercialization activities under a Licensed Program following the Discovery Term for such Program (other than with respect to a Buy-In Program for which Agios is the Commercializing Party and, to the extent that Agios has the right to use a Third Party to fulfill its Manufacturing obligations, other than a Split Program in the US Territory), or following Celgene's exercise of the Celgene Program Option, as applicable, the Third Party and the terms of the agreement with such Third Party must be reasonably acceptable to the JDC by Mutual Consent.

(h) No Reimbursement. For clarity, Celgene shall not be responsible for any Manufacturing Costs associated with a Discovery Program or Licensed Program incurred prior to Celgene's exercise of the Celgene Program Option or Development Cost Initiation Date with respect to such Program.

Section 4.2 Transfer of Manufacturing Responsibility.

(a) Transfer. Notwithstanding the foregoing, the Parties may mutually agree to have Agios transfer Manufacturing responsibility with respect to any Discovery Program or Licensed Program to Celgene at any time. Upon any transfer of Manufacturing responsibility to Celgene, Agios[**] shall (i) transfer, or have transferred, to Celgene or its designee, pursuant to a technology transfer plan to be mutually agreed by the Parties, all Manufacturing Technology Controlled by Agios and used in Manufacturing Collaboration Compounds, Licensed Compounds and/or Licensed Products under the applicable Program at the time of such transfer, and (ii) provide reasonable assistance in connection with the transfer of such Manufacturing responsibility to Celgene or its designee.

(b) Celgene Responsibility. Upon transfer of Manufacturing responsibility to Celgene under this Section 4.2 with respect to a Discovery Program or Licensed Program, Celgene shall be solely responsible for Manufacturing all Collaboration Compounds, Licensed Compounds and Licensed Products under such Discovery Program or Licensed Program, including both preclinical and clinical materials and commercial product, subject to any cost sharing as described in Section 4.1.

Section 4.3 Manufacturing Efforts. The Party that is responsible for Manufacturing hereunder shall use Commercially Reasonable Efforts to ensure adequate manufacturing capacity to meet forecast demand for such Collaboration Compounds, Licensed Compounds and/or Licensed Products, as applicable, including, if deemed necessary by the JRC, JDC or JCC, as applicable, the establishment of an alternative supply source. Such Party shall also use Commercially Reasonable Efforts to ensure adequate pre-clinical, clinical and commercial supply of such Collaboration Compounds, Licensed Compounds and Licensed Products, as applicable, for both Parties to Develop and/or Commercialize, as applicable, such Collaboration Compounds, Licensed Compounds and Licensed Products as contemplated under the applicable Discovery Plan, Development Plan and/or Commercialization Plan.

Section 4.4 Agios Reverted Compounds. If Celgene or the JDC determines that a Clinical Trial using a Licensed Compound or Licensed Product in combination with an Agios Reverted Compound or Agios Reverted Product would be necessary or useful under a Licensed Program, upon notice from Celgene or the JDC, Agios shall consider such combination in good faith and, subject to Agios' approval in its sole discretion, Agios shall use Commercially Reasonable Efforts to procure adequate quantities of pre-clinical and clinical supply of any Agios Reverted Compound or Agios Reverted Product for Celgene to conduct such combination Clinical Trial; provided, however, that (a) the Parties shall agree by Mutual Consent on the appropriate protocol for such Clinical Trial; (b) Celgene shall regularly update Agios on the progress of such Clinical Trial, shall promptly report to Agios any safety issues arising under such Clinical Trial, shall consult and coordinate with Agios with respect to any termination of such Clinical Trial, and shall provide to Agios all data and results generated in the course of such

Clinical Trial and a final report following completion thereof, which shall be Celgene Confidential Information but which may be used by Agios in the conduct of the applicable Agios Reverted Program; and (c) Celgene will pay Agios its Manufacturing Costs for such pre-clinical and clinical supply of Agios Reverted Compounds or Agios Reverted Products.

## Article V
## Regulatory Matters

Section 5.1 Lead Responsibility for Regulatory Interactions. Except as may otherwise be mutually agreed by the Parties or the JSC, JRC, JDC or JCC, as applicable, and subject to oversight by the JSC, JRC, JDC or JCC, as applicable to the extent such Committee has oversight over a Program:

(a) Discovery Term. Agios shall have lead responsibility for all Regulatory Interactions with respect to the Collaboration Compounds, Licensed Compounds and Licensed Products Developed under (A) each Discovery Program through the Discovery Term and (B) each Split Program or Co-Commercialized Program through Completion of Phase I MAD; provided that, with respect to each Co-Commercialized Program, Celgene may, by written notice to Agios, assume such responsibility with respect to such Program (and the Collaboration Compounds, Licensed Compounds and Licensed Products Developed under such Program) following the Discovery Term for such Program. Agios shall own all INDs and other submissions made to Regulatory Authorities during the time that it has such lead responsibility.

(b) Co-Commercialized Programs. Promptly following Completion of Phase I MAD with respect to each Co-Commercialized Program (or earlier as set forth in Section 5.1(a) above), Celgene shall have lead responsibility for all Regulatory Interactions with respect to the Collaboration Compounds, Licensed Compounds and Licensed Products Developed or Commercialized under each Co-Commercialized Program.

(c) Picked Validated Programs. Promptly following the Discovery Term, Celgene shall have sole responsibility for all Regulatory Interactions with respect to the Collaboration Compounds, Licensed Compounds and Licensed Products Developed or Commercialized under each Picked Validated Program selected by Celgene.

(d) Buy-In Programs. With respect to each Buy-In Program, the Commercializing Party for a Buy-In Program shall have lead responsibility for all Regulatory Interactions with respect to the Buy-In Compounds and Buy-In Products Developed or Commercialized under such Buy-In Program.

(e) Independent Programs; Celgene Reverted Programs. With respect to each Independent Program, the Party conducting the Independent Program shall have lead responsibility for all Regulatory Interactions with respect to the Independent Compounds Developed under such Independent Program. At such time as an Independent Program becomes a Celgene Reverted Program, Celgene shall have sole responsibility for all Regulatory Interactions with respect to the Celgene Reverted Compounds and Celgene Reverted Products Developed or Commercialized under such Celgene Reverted Program.

(f) Split Programs. With respect to each Split Program following the Discovery Term, (A) Agios shall have lead responsibility for all Regulatory Interactions with Regulatory Authorities in the US Territory with respect to the Collaboration Compounds, Licensed Compounds and Licensed Products Developed or Commercialized under such Split Program; and (B) Celgene shall have lead responsibility for all Regulatory Interactions with Regulatory Authorities in the ROW Territory with respect to the Collaboration Compounds, Licensed Compounds and Licensed Products Developed or Commercialized under such Split Program; provided that the JDC may determine by Mutual Consent that one Party shall have lead responsibility for all Regulatory Interactions in the Territory with respect to a Global Study.

(g) Transfer of Regulatory Responsibility. At such time as Celgene is assigned or is entitled to assume lead or sole responsibility for Regulatory Interactions with respect to a Program under this Section 5.1, upon Celgene's written request to Agios,

(i) Agios shall (1) at Celgene's option, either close or inactivate its IND(s) for the Licensed Compounds Developed under such Program, or transfer such IND(s) to Celgene, [**] and (2) with Celgene input, complete all relevant regulatory and clinical activities related to such IND and/or NDA as required for Celgene to assume regulatory ownership, as applicable; provided that, with respect to a Split Program, the foregoing shall not apply to the US Territory.

(ii) With respect to new INDs to be filed after the date Celgene assumes such lead or sole responsibility for such Program, Celgene shall be responsible for the preparation and filing of all subsequent INDs and other regulatory filings with respect to any subsequent Development or Commercialization for such Licensed Compounds or Licensed Products in such Program.

(iii) Agios shall provide to Celgene, [**] and in support of any such Celgene IND or other regulatory filings, all relevant clinical and non-clinical data reasonably requested by Celgene or a Regulatory Authority, including CMC, pharmacology and toxicology generated by Agios with respect to such Licensed Compounds or Licensed Products.

(h) Regulatory Interactions Defined. For purposes of this Agreement, "Regulatory Interactions" means (i) monitoring and coordinating all regulatory actions, communications and filings with, and submissions to, all Regulatory Authorities with respect to a Program and (ii) interfacing, corresponding and meeting with the Regulatory Authorities with respect to a Program.

Section 5.2 Participation Rights.

(a) Review of Regulatory Documentation. To the extent the JRC or JDC has oversight of a Program, each Party shall keep the JRC and JDC, as applicable, reasonably informed in connection with the preparation of all Regulatory Documentation, Regulatory Authority review of Regulatory Documentation, Regulatory Approvals, annual reports, including annual safety reports to the respective health authorities, annual re-assessments, any subsequent variations and changes to labeling, in each case with respect to Collaboration Compounds, Licensed Compounds and Licensed Products. Each Party shall respond within a reasonable time frame to all reasonable inquiries by the other Party with respect to any information provided pursuant to this Section 5.2(a) (and sufficiently promptly for the other Party to provide meaningful input with respect to responses to Regulatory Authorities).

(b) Participating in Meetings. The Party not having the lead responsibility for Regulatory Interactions in a country with respect to a Split Product or Buy-In Product shall have the right to have two senior, experienced employees reasonably acceptable to the responsible Party, participate as an observer in material or scheduled face-to-face meetings, video conferences and any teleconferences with the applicable Regulatory Authority, and shall be provided with advance access to the responsible Party's material documentation prepared for such meetings.

(c) Review. Prior to submission of material correspondence to any Regulatory Authority with respect to a Split Product or Buy-In Product, the Party having the lead responsibility for Regulatory Interactions shall, sufficiently in advance for the other Party to review and comment, provide the other Party any material correspondence with the Regulatory Authority related to such meetings. The responsible Party shall also provide the other Party with copies of any material correspondence with Regulatory Authorities relating to Development of, or the process of obtaining Regulatory Approval for, the Split Product in such Party's territory (*i.e.*, the US Territory if the responsible Party is Agios, or the ROW Territory if the responsible Party is Celgene) or the Buy-In Product, and respond within a reasonable time frame to all reasonable inquiries by the other Party with respect thereto.

Section 5.3 Global Safety Database; Pharmacovigilance Agreement. At a time to be mutually agreed by the Parties, the Parties shall establish, hold and maintain a single electronic system for the collection and storage of all safety information for each Licensed Compound and/or Licensed Product (the "Global Safety Database"). Such database shall comply in all material respects with all Laws reasonably applicable to pharmacovigilance anywhere where the Licensed Compounds and Licensed Products are being or have been Developed or Commercialized. Unless the Parties otherwise agree in the Pharmacovigilance Agreement, Agios shall initially be responsible for the Global Safety Database, and on a Program-by-Program basis Celgene shall assume control following the transfer of all INDs for such Program to Celgene (excluding Buy-In Programs for which Agios is the Commercializing Party); provided that the JDC shall determine by Mutual Consent which Party shall be responsible for the Global Safety Database for Split Programs, with the other Party providing support to such first Party. The Party not maintaining the Global Safety Database may hold and maintain a parallel safety database for any Licensed Compound or Licensed Product as needed or required according to applicable Laws. The Parties will use Commercially Reasonable Efforts to negotiate a pharmacovigilance agreement (the "Pharmacovigilance Agreement") to govern cooperation between the Parties that will enable each of them to comply with its respective obligations under applicable Laws and to satisfy its duty of care with respect to Licensed Compounds and Licensed Products, including with regard to ownership of the Global Safety Database, adverse event data collection, analysis and reporting. The Pharmacovigilance Agreement will be entered by the Parties either prior to the FPD for the first Clinical Trial related to a Discovery Program or Licensed Program or, at Celgene's election, upon transfer of all INDs for such Program to Celgene.

## Article VI
## Commercialization

Section 6.1 Commercialization Responsibilities for Licensed Products.

(a) Celgene Responsibility for Picks & Celgene Reverted Products. With respect to Licensed Products under a Picked Validated Program selected by Celgene and Celgene Reverted Products, (i) Celgene shall have sole responsibility for the Commercialization of such Licensed Products or such Celgene Reverted Products, including distribution, marketing and promotion thereof, and (ii) all business decisions regarding Commercialization of such Licensed Products and such Celgene Reverted Products, including the branding, design, sale, pricing, and promotion thereof, shall be within the sole discretion of Celgene.

(b) Responsibility for Co-Commercialized Products. With respect to Co-Commercialized Products, subject to oversight by the JCC, (i) Celgene shall have sole responsibility for the Commercialization of such Co-Commercialized Products, including distribution, marketing and promotion thereof, except that Agios shall be responsible for undertaking the Commercialization Activities assigned to Agios under the Commercialization Plan for such Co-Commercialized Product pursuant to Section 6.3, and (ii) all business decisions regarding Commercialization of such Co-Commercialized Products, including the branding, design, sale, pricing, and promotion thereof, shall be within the sole discretion of Celgene.

(c) Responsibility for Split Products. With respect to Split Products, subject to oversight by the JCC, (1) Agios shall have sole responsibility for the Commercialization of Split Products in the US Territory, including distribution, marketing and promotion thereof; (2) Celgene shall have sole responsibility for the Commercialization of Split Products in the ROW Territory, including distribution, marketing and promotion thereof (unless and until any Agios Opt-Out, in which event Celgene shall have sole responsibility for the Commercialization of Split Products in the entire Territory if Celgene elects to assume US Territory rights pursuant to Section 3.10(c)); and (3) the Commercializing Party shall make all business decisions regarding Commercialization of Split Products, including the branding, design, sale, pricing, and promotion thereof (subject to consultation with, and due consideration of the non-Commercializing Party's comments with respect to such Split Products, including comments on marketing strategies). Notwithstanding the foregoing,

(i) On an activity-by-activity basis, either Party may propose to the other that they undertake joint Commercialization activities, and, if both Parties agree to do so, the costs associated with such joint activities (A) will be included in the approved budget under the applicable Commercialization Plan pursuant to Section 6.2(a)(i) and (B) will be deemed Global Development Costs and shared in accordance with Section 9.4(b).

(ii) Following the receipt of the Regulatory Approval for a Split Product, the Parties shall not pursue the Development and Commercialization of a Second Generation Product except through Mutual Consent and coordination of the Parties (or the applicable Committees).

(iii) If either Party proposes to take any Commercialization action (or make any business decision) that the other Party reasonably determines is reasonably likely to have a material adverse impact on the Commercialization of a Split Product in the other Party's portion of the Territory, such proposing Party shall not proceed with such Commercialization action (or such business decision) unless approved by the JCC (with any disputes resolved in accordance with the dispute resolution procedure of Section 2.8, including [**] having the final decision-making authority to the extent provided in Section 2.8(b)).

(d) Responsibility for Buy-In Products. With respect to Buy-In Products, subject to oversight by the JCC, (i) the Commercializing Party shall have sole responsibility for the Commercialization of such Buy-In Products, including distribution, marketing and promotion thereof, and (ii) all business decisions regarding Commercialization of such Buy-In Products, including the branding, design, sale, pricing, and promotion thereof, shall be within the sole discretion of the Commercializing Party.

(e) Sales. The Commercializing Party will book all sales of the applicable Licensed Product or Celgene Reverted Product and will have the sole responsibility for the sale, invoicing and distribution of such Licensed Product or Celgene Reverted Product in the Territory.

Section 6.2 Commercialization Plan.

(a) Initial Commercialization Plan.

(i) Commercialization under each Co-Commercialized Program in the US Territory and each Split Program shall be governed by a Commercialization Plan (the "Commercialization Plan") that describes the Commercialization activities (including pre-launch and launch activities, if applicable) to be undertaken with respect to each such Licensed Product. Except as provided in Section 6.1(c)(i) above or Section 6.2(a)(ii) below, the Commercialization Plan need not include a budget.

(ii) Commencing no later than [**] months prior to the anticipated commercial launch of the first Co-Commercialized Product in the US Territory and thereafter at least [**] days prior to the start of each Calendar Year, Celgene shall prepare a Commercialization Plan for each Co-Commercialized Product in the US Territory in the next Calendar Year. Such Commercialization Plan for each Co-Commercialized Product shall include a budget for Field-Based Costs of Agios and shall include in reasonable detail the type and allocation of Commercialization Activities between the Parties with respect to such Co-Commercialized Product in the US Territory pursuant to Section 6.3.

(iii) Commencing no later than [**] months prior to the anticipated commercial launch of the first Split Product in the Territory and thereafter at least [**] days prior to the start of each Calendar Year, Agios with respect to the US Territory and Celgene with respect to the ROW Territory shall prepare the initial Commercialization Plan for each Split Product, with input and guidance from the JDC and JCC. Such Commercialization Plan shall describe Commercialization activities to be undertaken by Agios in the US Territory and Celgene in the ROW Territory. In connection with JCC approval under Section 6.2(b) below,

Agios shall have final decision-making authority with respect to any matters to the extent related to the US Territory, Celgene shall have final decision-making authority with respect to any matters to the extent related to the ROW Territory, and neither Party (nor the JCC) may amend the Commercialization Plan as it relates to the other Party's portion of the Territory except by Mutual Consent.

(b) JCC Approval; Amendments. The JCC shall approve the first Commercialization Plan for each Co-Commercialized Program in the US Territory and each Split Program no later than [**] prior to the anticipated commercial launch of each Licensed Product under such Licensed Program. Thereafter, the JCC shall review the Commercialization Plan not less frequently than [**] and shall propose updates to the Commercialization Plan for [**]. Either Party may also develop and submit to the JCC for review from time to time other proposed amendments to the applicable Commercialization Plan. The initial Commercialization Plan, and any amendments and updates to the Commercialization Plan, including any budgets for Co-Commercialized Products in the US Territory contained in the Commercialization Plan, shall be effective upon the approval of the JCC.

Section 6.3 Co-Commercialization Activities.

(a) General. The JCC shall determine the type and scope of field-based marketing efforts to be used for Commercialization of each Co-Commercialized Product in the US Territory (*e.g.*, sales force (and the number of physicians to be called on and call frequency), field-based medical affairs, and field-based market access resources) (collectively, "Commercialization Activities"), and the Commercialization Plan for each Co-Commercialized Product in the US Territory shall set forth such efforts for each Indication which is marketed in the US Territory. Celgene shall be responsible for all Field-Based Costs incurred by Agios as provided in Section 9.5(d).

(b) Allocation of Activities. The Commercialization Plan will allocate to each Party its portion of the total Commercialization Activities for each Co-Commercialized Product in the US Territory; provided that, unless otherwise agreed to by the Parties, Agios will be allocated approximately [**]% of the Commercialization Activities in the US Territory. The Commercialization Plan will attempt to provide that Agios' assigned Commercialization Activities are distributed geographically within the US Territory in a manner reasonably consistent with the distribution of the U.S. population and that each Party's detailing effort, if applicable, will be directed to physicians of similar prescribing potential but shall take into account the competitive situation of the applicable Co-Commercialized Product. In overseeing the Commercialization Activities, the JCC will take into account the Co-Commercialized Product's customer base and call volume measured against the customer base, geographic scope of activities, and the competitive market for the Co-Commercialized Product.

(c) Sales Force. To the extent the Commercialization Activities include detailing efforts, the JCC shall determine the number of sales representatives needed to carry out the required Commercialization Activities for each Co-Commercialized Program. Each Party, in its sole discretion, shall create a field management structure for its sales effort. Each sales representative shall have a sales territory that allows such sales representative to perform a reasonable number of details within a reasonable geographic area (*i.e.*, without overly-

burdensome travel requirements but avoiding sales representatives detailing the same persons). The effort of the Agios and Celgene sales forces in promoting Co-Commercialized Products will be organized under the supervision of the JCC as to qualifications of sales representatives and field-based sales managerial personnel and the timing of hiring in light of the then-current Commercialization Plan; provided that the Commercialization Plan shall identify the portion of the detailing effort to be undertaken by Agios no later than [**] months before the planned date of the NDA submission in the US Territory. At Celgene's election, Agios shall use Commercially Reasonable Efforts to have hired, no later than [**] months before the applicable PDUFA date, [**]% of Agios' sales force planned to be available upon launch of the Co-Commercialized Product in the US Territory and to have Agios' sales force trained within [**] months of hiring.

(d) Training Materials and Sessions. The JCC will develop Co-Commercialized Product-specific training materials and arrange for provision of such materials to each Party's sales forces, if applicable. The JCC will develop a sales training program directed towards the Co-Commercialized Products in the US Territory. Unless otherwise mutually agreed by the Parties, Celgene and Agios sales representatives will participate in a launch meeting(s) (which may be held together or separately) for each Co-Commercialized Product in the US Territory, which shall include training sessions of Co-Commercialized Product-specific sales skills with respect to the approved indications for the Co-Commercialized Products. Subsequent to launch, Celgene and Agios shall periodically hold meetings with Agios and Celgene field management (down to and including district managers or their equivalents who are directly supervising territory sales representatives) to coordinate promotion of the Co-Commercialized Products in the US Territory. As requested by Agios, Celgene shall make its management, marketing, training and other personnel reasonably available to participate in Agios' national and regional sales meetings and Co-Commercialized Product-training events for the US Territory.

(e) Promotional Materials. Celgene, [**] shall provide Agios with sales, promotional and communication materials sufficient to permit Agios to perform the Commercialization Activities in a manner consistent with the Commercialization Activities performed by Celgene. Agios will utilize only those sales, promotional and communication materials provided to Agios by Celgene and will not utilize any other materials relating to or referring to the Co-Commercialized Product.

(f) Other Obligations. In conducting the Commercialization Activities, the Parties will comply with all applicable Laws, applicable industry professional standards and compliance policies of Celgene that have been previously furnished to Agios, as the same may be updated from time to time and provided to Agios. Celgene will reasonably assist Agios in training sales representatives in such standards. Neither Party shall make any claims or statements with respect to the Co-Commercialized Products that are not strictly consistent with the product labeling and the sales and marketing materials approved for use pursuant to the Commercialization Plan.

(g) Termination of Commercialization Activities.

(i) Agios shall have the right to terminate its Commercialization obligations with respect to any Co-Commercialized Product by providing at least [**] months' prior written notice to Celgene (or sooner as Celgene may determine, in its sole discretion). Upon exercise of such termination right, effective upon the expiration of such [**]-month (or, if applicable, shorter) notice period, Agios' obligations to perform Commercialization Activities under this Section 6.3 shall terminate, and Celgene shall no longer be required to maintain the Commercialization Plan for such Co-Commercialized Product.

(ii) On a Co-Commercialized Product-by-Co-Commercialized Product basis, on the date on which in the US Territory there is [**] Generic Product relating to such Co-Commercialized Product, then Celgene shall no longer be responsible for Agios' Field-Based Costs with respect to such Co-Commercialized Product, and Agios shall have no further obligation to perform the Commercialization Activities for such Co-Commercialized Product or maintain a sales force for the purpose of promoting such Co-Commercialized Product.

(iii) As described in Section 3.10(c)(i), upon a Split Program becoming a Co-Commercialized Program, Agios shall not be entitled to perform Commercialization Activities for such Program. Agios' Commercialization Activities shall also terminate as provided in Section 15.5.

Section 6.4 Trademarks.

(a) The JCC shall select the trademark(s) to be used in connection with the marketing and sale of Co-Commercialized Products in the US Territory (provided that such trademark(s) shall not contain the name of either Party except with such Party's prior written consent), and the Parties shall adhere to the use of such trademark(s) in their Commercialization of Co-Commercialized Products in the US Territory hereunder, to the extent permitted by Law.

(b) Celgene shall own all product trademarks for all Licensed Products for which Celgene is the Commercializing Party, including for the Split Product in the ROW Territory. Agios shall own all product trademarks for any Split Product in the US Territory and for any Buy-In Product with respect to which Agios is the Commercializing Party.

(c) Celgene shall use, in connection with all packaging, literature, labels and other printed matters, to the extent permitted by Law, an expression to the effect that the Licensed Products were developed under license from Agios, together with the Agios logo, and Agios hereby grants Celgene a license to use Agios' name and logo to comply with such obligation.

## Article VII
## Diligence

Section 7.1 Collaboration Activities.

(a) General. Each Party shall use Commercially Reasonable Efforts to perform all Collaboration activities for which such Party is responsible hereunder in compliance with the applicable Discovery Plan, Development Plan or Commercialization Plan, including any budget(s) and timeframe(s) set forth therein and including making available those resources set forth in any applicable Discovery Plan, Development Plan or Commercialization Plan, and the terms of this Agreement.

(b) Compliance with Laws. Each Party shall:

(i) perform its obligations under this Agreement in a scientifically sound and workmanlike manner; and

(ii) carry out all work done in the course of the Collaboration in compliance with all applicable Laws governing the conduct of such work.

Section 7.2 Diligence Obligations.

(a) In addition to the diligence obligations set forth in Section 7.1,

(i) the Commercializing Party with respect to each Buy-In Program,

(ii) Agios with respect to each Split Program in the US Territory, and

(iii) Celgene with respect to each Split Program in the ROW Territory and each Co-Commercialized Program,

shall use Commercially Reasonable Efforts to Develop and achieve Regulatory Approval for Licensed Products under such Program in each of the Major Markets (or, with respect to Split Programs, in the US Territory with respect to Agios' obligations and in Japan and the Major European Countries with respect to Celgene's obligations) and, following such Regulatory Approval, to Commercialize such Licensed Products in each of the Major Markets (or, with respect to Split Programs, in the US Territory with respect to Agios' obligations and in Japan and the Major European Countries with respect to Celgene's obligations).

(b) A breach of the diligence obligations set forth in this Section 7.2 shall be deemed a material breach and shall be subject to termination under Section 14.2(b)(i). Notwithstanding the foregoing, the Parties acknowledge that it might be commercially reasonable, under certain circumstances, for the applicable Commercializing Party to determine not to launch a Licensed Product in [**] Major Markets, and failure under such circumstances to launch such Licensed Product shall not be a breach of this Agreement.

Section 7.3 Celgene's Picks. The Parties agree that, if Celgene has not obtained at least a submission of an IND with respect to a Picked Validated Program selected by Celgene by the [**] anniversary of such Program being selected by Celgene, then Agios' obligations under Section 8.8(c) with respect to the Collaboration Target associated with such Picked Validated Program shall cease.

Article VIII
Grant of Rights; Exclusivity

Section 8.1 Research Licenses. Subject to the terms and conditions of this Agreement:

(a) Licenses Granted to Celgene. Agios hereby grants to Celgene a non-exclusive, non-royalty-bearing, non-transferable (except as set forth in Section 15.4), worldwide right and license in the Field, with the right to grant sublicenses solely to Affiliates and Third Party Contractors subject to Section 8.4(a), under Agios' rights in Agios Intellectual Property and Agios Collaboration Intellectual Property:

(i) to perform Celgene's obligations and exercise its rights under each Discovery Program; and

(ii) to exercise Celgene's rights and perform its obligations with respect to any Independent Program assumed by Celgene pursuant to Section 3.5(a) or Section 3.5(b), up to and including the expiration of the applicable Buy-In Right Term or Agios' exercise or waiver of the Buy-In Right (at which point Celgene's license under Section 8.2(d) or 8.2(e) will apply).

(b) Licenses Granted to Agios. Celgene hereby grants to Agios a non-exclusive, non-royalty-bearing, non-transferable (except as set forth in Section 15.4), worldwide right and license in the Field, with the right to grant sublicenses solely to Affiliates and Third Party Contractors subject to Section 8.4(a):

(i) under Celgene's rights in Celgene Intellectual Property and Celgene Collaboration Intellectual Property, to perform Agios' obligations under each Discovery Program to Develop and/or Manufacture, for purposes of such Discovery Program, Collaboration Compounds and/or Development Candidates during the Discovery Term; and

(ii) under Celgene's rights in Celgene Collaboration Intellectual Property, to exercise Agios' rights and perform its obligations with respect to any Independent Program assumed by Agios pursuant to Section 3.5(a) or 3.5(b), up to and including the expiration of the applicable Buy-In Right Term or Celgene's exercise or waiver of the Buy-In Right (at which point Agios' license under Section 8.2(d) or 8.2(f)(iii) will apply); provided that, for this purpose, "Celgene Collaboration Intellectual Property" means Celgene Collaboration Intellectual Property only to the extent that it (A) is actually used in the corresponding Discovery Program immediately prior to such Discovery Program becoming such Independent Program and (B) is necessary for the Development and/or Manufacture of Independent Compounds under such Independent Program.

Section 8.2 Development and Commercialization Licenses. Subject to the terms and conditions of this Agreement:

(a) Co-Commercialized Programs. Effective as of the Option Exercise Date with respect to each Co-Commercialized Program:

(i) Agios hereby grants to Celgene an exclusive (even as to Agios except as provided in Section 8.10(b)), non-transferable (except as set forth in Section 15.4), royalty-bearing, worldwide right and license in the Field, with the right to grant sublicenses as set forth in Sections 8.4(a) and 8.4(c), under Agios' rights in Agios Intellectual Property and Agios Collaboration Intellectual Property, to Develop, Manufacture and/or Commercialize Licensed Compounds and/or Licensed Products under such Co-Commercialized Program.

(ii) Celgene hereby grants to Agios a non-exclusive, non-transferable (except as set forth in Section 15.4), worldwide right and license in the Field, without the right to grant sublicenses (except as set forth in Section 8.4(a)), under Celgene's rights in Celgene Intellectual Property and Celgene Collaboration Intellectual Property, to perform Agios' obligations under a Development Plan or Commercialization Plan to Develop, Manufacture and/or Commercialize Licensed Compounds and/or Licensed Products under such Co-Commercialized Program. Such license shall be fully paid-up and non-royalty-bearing.

(b) Picked Validated Programs Selected by Celgene. Effective as of the date of Celgene's Pick, with respect to each Picked Validated Program selected by Celgene pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii), Section 3.6(c) or Section 15.5):

(i) Agios hereby grants to Celgene an exclusive (even as to Agios except as provided in Section 8.10(b)), non-transferable (except as set forth in Section 15.4), royalty-bearing, worldwide right and license in the Field, with the right to grant sublicenses as set forth in Sections 8.4(a) and 8.4(c), under Agios' rights in Agios Intellectual Property and Agios Collaboration Intellectual Property, to Develop, Manufacture and/or Commercialize Licensed Compounds and/or Licensed Products under such Picked Validated Program.

(ii) Celgene hereby grants to Agios a non-exclusive, non-transferable (except as set forth in Section 15.4), worldwide right and license in the Field, without the right to grant sublicenses (except as set forth in Section 8.4(a)), under Celgene's rights in Celgene Intellectual Property and Celgene Collaboration Intellectual Property, to perform Agios' obligations under a Development Plan to Develop Licensed Compounds and/or Licensed Products under such Picked Validated Program. Such license shall be fully paid-up and non-royalty-bearing.

(c) Split Programs. Effective upon the Option Exercise Date for each Split Program:

(i) Agios hereby grants to Celgene an exclusive (even as to Agios except as provided in Section 8.10(b)), non-transferable (except as set forth in Section 15.4), royalty-bearing right and license in the Field, with the right to grant sublicenses as set forth in Sections 8.4(a) and 8.4(d), under Agios' rights in Agios Intellectual Property and Agios Collaboration Intellectual Property:

(A) to Develop, Manufacture and/or Commercialize Split Compounds and/or Split Products under such Split Program in the ROW Territory; and

(B) to Develop and/or Manufacture Split Compounds and/or Split Products under such Split Program in the US Territory for the sole purpose of using, offering for sale and selling Split Compounds and/or Split Products in, and importing Split Compounds and/or Split Products into, the ROW Territory.

(ii) Celgene hereby grants to Agios a non-exclusive, non-transferable (except as set forth in Section 15.4), royalty-bearing right and license in the Field, with the right to grant sublicenses as set forth in Sections 8.4(a) and 8.4(d), under Celgene's rights in Celgene Intellectual Property and Celgene Collaboration Intellectual Property:

(A) to Develop, Manufacture and/or Commercialize Split Compounds and/or Split Products under such Split Program in the US Territory; and

(B) to Develop and/or Manufacture Split Compounds and/or Split Products under such Split Program in the ROW Territory for the sole purpose of using, offering for sale and selling Split Compounds and/or Split Products in, and importing Split Compounds and/or Split Products into, the US Territory;

provided that the foregoing license under Section 8.2(c)(ii)(A) shall be exclusive (even as to Celgene except as provided in Section 8.10(b)) with respect to the applicable Split Program only to the extent of claims within the Celgene Collaboration Patent Rights Covering a composition of matter on the Split Compound or Split Product in such Split Program.

(iii) For purposes of clarity, upon the Agios Opt-Out Date under any Split Program, (A) if Celgene elects to assume US Territory rights under such Split Program in accordance with Section 3.10, the licenses granted to each Party with respect to such Split Program under this Section 8.2(c) shall convert to the licenses granted to each Party with respect to a Co-Commercialized Program under Section 8.2(a), and (B) if Celgene does not elect to assume US Territory rights under such Split Program, then the licenses granted to Agios under Section 8.2(c)(ii) shall terminate.

(d) Buy-In Programs. Effective upon the date of the Buy-In Party's exercise of any Buy-In Right for a Buy-In Program pursuant to Section 3.11, with respect to each such Buy-In Program:

(i) If Celgene is the Commercializing Party, Agios hereby grants to Celgene an exclusive (even as to Agios except as provided in Section 8.10(b)), non-transferable (except as set forth in Section 15.4), royalty-bearing, worldwide right and license in the Field, with the right to grant sublicenses as set forth in Sections 8.4(a) and 8.4(e), under Agios' rights in Agios Intellectual Property and Agios Collaboration Intellectual Property, to Develop, Manufacture and/or Commercialize the Buy-In Compounds and/or Buy-In Products under such Buy-In Program.

(ii) If Agios is the Commercializing Party, Celgene hereby grants to Agios a non-exclusive, non-transferable (except as set forth in Section 15.4), royalty-bearing, worldwide right and license in the Field, with the right to grant sublicenses as set forth in Sections 8.4(a) and 8.4(e), under Celgene's rights in Celgene Collaboration Intellectual Property, to Develop, Manufacture and/or Commercialize the Buy-In Compounds and/or Buy-In Products under such Buy-In Program; provided that, for this purpose, "Celgene Collaboration Intellectual Property" means Celgene Collaboration Intellectual Property only to the extent that it (A) is actually used in the applicable Discovery Program immediately prior to such Discovery Program becoming the Independent Program that preceded such Buy-In Program and (B) is necessary for the Development, Manufacture and/or Commercialization of Buy-In Product under such Buy-In Program; provided further that the foregoing license under this Section 8.2(d)(ii) shall be exclusive (even as to Celgene except as provided in Section 8.10(b)) with respect to the applicable Buy-In Program only to the extent of claims within the Celgene Collaboration Patent Rights Covering a composition of matter on the Buy-In Product in such Buy-In Program.

(e) Celgene Reverted Programs. Effective upon the date of rejection or waiver by Agios of any Buy-In Right for an Independent Program independently Developed by Celgene pursuant to Section 3.11(c), for each such Celgene Reverted Program, Agios hereby grants to Celgene an exclusive (even as to Agios except as provided in Section 8.10(b)), non-transferable (except as set forth in Section 15.4), royalty-bearing worldwide right and license in the Field, with the right to grant sublicenses as set forth in Sections 8.4(a) and 8.4(f), under Agios' rights in Agios Intellectual Property and Agios Collaboration Intellectual Property, to Develop, Manufacture and/or Commercialize Celgene Reverted Compounds and/or Celgene Reverted Products under such Celgene Reverted Program.

(f) Agios Reverted Programs.

(i) Optionable Programs for which Celgene does not exercise the Celgene Program Option. Effective as of Celgene's failure to make (or decision not to make) a DC Commitment within the period required under a Discovery Program or, after making a DC Commitment, Celgene's failure to exercise (or decision not to exercise) the Celgene Program Option during the applicable Celgene Option Exercise Period for such Discovery Program, Celgene hereby grants to Agios a non-exclusive, non-transferable (except as set forth in Section 15.4), worldwide right and license in the Field, with the right to grant sublicenses as set forth in Sections 8.4(a) and 8.4(g), under Celgene's rights in Celgene Collaboration Intellectual Property, to Develop, Manufacture and/or Commercialize Agios Reverted Compounds and/or Agios Reverted Products that contain such Agios Reverted Compound under such Discovery Program; provided that, for this purpose, "Celgene Collaboration Intellectual Property" means Celgene Collaboration Intellectual Property only to the extent that it (A) is actually used in such Discovery Program immediately prior to such Program becoming an Agios Reverted Program and (B) is necessary for the Development, Manufacture and/or Commercialization of Agios Reverted Compounds and/or Agios Reverted Products that contain such Agios Reverted Compounds under such Discovery Program; provided further that the foregoing license under this Section 8.2(f)(i) shall be exclusive (even as to Celgene except as provided in Section 8.10(b)) with respect to the applicable Agios Reverted Program only to the extent of claims within the Celgene Collaboration Patent Rights Covering a composition of matter on the Agios Reverted Compound or Agios Reverted Product that contains such Agios Reverted Compound in such Agios Reverted Program.

(ii) Picked Validated Programs. Effective as of the date of Agios' Pick, with respect to each Picked Validated Program selected by Agios pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii) or Section 15.5), Celgene hereby grants to Agios a non-exclusive, non-transferable (except as set forth in Section 15.4), worldwide right and license in the Field, with the right to grant sublicenses as set forth in Sections 8.4(a) and 8.4(g), under Celgene's rights in Celgene Collaboration Intellectual Property, to Develop, Manufacture and/or Commercialize Picked Compounds and Agios Reverted Products that contain such Picked Compounds under such Picked Validated Program; provided that, for this purpose, "Celgene Collaboration Intellectual Property" means Celgene Collaboration Intellectual Property only to the extent that it (A) is actually used in such Picked Validated Program immediately prior to such Program becoming an Agios Reverted Program and (B) is necessary for the Development, Manufacture and/or Commercialization of Agios Reverted Compounds and/or Agios Reverted Products that contain such Agios Reverted Compounds under such Picked Validated Program;

provided further that the foregoing license under this Section 8.2(f)(ii) shall be exclusive (even as to Celgene except as provided in Section 8.10(b)) with respect to the applicable Agios Reverted Program only to the extent of claims within the Celgene Collaboration Patent Rights Covering a composition of matter on the Agios Reverted Compound or Agios Reverted Product that contains such Agios Reverted Compound in such Agios Reverted Program.

(iii) Independent Programs. Effective upon the date of rejection or waiver by Celgene of any Buy-In Right for an Independent Program independently Developed by Agios pursuant to Section 3.11(c), for each such Agios Reverted Program, Celgene hereby grants to Agios a non-exclusive, non-transferable (except as set forth in Section 15.4), worldwide right and license in the Field, with the right to grant sublicenses as set forth in Sections 8.4(a) and 8.4(g), under Celgene's rights in Celgene Collaboration Intellectual Property, to Develop, Manufacture and/or Commercialize Agios Reverted Compounds and/or Agios Reverted Products that contain such Agios Reverted Compounds under such Agios Reverted Program; provided that, for this purpose, "Celgene Collaboration Intellectual Property" means Celgene Collaboration Intellectual Property only to the extent that it (A) is actually used in the applicable Discovery Program immediately prior to such Discovery Program becoming such Independent Program and (B) is necessary for the Development, Manufacture and/or Commercialization of Agios Reverted Compounds and/or Agios Reverted Products that contain such Agios Reverted Compounds under such Agios Reverted Program; provided further that the foregoing license under this Section 8.2(f)(iii) shall be exclusive (even as to Celgene except as provided in Section 8.10(b)) with respect to the applicable Agios Reverted Program only to the extent of claims within the Celgene Collaboration Patent Rights Covering a composition of matter on the Agios Reverted Compound or Agios Reverted Product that contains such Agios Reverted Compound in such Agios Reverted Program.

(iv) Agios shall not owe royalties or milestones with respect to the licenses in this Section 8.2(f), but Agios shall be solely responsible for any payments owed by Celgene to any Third Party licensors of Celgene Collaboration Intellectual Property, and shall be responsible for complying with the terms of any license agreements with such Third Party licensors, in either case, directly related to Agios' exercise of such licenses.

Section 8.3 Collaboration Compounds. The Parties agree as follows:

(a) Celgene's Use of Licensed Compounds. It is agreed that each of the licenses granted to Celgene from Agios under Section 8.2 includes the right to use Collaboration Compounds, Licensed Compounds or Celgene Reverted Compounds associated with one Discovery Program, Independent Program conducted by Celgene, Licensed Program for which Celgene is the Commercializing Party, or Celgene Reverted Program, as applicable, in connection with any other Discovery Program, Independent Program conducted by Celgene, Licensed Program for which Celgene is the Commercializing Party, or Celgene Reverted Program.

(b) Agios' Use of Licensed Compounds. Agios and, subject to Sections 15.4(b) and 15.4(c), its Affiliates shall not, and shall not grant any Third Party the right to, Develop, Manufacture and/or Commercialize any Licensed Compound, Licensed Product, Celgene Reverted Compound or Celgene Reverted Product for any purpose, other than in connection with a Licensed Program or Celgene Reverted Program pursuant to the Collaboration under this Agreement.

Section 8.4 Sublicense Rights. Subject to Section 8.5, the Parties have the following sublicensing rights.

(a) Sublicenses to Affiliates and Subcontractors. Each Party shall have the right to grant sublicenses within the scope of the licenses under Sections 8.1, 8.2 and 8.3, as applicable:

(i) to such Party's Affiliates; and

(ii) to Third Parties for the purpose of engaging Third Parties as contract research organizations, contract manufacturers, contract sales forces, consultants, academic researchers and the like ("Third Party Contractors") in connection with Development, Manufacturing or Commercialization activities on behalf of such Party or its Affiliates with respect to [**] in the Field in the Territory under this Agreement, subject to the following with respect to [**] (except only the obligations under Section 8.4(a)(ii)(A) shall apply with respect to Agios Reverted Programs or Celgene Reverted Programs and, for all other purposes of this Section 8.4(a)(ii), "[**]" shall not include Agios Reverted Compounds, Agios Reverted Products, Celgene Reverted Compounds or Celgene Reverted Products):

(A) unless otherwise agreed by the JSC by Mutual Consent, each Party shall require any such Third Party to whom such Party discloses Confidential Information to enter into an appropriate written agreement obligating such Third Party to be bound by obligations of confidentiality and restrictions on use of such Confidential Information that are no less restrictive than the obligations set forth in Article XI, including requiring such Third Party to agree in writing not to issue any Publications except in compliance with the terms of this Agreement (including approval by the JSC, pursuant to the Publication Guidelines, and the obligations set forth in Section 11.4, except that Publications by academic collaborators shall be permitted (without JSC consent) if the academic collaborator (i) provides an advance copy of the proposed Publication (under the same time periods as described in Section 11.4(a)), which may be shared with the other Party, (ii) agrees to delay such Publication sufficiently long enough to permit the timely preparation and filing of a patent application, and (iii) upon the request of either Party, removes from such Publication any Confidential Information of such Party);

(B) unless otherwise agreed by the JSC by Mutual Consent, each Party will obligate such Third Party to agree in writing to [**] to, any inventions arising under its agreement with such Third Party to the extent related to Development, Manufacturing or Commercialization with respect to such Agreement Compounds in the Field in the Territory; and such Party shall structure such [**] so as to enable such Party to sublicense such Third Party inventions to the other Party pursuant to Section 8.1, 8.2, 8.3 or 8.9, as applicable (including permitting such other Party to grant further sublicenses); provided that, in connection with any academic collaborator performing research work to discover or research Targets (but only if such academic collaborator is not provided [**]), each Party will only be required to obligate such academic collaborator to agree in writing to grant [**] to, and a right to negotiate for [**] to, any such inventions, which must be sublicensable to the other Party pursuant to Section 8.1, 8.2, 8.3 or 8.9, as applicable (including permitting such other Party to grant further sublicenses);

(C) each Party shall notify the JRC, JDC or JCC, as applicable, at a regular meeting of the JRC, JDC or JCC, as applicable, of the execution any such agreement with such Third Party and, if requested, shall provide the other Party with a copy of such agreement, which copy may be redacted with respect to matters that do not relate to the Collaboration; and

(D) unless otherwise agreed by the JSC by Mutual Consent, each Party will require any such Third Party to grant to the other Party access to [**] generated by such Third Party's work with respect to such [**] to the same extent as such other Party's licenses under Section 8.1, 8.2, 8.3 or 8.9, as applicable, and grant the other Party the right to audit the records of such Third Party.

(b) Sublicenses under Independent Programs.

(i) Celgene shall not have the right to grant sublicenses or licenses within the scope of the license under Section 8.1(a)(ii) to any Third Party to Develop and Manufacture any Independent Compounds under an Independent Program Developed by Celgene in accordance with Section 3.11 (except to Affiliates and Third Party Contractors as permitted under Section 8.4(a) above), without the prior written consent of Agios, unless and until such Independent Program becomes a Buy-In Program (in which event Section 8.4(e) shall apply with respect to sublicense rights) or a Celgene Reverted Program (in which event Section 8.4(f) shall apply with respect to sublicense rights).

(ii) Agios shall not have the right to grant sublicenses or licenses within the scope of the license under Section 8.1(b)(ii) to any Third Party to Develop and Manufacture any Independent Compounds under an Independent Program Developed by Agios in accordance with Section 3.11 (except to Affiliates and Third Party Contractors as permitted under Section 8.4(a) above), without the prior written consent of Celgene, unless and until such Independent Program becomes a Buy-In Program (in which event Section 8.4(e) shall apply with respect to sublicense rights) or an Agios Reverted Program (in which event Section 8.4(g) shall apply with respect to sublicense rights).

(c) Sublicenses under Picked Validated Programs selected by Celgene and Co-Commercialized Programs. Celgene shall have the right to grant sublicenses or licenses within the scope of the licenses under Sections 8.2(a) and 8.2(b) to any Third Party to Develop, Manufacture or Commercialize Licensed Compounds and/or Licensed Products under Picked Validated Programs selected by Celgene pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii), Section 3.6(c) or Section 15.5) and under Co-Commercialized Programs in the Territory.

(d) Sublicenses under Split Programs. Subject to Section 3.10(e), Agios shall have the right to grant sublicenses or licenses within the scope of the license under Section 8.2(c)(ii) to any Third Party to Develop, Manufacture or Commercialize Split Products under a Split Program without Celgene's consent; provided that any such sublicenses or licenses do not

modify Celgene' rights in the Split Product or the Split Program. Celgene shall have the right to grant sublicenses or licenses within the scope of the license under Section 8.2(c)(i) to any Third Party to Develop, Manufacture or Commercialize Split Products under a Split Program without Agios' consent; provided that any such sublicenses or licenses do not modify Agios' rights in the Split Product or the Split Program.

(e) Sublicenses under Buy-In Programs. The Commercializing Party for a Buy-In Program shall have the right to grant sublicenses or licenses within the scope of the license under Section 8.2(d) to any Third Party to Develop, Manufacture or Commercialize Buy-In Products in the Territory under a Buy-In Program without the other Party's consent; provided that any such sublicenses or licenses do not modify the other Party's rights in the Buy-In Product or Buy-In Program.

(f) Sublicenses under Celgene Reverted Programs. Celgene shall have the right to grant sublicenses or licenses, within the scope of the license under Section 8.2(e) above, to Third Parties to Develop, Manufacture or Commercialize Celgene Reverted Compounds and/or Celgene Reverted Products.

(g) Sublicenses under Agios Reverted Programs. Agios shall have the right to grant sublicenses or licenses, within the scope of the license under Section 8.2(f) above, to Third Parties to Develop, Manufacture or Commercialize Agios Reverted Compounds and/or Agios Reverted Products.

Section 8.5 Sublicense Requirements. Any sublicense granted by a Party pursuant to this Agreement shall be subject to the following:

(a) each sublicense granted hereunder by a Party shall be consistent with the requirements of this Agreement;

(b) any transfer of rights between Celgene and its Affiliates shall not be deemed a sublicense by Celgene but shall be deemed a direct license by Agios to Celgene's Affiliate; provided that Celgene shall remain responsible for the activities of its Affiliate;

(c) a Party's or its Affiliates' Third Party sublicensees shall have no right to grant further sublicenses without the other Party's prior written consent, which consent shall not be unreasonably withheld, conditioned or delayed;

(d) such Party shall be primarily liable for any failure by its sublicensees to comply with all relevant restrictions, limitations and obligations in this Agreement;

(e) such sublicense must be granted pursuant to a written sublicense agreement and such Party must provide the other Party with a copy of any sublicense agreement entered into under Sections 8.4(c), 8.4(d), and 8.4(e) above within [**] days after the execution of such sublicense agreement; provided that any such copy may be redacted to remove any confidential, proprietary or competitive information, but such copy shall not be redacted to the extent that it impairs the other Party's ability to ensure compliance with this Agreement. Such sublicense agreement shall be treated as Confidential Information of the sublicensing Party; and

(f) except as otherwise provided in the sublicense agreement, if this Agreement terminates for any reason, any Third Party sublicensee of Celgene shall, from the effective date of such termination, automatically become a direct licensee of Agios with respect to the rights licensed to Celgene hereunder and sublicensed to the sublicensee by Celgene; provided, however, that such sublicensee is not in breach of its sublicense agreement and continues to perform thereunder.

Section 8.6 Affiliates and Third Party Contractors. Either Party may exercise its rights and perform its obligations hereunder itself or through its Affiliates and sublicensees. Each Party shall be primarily liable for any failure by its Affiliates and Third Party Contractors to comply with all relevant restrictions, limitations and obligations in this Agreement.

Section 8.7 Existing Third Party Agreements.

(a) Acknowledgement. Except as provided in Section 8.7(b), Agios acknowledges that it is responsible for the fulfillment of its obligations under the Existing Third Party Agreements and agrees to fulfill the same, including any provisions necessary to maintain in effect any rights sublicensed to Celgene hereunder and the exclusive nature of such rights, subject to Celgene's compliance with its obligations hereunder. In the event of any conflict between the terms of this Agreement and the Existing Third Party Agreements, the Parties will discuss in good faith how to address the conflict; provided that, if the Parties are unable to agree on how to address the conflict, the terms of this Agreement shall govern.

(b) Incorporation of Certain Provisions. Celgene acknowledges and agrees that it shall be bound by the following provisions of the Existing Third Party Agreements, as a sublicensee of the rights licensed to Agios thereunder but only to the extent applicable to the rights sublicensed to Celgene hereunder and to the extent that Celgene exercises its Celgene Program Option with respect to an Optionable Program, selects Picked Validated Programs or is the Commercializing Party for a Buy-In Program or Celgene Reverted Program (but specifically excluding with respect to any Agios Reverted Programs or any Terminated Programs under Section 14.3(a)):

(i) Sections 2.3 (as described in Section 8.10(b)(iii) hereof), 4.1 (with respect to the diligence obligations but not the reporting obligations), 4.2 and 12.3(c) of the [**] Agreement,

(ii) Sections 2.2, 2.4 (as described in Section 8.10(b)(iii) hereof), 3.1, 3.2, 5.5, 8.1 (as provided in Section 13.3), 8.2, 8.3, 10.2 and 10.3 (to the extent of the rights of the licensor under the [**] Agreement to terminate the [**] Agreement), 10.4, 10.7(b), 11.1, 11.2 and 14.6 of the [**] Agreement, and

(iii) Sections 1.3 (as described in Section 8.10(b)(iii) hereof), 2.1, 2.3, 5.2, 5.3, 5.4, 5.5, 6.2, 7.1, 8.1 (with respect to information of the licensors under the [**]Agreement or with respect to the licensor's obligation to keep information of either Party confidential), 10.1 and 10.4 of the [**] Agreement.

Furthermore, Celgene acknowledges that Agios is required to share certain reports and copies of sublicense agreements provided by Celgene to Agios hereunder with the licensors under the Existing Third Party Agreements, and Celgene consents to the sharing of such reports and such copies of such sublicense agreements to the extent required under such Existing Third Party Agreements to the same extent as disclosures are permitted under Section 11.3(b)(ii)(B) hereunder; provided that any such copies of sublicense agreements must be redacted to the extent permitted under such Existing Third Party Agreement.

(c) Covenants Regarding the Existing Third Party Agreements. Agios agrees that during the Term:

(i) Agios shall not modify or amend the Existing Third Party Agreements in any way without Celgene's prior written consent;

(ii) Agios shall not terminate any Existing Third Party Agreement, in whole or in part, without Celgene's prior written consent;

(iii) Agios shall be solely responsible for, and shall make, all royalty payments, milestone payments, yearly fees, sublicensee fees, Prosecution fees, and all other payments owed to the licensors under and pursuant to the Existing Third Party Agreements;

(iv) Agios shall not exercise or fail to exercise any of Agios' rights, or fail to perform any of Agios' obligations, under the Existing Third Party Agreements that relate to Celgene's rights hereunder without the prior written consent of Celgene, including rights with respect to including improvements within the licenses granted under the Existing Third Party Agreements; and, at the reasonable request of Celgene, Agios shall exercise such rights and make such requests that relate to Celgene's rights hereunder as are permitted under the Existing Third Party Agreements;

(v) Agios shall promptly furnish Celgene with copies of all reports and other communications that Agios furnishes to the licensors under the Existing Third Party Agreements to the extent that such reports relate to this Agreement;

(vi) Agios shall promptly furnish Celgene with copies of all reports and other communications that Agios receives from the licensors under the Existing Third Party Agreements that relate to the subject of this Agreement (including notices relating to improvements under the Existing Third Party Agreements);

(vii) Agios shall furnish Celgene with copies of all notices received by Agios relating to any alleged breach or default by Agios under the Existing Third Party Agreements within [**] Business Days after Agios' receipt thereof; in addition, if Agios should at any time breach the Existing Third Party Agreements or become unable to timely perform its obligations thereunder, Agios shall immediately notify Celgene;

(viii) If Agios cannot or chooses not to cure or otherwise resolve any alleged breach or default under the Existing Third Party Agreements, (A) Agios shall so notify Celgene within [**] Business Days of such decision, which shall not be less than [**] Business Days prior to the expiration of the cure period under the Existing Third Party Agreements; provided that Agios shall use Commercially Reasonable Efforts to cure any such breach or default; and (B) Celgene, in its sole discretion, shall be permitted (but shall not be obligated), on

behalf of Agios, to cure any breach or default under the Existing Third Party Agreements in accordance with the terms and conditions of the Existing Third Party Agreements or otherwise resolve such breach directly with the licensors under the Existing Third Party Agreements; and (C) if Celgene pays any such licensor any amounts owed by Agios under the Existing Third Party Agreements, Celgene may deduct such amounts from payments Celgene is required to make thereafter to Agios hereunder or, at Celgene's election, may otherwise seek reimbursement of such amounts from Agios; and

(ix) Agios shall not provide any [**] to the licensors under the Existing Third Party Agreements without Celgene's prior written consent.

(d) Expiration of Option Term. Upon the expiration of the Option Term or at any other time during the Option Term, upon Agios' request, the Parties will discuss in good faith whether any sublicense of rights under any Existing Third Party Agreement granted to Celgene hereunder may be terminated as a result of such sublicensed rights not being necessary or useful for the exercise of Celgene's rights or performance of Celgene's obligations hereunder. If the Parties agree by Mutual Consent to terminate any rights under Existing Third Party Agreements licensed to Celgene hereunder, this Agreement shall be amended to reflect such agreement, including an amendment of the provisions of Section 8.7(c) to the extent applicable.

(e) Survival of Celgene's Rights Following Termination of Existing Third Party Agreements. The Parties agree that in the event of any termination of any Existing Third Party Agreement with respect to any intellectual property rights licensed to Celgene hereunder (other than a termination under Section 8.7(d) above), Celgene shall have any rights available under such Existing Third Party Agreements to become a direct licensee of the Third Party licensor under such Existing Third Party Agreement and Agios shall use Commercially Reasonable Efforts to assist Celgene in exercising such rights; provided that Celgene has not breached this Agreement with respect to the applicable Licensed Program or Celgene Reverted Program, or breached the applicable Third Party Rights under such Existing Third Party Agreement. In addition, notwithstanding the foregoing, in the event of such termination, Celgene may in any event approach the licensor under the applicable Existing Third Party Agreement for a direct license. In the event of any such direct license following any termination of the related Existing Third Party Agreement without Celgene's consent, Celgene shall be entitled to deduct from any payments owed to Agios hereunder [**] percent ([**]%) of the amounts paid by Celgene to such licensor under such direct license with respect to licenses within the scope of the licenses previously granted to Agios under the applicable Existing Third Party Agreement.

(f) Termination of Existing Third Party Agreement. The Parties agree that termination, without Celgene's prior written consent, of any Existing Third Party Agreement with respect to Patent Rights or Know-How that is necessary to use a Collaboration Target or Celgene Reverted Target, or to Develop, Manufacture or Commercialize Collaboration Compounds, Licensed Compounds, Licensed Products, Celgene Reverted Compounds or Celgene Reverted Products under the applicable Licensed Program or Celgene Reverted Program hereunder shall be deemed a material breach of this Agreement by Agios; provided that (i) if Celgene's breach of this Agreement results in a breach of the Existing Third Party Agreements, Celgene agrees to use Commercially Reasonable Efforts to assist Agios in curing such breach of

the Existing Third Party Agreements, and (ii) if Celgene's breach of this Agreement results in a termination of the Existing Third Party Agreements, such termination of the Existing Third Party Agreements shall not be deemed a material breach by Agios of this Agreement.

(g) Agios' Allocation of Consideration. Agios has disclosed to Celgene, and Celgene understands, that Agios intends to allocate a portion of the total consideration paid by Celgene pursuant to Section 9.1 and Section 9.2 of this Agreement, to the Existing Third Party Agreements as set forth on Schedule 1.53.

Section 8.8 Exclusivity.

(a) During the Option Term, Agios and, subject to Sections 15.4(b) and 15.4(c), its Affiliates shall not, directly or indirectly, Develop, Manufacture or Commercialize (i) any therapeutic modality (including any small molecule or biologic) for Indications in the Oncology Field that [**] or (ii) any therapeutic modality (including any small molecule or biologic) in any field or application that either activates or inhibits through direct binding to a Target on the Target List or to a Celgene Reverted Target, in each case with an EC50 or IC50 at or less than 800nM, except for the following:

(A) in the case of either clause (i) or (ii), Collaboration Compounds, Development Candidates, Licensed Compounds, Independent Compounds and products that contain any of the foregoing pursuant to the Collaboration under this Agreement,

(B) in the case of either clause (i) or (ii), Agios Reverted Compounds (other than Agios Reverted Compounds that activate or inhibit through direct binding to Released Targets) and Agios Reverted Products that contain any such Agios Reverted Compound, and

(C) in the case of the foregoing clause (i), compounds and products that [**] and that are Developed or Commercialized with for-profit Third Parties pursuant to collaboration or licensing agreements that requires the first Clinical Trial in patients be conducted for an Indication [**] ("Partnered Programs"); provided that, during the Option Term, Agios and, subject to Sections 15.4(b) and 15.4(c), its Affiliates shall not collaborate with or otherwise assist any Third Party with respect to Development, Manufacturing or Commercialization activities pursuant to any Partnered Program to the extent directed to any Indication [**].

Notwithstanding the foregoing, with respect to any Extended Program, the obligations set forth in clause (ii) above shall continue to apply following the Option Term for any Target on the Target List that continues to be part of an Extended Program until the expiration of the Post-Option Extension.

(b) During the Option Term, Celgene and, subject to Sections 15.4(b) and 15.4(c), its Affiliates shall not, directly or indirectly, Develop, Manufacture or Commercialize any therapeutic modality (including any small molecule or biologic) for Indications in the Oncology Field that [**], except for Collaboration Compounds, Development Candidates, Licensed Compounds, Independent Compounds, Celgene Reverted Compounds and products that contain any of the foregoing pursuant to this Agreement. Notwithstanding the foregoing,

with respect to any Extended Program, the obligations set forth in this Section 8.8(b) shall continue to apply following the Option Term for any Target on the Target List that continues to be part of an Extended Program until the expiration of the Post-Option Extension.

(c) On a Collaboration Target-by-Collaboration Target and Celgene Reverted Target-by-Celgene Reverted Target basis, during the applicable Exclusivity Period, neither Party nor, subject to Sections 15.4(b) and 15.4(c), any of its respective Affiliates shall, directly or indirectly, Develop, Manufacture or Commercialize any therapeutic modality (including any small molecule or biologic) in any field or application that [**] that is within a Licensed Program or an Independent Program (except, in the case of Celgene, with respect to Independent Programs of Agios pursuant to Section 3.5(a)(i) or Section 3.5(b)(i)), or a Celgene Reverted Target that is within a Celgene Reverted Program, except for Collaboration Compounds, Development Candidates, Licensed Compounds, Independent Compounds, Celgene Reverted Compounds and products that contain any of the foregoing pursuant to this Agreement.

(d) A Party shall not be deemed to be, directly or indirectly, Developing, Manufacturing or Commercializing in violation of the provisions of Section 8.8(b) or 8.8(c) as a result of conducting a research program or discovery effort (or manufacturing or commercializing a therapeutic modality resulting from such research program or discovery effort) that has as its specified and primary goal, as evidenced by laboratory notebooks or other relevant documents contemporaneously kept, taken as a whole, to discover or Develop compounds that [**], as applicable, that is subject to the prohibitions of Section 8.8(b) or 8.8(c).

(e) It is agreed and understood by the Parties that any Celgene research, discovery and commercialization activities existing as of the Effective Date (other than activities directed to [**]), whether such activities are undertaken by Celgene alone or in conjunction with one or more partners, licensors, licensees, and/or collaborators, are expressly excluded from the provisions of this Section 8.8. In particular and without limitation, Celgene research, discovery, and commercialization activities related to (i) the [**]; (ii) the [**]; (iii) [**]; (iv) [**]; (v) [**]; or (vi) [**]. With respect to any Celgene program directed at [**], the provisions of this Section 8.8 shall apply to such program as of the Effective Date; provided that Celgene shall not be required to contribute any compounds from such Celgene program to this Collaboration.

Section 8.9 Targets. Notwithstanding anything herein to the contrary, the Parties agree that, at such point as a Target is removed from the Target List (whether removed by Mutual Consent of the JRC, upon expiration of the Option Term (or, if applicable, with respect to any Extended Program, following any Post-Option Extension), or otherwise), both Parties shall be entitled to use such Target for any purpose, subject to Section 8.8. On a Target-by-Target basis, Agios hereby grants to Celgene a non-exclusive, non-transferable (except as set forth in Section 15.4), worldwide right and license, with the right to grant sublicenses, under the Agios Intellectual Property and Agios Collaboration Intellectual Property to the extent (a) directed to a Target per se and (b) in existence, or developed or generated, during the Option Term, with respect to each Target that was on but is removed from the Target List (whether removed by Mutual Consent of the JRC, upon expiration of the Option Term (or, if applicable, with respect to any Extended Program, following any Post-Option Extension), or otherwise), subject to Section 8.8. Such license shall be perpetual, irrevocable, fully paid-up, and non-royalty-bearing, but Celgene shall be solely responsible for any payments owed by Agios to any

Third Party licensors of Agios Intellectual Property or Agios Collaboration Intellectual Property and shall be responsible for complying with the terms of any license agreements with such Third Party licensors, in either case, directly resulting from Celgene's exercise of the foregoing license.

Section 8.10 Retained Rights.

(a) No Implied Licenses or Rights. Except as expressly provided in Section 8.1, 8.2, 8.3 or 8.9, and subject to Section 3.5(a)(i) and Section 8.8, all rights in and to the Agios Intellectual Property, Agios' and its Affiliates' interests in Agios Collaboration Intellectual Property and any other Patent Rights or Know-How of Agios and its Affiliates, are hereby retained by Agios and its Affiliates. Except as expressly provided in Sections 8.1, 8.2, 8.3 and 8.9, and subject to Section 8.8, all rights in and to the Celgene Intellectual Property, Celgene's and its Affiliates' interests in Celgene Collaboration Intellectual Property and any other Patent Rights or Know-How of Celgene and its Affiliates, are hereby retained by Celgene and its Affiliates.

(b) Other Retained Rights.

(i) Notwithstanding the licenses granted to Agios pursuant to Section 8.2, Celgene retains the right to practice under the Celgene Intellectual Property and Celgene Collaboration Intellectual Property to perform (and to sublicense Third Parties to perform) its obligations under this Agreement, including for the purpose of performing its activities in connection with the Clinical Trials, any Manufacturing activities, or any Commercialization activities.

(ii) Notwithstanding the licenses granted to Celgene pursuant to Section 8.2, Agios retains the right to practice under the Agios Intellectual Property and Agios Collaboration Intellectual Property to perform (and to sublicense Third Parties to perform) its obligations under this Agreement, including for the purpose of performing its activities in connection with the Clinical Trials, any Manufacturing activities, or any Commercialization activities.

(iii) The Parties acknowledge that the licenses granted hereunder are subject to the rights retained by (A) the licensor under the [**] Agreement pursuant to Section 2.3 of the [**] Agreement, (B) the licensor under the [**] Agreement pursuant to Section 2.4 of the [**] Agreement, and (C) the licensors under the [**] Agreement pursuant to Sections 1.3 and 2.3 of the [**] Agreement; provided that, upon Celgene's reasonable request, Agios shall cooperate fully in requesting and obtaining any waiver with respect to the requirement, if applicable under such agreements, that Licensed Products or Celgene Reverted Products used or sold in the United States be manufactured substantially in the United States.

Section 8.11 Section 365(n) of the Bankruptcy Code. All rights and licenses granted under or pursuant to any section of this Agreement are and will otherwise be deemed to be for purposes of Section 365(n) of the United States Bankruptcy Code (Title 11, U.S. Code), as amended (the "Bankruptcy Code"), licenses of rights to "intellectual property" as defined in Section 101(35A) of the Bankruptcy Code. The Parties will retain and may fully exercise all of their respective rights and elections under the Bankruptcy Code. The Parties agree that each

Party, as licensee of such rights under this Agreement, will retain and may fully exercise all of its rights and elections under the Bankruptcy Code or any other provisions of applicable law outside the United States that provide similar protection for "intellectual property." The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against a Party under the U.S. Bankruptcy Code or analogous provisions of applicable law outside the United States, the Party that is not subject to such proceeding will be entitled to a complete duplicate of (or complete access to, as appropriate) such intellectual property and all embodiments of such intellectual property, which, if not already in the non-subject Party's possession, will be promptly delivered to it upon the non-subject Party's written request thereof. Any agreements supplemental hereto will be deemed to be "agreements supplementary to" this Agreement for purposes of Section 365(n) of the Bankruptcy Code.

## Article IX
## Financial Provisions

Section 9.1 Initial Payment. In consideration of Agios' performance of its obligations under the Collaboration, Celgene shall make an initial, non-refundable payment to Agios of One Hundred Twenty-One Million One Hundred Seventy-Six Thousand Sixty-Three Dollars (US$121,176,063) within [**] days following the Effective Date.

Section 9.2 Equity Investment. As of the Effective Date, the Parties have entered into a Stock Purchase Agreement pursuant to which, as of the Effective Date, Celgene shall purchase from Agios, and Agios shall sell to Celgene, shares of Series B Convertible Preferred Stock of Agios, as more specifically set forth in such Stock Purchase Agreement.

Section 9.3 Option Exercise Payments.

(a) Payments for Co-Commercialized Programs. Following Celgene's selection of a Development Candidate at the DC Selection Stage under a Co-Commercialized Program pursuant to Section 3.6(b), on a Program-by-Program basis:

(i) Celgene shall pay Agios Twenty-Two Million Five Hundred Thousand Dollars (US$22,500,000) (the "IND Amount") upon an IND Acceptance achieved by Agios for such Development Candidate in such Co-Commercialized Program pursuant to Section 3.6(b)(iii)(A); provided that (A) no such IND Amount will be due with respect to the first [**] IND Acceptances achieved by Agios under Co-Commercialized Programs for which IND Acceptance is achieved; (B) no such IND Amount will be due prior to [**]; and (C) no such IND Amount will be due with respect to any IND Acceptance achieved by Agios under an Optionable Program that becomes a Split Program pursuant to Section 3.10.

(ii) If Celgene has requested Agios to conduct a Phase I MAD Study pursuant to Section 3.6(b)(iii)(A)(2), then, unless the applicable Program becomes a Split Program, Celgene shall pay Agios Five Million Dollars (US$5,000,000) upon enrollment of the last patient in such first Phase I MAD Study (whether successful or not) conducted by Agios (the "Phase I Amount"); provided, however, that, if the JDC by Mutual Consent adopts a Development Plan and related Development Budget pursuant to which Agios undertakes significant additional Development activities under such Program following IND Acceptance in parallel with such

Phase I MAD Study, then the JDC by Mutual Consent will determine the amount of an increase to such Phase I Amount necessary to cover such excess costs and expenses pursuant to such Development Plan. For clarity, Celgene shall not be responsible for the Phase I Amount with respect to any Split Program.

(iii) For clarity, Celgene shall not owe the IND Amount with respect to any Picked Validated Program selected by Celgene or for any Buy-In Program (whether Celgene is the Buy-In Party or Agios is), and Celgene shall not owe the Phase I Amount with respect to any Phase I MAD Study other than that conducted at Celgene's request pursuant to Section 3.6(b)(iii)(A)(2).

(b) Reimbursement for Picked Validated Programs Selected by Celgene. Except as provided in Section 3.3(b)(iii)(B), 3.3(b)(iii)(C) or 15.5, on a Validated Program-by-Validated Program basis, Celgene shall pay to Agios the Validated Program Discovery Costs for each Pick selected by Celgene pursuant to Section 3.7 that is directed to a Collaboration Target that was not on the Target List as of the Effective Date.

(c) Payment. Celgene shall make the payments set forth in this Section 9.3 within [**] days following receipt of an invoice from Agios notifying Celgene that the event triggering the payment has occurred (or, if Section 9.3(a)(i)(B) is applicable, within [**] days after receipt of an invoice or [**], whichever is later).

Section 9.4 Development Costs.

(a) For Licensed Programs. Except as set forth in clauses (b) and (c) below with respect to Split Programs and Buy-In Programs, the following shall apply:

(i) With respect to each Co-Commercialized Program and Picked Validated Program selected by Celgene under which Agios performs Development activities hereunder, Celgene shall be responsible for bearing one hundred percent (100%) of the Development Costs for such Licensed Program, including the Development Costs of any Clinical Trials or other Licensed Program activities conducted by Agios (at Celgene's request pursuant to Section 3.6(b)(iv)(B) and as agreed to by Agios), that (A) are incurred after the Development Cost Initiation Date for such Licensed Program and (B) are within [**] percent ([**]%) of the approved Development Budget under the Development Plan for such Licensed Program. Notwithstanding anything herein to the contrary, any costs of the first Phase 1 MAD Study for which Agios is paid the Phase I Amount shall not be included in the Development Costs under this Section 9.4(a).

(ii) Within [**] days following the end of each [**], Agios shall prepare and deliver to Celgene a [**] report detailing its Development Costs incurred during such period with respect to which Celgene is required to pay pursuant to Section 9.4(a)(i). Agios shall submit any supporting information reasonably requested by Celgene related to such Development Costs included in Agios' report within [**] days after Agios' receipt of such request. Celgene shall pay all amounts of such Development Costs within [**] days following the later of Celgene's receipt of such report and Celgene's receipt of such supporting information.

(b) For Split Programs. Effective as of the Option Exercise Date for any Split Program, each party shall be responsible for fifty percent (50%) of Global Development Costs of such Split Program that (i) are incurred after the Development Cost Initiation Date for such Split Program (as further described in Section 3.10(b)(ii)) and (ii) are within [**] percent ([**]%) of the approved Development Budget under the Development Plan for such Split Program (or the Commercialization budget under the Commercialization Plan, as described in Sections 6.1(c)(i) and 6.2(a)(i)). For purposes of clarity, (x) Agios shall be responsible for one hundred percent (100%) of Territory-Specific Development Costs of such Split Program incurred by Agios, (y) Celgene shall be responsible for one hundred percent (100%) of Territory-Specific Development Costs of such Split Program incurred by Celgene, and (z) Agios shall be responsible for [**] percent ([**]%) of its Global Development Costs of such Split Program incurred prior to [**].

(c) For Buy-In Programs. Effective as of the date of the Buy-In Party's exercise of its Buy-In Rights with respect to each Buy-In Program as set forth in Section 3.11, the Buy-In Party shall be responsible for [**] percent ([**]%) of all Development Costs and the other Party shall be responsible for all remaining Development Costs of such Buy-In Program that (i) are incurred after the Development Cost Initiation Date for such Buy-In Program and (ii) are within [**] percent ([**]%) of the approved Development Budget under the Development Plan for such Buy-In Program.

(d) Reconciliation of Development Costs for Split Programs and for Buy-In Programs. Within [**] days following the end of each [**], each Party shall prepare and deliver to the other Party a [**] report detailing its Development Costs for Buy-In Products and Global Development Costs for Split Products, in either case, incurred during such period with respect to which the Parties are required to share pursuant to Section 9.4(b) or 9.4(c). The Party incurring such costs shall submit any supporting information reasonably requested by the other Party related to such costs included in the incurring Party's report within [**] days after the incurring Party's receipt of such request. The Parties shall conduct a reconciliation of such Development Costs or Global Development Costs, as applicable, within [**] days after receipt of all such supporting information, and an invoice shall be issued to the Party (if any) that has not paid for its full share of the Development Costs or Global Development Costs, as applicable, identified in such reconciliation. The paying Party shall pay all amounts payable under any such invoice within [**] days after its receipt of such invoice.

Section 9.5 Manufacturing Costs; Commercialization Costs.

(a) Each Party shall be solely responsible for Manufacturing Costs as provided in Section 4.1.

(b) Subject to Section 9.5(a), Celgene shall be [**] responsible for [**] percent ([**]%) of Celgene's expenses incurred in connection with the Commercialization of the Picked Products and Celgene Reverted Products. Subject to Section 9.5(a), the Commercializing Party shall be [**] responsible for [**] percent ([**]%) of its expenses incurred in connection with the Commercialization of Buy-In Products.

(c) Subject to Section 9.5(a) and Section 6.1(c)(i), the Commercializing Party shall be [**] responsible for [**] percent ([**]%) of its expenses incurred in connection with the Commercialization of the Split Products in such Commercializing Party's portion of the Territory (*i.e.*, the US Territory if Agios is the Commercializing Party, and the ROW Territory if Celgene is the Commercializing Party).

(d) Subject to Section 9.5(a), Celgene shall be [**] responsible for [**] percent ([**]%) of Celgene's expenses incurred in connection with the Commercialization of the Co-Commercialized Products. In addition, with respect to each Co-Commercialized Program, Celgene shall be responsible for bearing [**] percent ([**]%) of the Field-Based Costs for Commercialization Activities of Agios under Section 6.3 for such Co-Commercialized Program pursuant to Section 6.3 that (i) are incurred after the Development Cost Initiation Date for such Co-Commercialized Program and (ii) are within [**] percent ([**]%) of the approved budget under the Commercialization Plan for such Co-Commercialized Program.

(e) Within [**] days following the end of each [**], Agios shall prepare and deliver to Celgene a [**] report detailing its Field-Based Costs pursuant to Section 6.3 for Co-Commercialized Products incurred during such period with respect to which Celgene is required to pay pursuant to Section 9.5(d). Agios shall submit any supporting information reasonably requested by Celgene related to such costs included in Agios' report within [**] days after Agios' receipt of such request. Celgene shall pay all amounts of such Field-Based Costs within [**] days following the later of Celgene's receipt of such report and Celgene's receipt of such supporting information.

Section 9.6 Milestone Payments.

(a) Development and Regulatory Milestones. With respect to each Split Program, Co-Commercialized Program and Picked Validated Program selected by Celgene pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii), Section 3.6(c) or Section 15.5), Celgene shall pay Agios the following amounts after the first achievement by or on behalf of Celgene, its Affiliates or its sublicensees of the corresponding milestone events set forth below with respect to each Licensed Product under such a Licensed Program, on a Licensed Program-by-Licensed Program basis.

| **Development Milestones** | **Each Program** |
|---|---|
| (1) FPD in a Phase III Study intended to support Regulatory Approval in ROW Territory | US$25,000,000 |
| (2) Filing of first NDA in ROW Territory | [**] |
| (3) First Regulatory Approval in any of China, Japan or a Major European Country | [**] |
| (4) Second Regulatory Approval in any of China, Japan or a Major European Country, but only if received in a different country or region, as applicable, than the first Regulatory Approval | [**] |

(i) For purposes of determining the occurrence of milestones under Section 9.6(a)(2), "[**]" shall be deemed to have occurred [**] days following [**]; provided that, if such [**]. For purposes of determining the occurrence of milestones under Section 9.6(a)(3) and Section 9.6(a)(4), the [**]. For purposes of clarity, no milestone amount shall be payable to Agios under Section 9.6(a)(4) if [**] for purposes of Section 9.6(a)(4).

(ii) For purposes of clarity, neither Buy-In Programs nor Celgene Reverted Programs shall be entitled to any milestones under this Section 9.6(a).

(iii) For purposes of determining the milestones owed under this Section 9.6(a) on Licensed Product in a Split Program, Co-Commercialized Program and Picked Validated Program selected by Celgene, a Licensed Product that achieves the applicable milestones in connection with [**] different Indications shall not be deemed to be [**] separate Licensed Products; provided that, if the Licensed Product achieves the applicable milestones for [**] in the Oncology Field and [**] Indications outside the Oncology Field, (A) Celgene shall pay the corresponding milestones described in this Section 9.6(a) with respect to the [**] Indication in the Oncology Field to achieve each such milestone event, and (B) upon achievement of the milestone events described in Sections 9.6(a)(3) and 9.6(a)(4) for the [**] Indication outside the Oncology Field, Celgene shall pay the corresponding milestone payment upon achievement of such event. Other than the foregoing payment, no milestone payments shall be due with respect to the achievement of any milestone event by a Licensed Product for [**] Indication.

(iv) For purposes of clarity, if Development of a Licensed Product directed to a particular Collaboration Target [**] (a "Failed Product") prior to [**], and Development of a Back-Up Compound directed to the same Collaboration Target as the Failed Product subsequently commences or continues, then any of the milestone payments previously made by Celgene in the table set forth above in connection with such Failed Product shall [**] achievement of such milestone event by such Back-Up Compound. However, in the event that a Licensed Product [**], a Licensed Product [**] shall be deemed a "Second Generation Product." If such Second Generation Product achieves the Regulatory Approval milestone events set forth in Section 9.6(a)(3) and Section 9.6(a)(4), then Celgene shall pay to Agios the associated milestone payments; provided that [**] with respect to the events set forth in Section 9.6(a)(1) or 9.6(a)(2); provided further that such Second Generation Product shall not be subject to the provisions of Section 9.6(a)(iii), and no milestone payments shall be due with respect to the [**] Indication for such Second Generation Product.

(v) For purposes of clarity, if for any reason a milestone event corresponding to a milestone payment in the table set forth above does not occur prior to the occurrence of the next milestone event listed in the table above for such Licensed Product, then such prior non-occurring milestone event shall be deemed to occur concurrently with the occurrence of the next milestone event; provided that [**].

(vi) Each milestone payment under this Section 9.6(a) shall be made within [**] days after the achievement of the applicable milestone by Celgene or any of its Affiliates or sublicensees (or, if achievement of such milestone is within the control of Agios, within [**] days following Celgene's receipt of written notice of the achievement of such milestone).

(vii) For clarity, the milestone payments set forth in the table above in this Section 9.6(a) (to the extent payable) shall be paid only for each Licensed Product containing the same Licensed Compound to achieve the applicable milestone event, except as provided in Section 9.6(a)(iii) for [**]. By way of example, a change in [**] with respect to a Licensed Compound will not trigger additional milestones for Licensed Product(s) containing such Licensed Compound.

(b) Phase II Study Milestone. Celgene shall pay Agios a one-time milestone of US $25 million upon the dosing of the final human subject with a Split Product designated by Agios in writing in a company-sponsored Phase II Study in the US Territory (or in the ROW Territory, if agreed by the Parties by Mutual Consent). Such milestone shall be paid within [**] days after Celgene's receipt of written notice of the achievement of such event by Agios or any of its Affiliates or sublicensees. Such milestone shall be paid only once with respect to only one Split Program.

(c) Sales Milestone. Celgene shall make the following non-refundable, non-creditable, one-time payment to Agios (i) with respect to each Co-Commercialized Product or Split Product within [**] days following the first achievement of aggregate Annual Net Sales in the [**] of each such Licensed Product that meet or exceed the threshold set forth below, and (ii) with respect to each Picked Product, within [**] days following the first achievement of aggregate [**] Annual Net Sales of each such Picked Product that meet or exceed the threshold set forth below. If a Second Generation Product is sold, the Annual Net Sales associated with such Second Generation Product will be aggregated with the Licensed Compound(s) to which it relates, and separate sales milestones under this Section 9.6(c) shall not be paid for such Second Generation Product.

| Annual Net Sales Threshold | Milestone Payment |
|---|---|
| Equal to or greater than US$[**] | US$25,000,000 |

Section 9.7 Royalty Payments.

(a) For Co-Commercialized Products. Celgene shall pay to Agios royalties on aggregate worldwide Annual Net Sales of each Co-Commercialized Product at the following rates:

| Annual Net Sales of Licensed Product | Royalty Rate |
|---|---|
| On the tranche of Annual Net Sales less than US$[**] | [**]% |
| On the tranche of Annual Net Sales equal to or greater than US$[**]and less than US$[**] | [**]% |
| On the tranche of Annual Net Sales equal to or greater than US$[**] | [**]% |

If a Second Generation Product is sold, the Annual Net Sales associated with such Second Generation Product will be aggregated with the Licensed Compound(s) to which it relates for purposes of determining the applicable royalty rate for such sales.

(b) For Split Products.

(i) Celgene shall pay to Agios royalties on aggregate Annual Net Sales of each Split Product in the ROW Territory at the rates set forth in the table above.

(ii) Agios shall pay to Celgene royalties on aggregate Annual Net Sales of each Split Product in the US Territory at the rates set forth in the table above (substituting Agios for Celgene as the royalty-paying Party and Celgene for Agios as the royalty-receiving Party).

(c) For Buy-In Products. The Commercializing Party for a Buy-In Program shall pay the Buy-In Party royalties on aggregate worldwide Annual Net Sales of Buy-In Products under such Buy-In Program at the rates set forth in the table above (substituting the Commercializing Party for Celgene as the royalty-paying Party and the Buy-In Party for Agios as the royalty-receiving Party).

(d) For Picked Products. Celgene shall pay to Agios royalties on aggregate worldwide Annual Net Sales of each Picked Product at the rates set forth in the table above.

(e) For Celgene Reverted Programs. Celgene shall pay to Agios royalties at a rate of [**] percent ([**]%) of aggregate worldwide Annual Net Sales of each Celgene Reverted Product.

(f) Royalty Term.

(i) Royalties payable under this Section 9.7 shall be paid by the Commercializing Party on a Royalty-Bearing Product-by-Royalty-Bearing Product and country-by-country basis from the date of First Commercial Sale of each Royalty-Bearing Product with respect to which royalty payments are due until the latest of:

(A) the last to expire of any Valid Claim of Agios Patent Rights or Agios Collaboration Patent Rights, in each case Covering such Royalty-Bearing Product in such country;

(B) [**] years following the date of First Commercial Sale in such country; and

(C) the expiration of Regulatory Exclusivity for such Royalty-Bearing Product in such country.

(each such term with respect to a Royalty-Bearing Product and a country, a "Royalty Term").

(ii) Notwithstanding the foregoing, (A) in the event that the Royalty Term for a Royalty-Bearing Product in a country continues solely due to Section 9.7(f)(i)(B) above (*i.e.*, the Royalty-Bearing Product is not Covered by a Valid Claim of Agios Patent Rights or Agios Collaboration Patent Rights in the applicable country, and such Royalty-Bearing Product is not subject to Regulatory Exclusivity in such country) or (B) in the event that, and for so long as, Generic Competition for a Royalty-Bearing Product occurs in a country, then, in either such event, the royalty rates in such country will be reduced to [**] percent ([**]%) of the applicable rate in Section 9.7(a), 9.7(b), 9.7(c), 9.7(d) or 9.7(e) in such country.

(iii) Upon the expiration of the Royalty Term with respect to a Royalty-Bearing Product in a country, the licenses granted by a Party to the Commercializing Party pursuant to Section 8.2 shall be deemed to be fully paid-up, irrevocable and perpetual with respect to such Royalty-Bearing Product in such country.

(g) Third Party Payments.

(i) Except as otherwise provided in Section 8.9 or Section 14.3(b)(viii)(B), [**] shall be [**] responsible for [**] amounts payable under the Existing Third Party Agreements with respect to Licensed Compounds and Licensed Products.

(ii) At any time, if either Party determines that the Parties should obtain a license under Third Party Patent Rights or Third Party Know-How [**] to use a Collaboration Target or to Develop, Manufacture or Commercialize Collaboration Compounds, Licensed Compounds and/or Licensed Products, then such Party shall notify the JRC or the JDC, as applicable.

(A) If the JRC or JDC agrees by Mutual Consent to obtain such license, the JRC or JDC shall determine which Party should obtain such license; provided that, if the JRC or JDC cannot agree on which Party should obtain such license, then Celgene shall be the Party to do so if Celgene has exercised the Celgene Program Option (or taken an exclusive license under Section 8.2) for the Program to which the license relates, and Agios shall do so if Celgene has not yet exercised such Celgene Program Option (or taken an exclusive license under Section 8.2); provided that, with respect to Split Programs, the Parties shall each be entitled to do so for their respective portions of the Territory; provided further that Agios shall be the Party to obtain such license with respect to any Buy-In Program for which Agios is the Commercializing Party.

(B) If such license is entered into following the Effective Date, then the costs of such license shall be shared as follows: (1) the Party who obtains such license shall be solely responsible for all costs under such license prior to the exercise of the Celgene Program Option (or prior to the effective date of Celgene's exclusive license under Section 8.2) with respect to the Program to which such license relates and all costs not described in clause (2); and (2) the Parties shall [**] all royalty and milestones costs incurred after the Option Exercise Date (or after the effective date of Celgene's exclusive license under Section 8.2) to the extent the costs directly relate to such Program and to events following such Option Exercise Date (or following the effective date of Celgene's exclusive license under Section 8.2); provided that, if such license is entered into following the Effective Date but prior to the exercise of the Celgene Program Option (or the effective date of Celgene's exclusive license under Section 8.2) with respect to such Program to which such license relates, Celgene may deduct [**] all costs

paid by Celgene under clause (2) from any milestone incurred after and including the milestone event described in Section 9.6(a)(3) or any royalty payments owed to Agios hereunder with respect to such Program; provided further that, with respect to Buy-In Programs, the foregoing payment obligations will be borne [**]% by the Commercializing Party and [**]% by the Buy-In Party, with the events described in this Section 9.7(g)(ii)(B) being based on the date the Buy-In Party exercises its Buy-In Right, rather than the Option Exercise Date.

(C) For purposes of this Agreement, the Third Party Patent Rights and Third Party Know-How licensed pursuant to this Section 9.7(g)(ii) shall be deemed "Collaboration Intellectual Property" of the Party obtaining such license.

(D) (1) The Party designated to pursue the license shall keep the other Party fully informed of the status of the negotiations with the Third Party and provide the other Party with copies of all draft agreements; (2) the other Party may provide comments and suggestions with respect to the negotiation of the agreement with the Third Party, and the Party seeking the license shall reasonably consider all comments and suggestions reasonably recommended by the other Party; and (3) the Party seeking the license shall obtain a license that is sublicensable to the other Party in accordance with the terms of this Agreement, treating (unless otherwise agreed by the Parties) the Third Party intellectual property as Collaboration Intellectual Property hereunder and treating the agreement licensing such Third Party intellectual property in the same way as the Existing Third Party Agreements (including as provided in Section 8.7), except for payment obligations, which will be treated as provided in this Section 9.7(g)(ii).

(E) If the JRC or JDC does not agree by Mutual Consent that a license proposed pursuant to this Section 9.7(g)(ii) should be obtained, either Party shall have the right to obtain the license at its own cost (a "Unilateral In-License"). In such event, no rights or licenses obtained under any such Third Party license shall be included in any license granted under this Agreement by the Party obtaining the license to the other Party, unless and until the other Party agrees to pay its share of the costs of such license as described in Section 9.7(g)(ii)(B) and to reimburse the other Party for the share of the costs of such license that the non-licensing Party would have paid under Section 9.7(g)(ii)(B) if the Unilateral In-License had been entered into pursuant to Section 9.7(g)(ii)(B). If a Party agrees to make such payments, such license shall cease to be a Unilateral In-License hereunder.

(iii) In the event that royalties are payable by a Party to the other Party with respect to any Royalty-Bearing Product(s) for which the paying Party is the Commercializing Party under this Section 9.7, such Commercializing Party shall have the right to deduct a maximum of [**] percent ([**]%) of any royalties or other amounts actually paid by the Commercializing Party to a Third Party with respect to a Unilateral In-License, but only to the extent that the Patent Rights and/or Know-How licensed under such Unilateral In-License are [**] to use the Collaboration Target to which such Royalty-Bearing Product(s) is directed, or to the Development, Manufacture or Commercialization of such Royalty-Bearing Product(s) in a country(ies) in the Territory (or the US Territory or ROW Territory, as applicable, with respect to Split Products), from royalty payments otherwise due and payable by such Commercializing Party to the other Party under this Section 9.7 with respect to such Royalty-Bearing Product(s) in such country(ies), on a Royalty-Bearing Product-by-Royalty-Bearing Product and country-by-

country basis; provided, however, that in no event shall the aggregate deductions permitted by this subsection (iii) reduce the royalties payable by the Commercializing Party to the other Party with respect to any such Royalty-Bearing Product(s) in such country(ies) for any Calendar Quarter to less than [**] percent ([**]%) of the royalties otherwise due in the absence of any deduction pursuant to this subsection (iii); provided further that on a Royalty-Bearing Product-by-Royalty-Bearing Product basis, any royalty deductions that are not credited against royalties payable by such Commercializing Party to such other Party for the Calendar Quarter in which they were accrued due to the limitation in the preceding proviso shall be carried forward and credited against royalties payable by such Commercializing Party to such other Party in subsequent Calendar Quarter(s) hereunder until such royalty credits are completely expended.

Section 9.8 Royalty Reports; Payments. Within [**] calendar days after the end of any [**], the Commercializing Party with respect to each Royalty-Bearing Product shall provide the other Party with a report stating the sales in units and in value of such Royalty-Bearing Product made by such Commercializing Party, its Affiliates, licensees and sublicensees, as applicable, in the Territory (or the US Territory or the ROW Territory, as applicable, with respect to Split Products), on a country-by-country basis, together with the calculation of the royalties due to the other Party, including the method used to calculate the royalties, the exchange rates used, and itemized deductions. Celgene shall also include in its report to Agios notice of the achievement of the sales milestone event set forth in Section 9.6(c), as applicable. Payments of all amounts payable under Section 9.6 or 9.7 shall be made by Celgene or Agios, as applicable, to the bank account indicated by the other Party concurrently with the delivery of such report.

Section 9.9 Financial Records. The Parties shall keep, and shall require their respective sublicensees to keep, complete and accurate books and records in accordance with the applicable Accounting Standards. The Parties shall keep, and shall require their respective sublicensees to keep, such books and records for at least [**] years following the end of the Calendar Year to which they pertain. Such books of accounts shall be kept at the principal place of business of the financial personnel with responsibility for preparing and maintaining such records. With respect to royalties, such records shall be in sufficient detail to support calculations of royalties due to the royalty-receiving Party. Celgene and Agios shall also keep, and require their respective sublicensees to keep, complete and accurate records and books of accounts containing all data reasonably required for the calculation and verification of Manufacturing Costs, Field-Based Costs, Development Costs, and Global Development Costs, including internal FTEs utilized by either Party in Global Studies or other Development activities.

Section 9.10 Audits.

(a) Each Party may, upon request and at its expense (except as provided for herein), cause an internationally recognized independent accounting firm selected by it (except one to whom the Auditee has a reasonable objection), (the "Audit Team") to audit during ordinary business hours the books and records of the other Party and the correctness of any payment made or required to be made to or by such Party, and any report underlying such payment (or lack thereof), pursuant to the terms of this Agreement. Prior to commencing its work pursuant to this Agreement, the Audit Team shall enter into an appropriate confidentiality agreement with the Auditee obligating the Audit Team to be bound by obligations of confidentiality and restrictions on use of such Confidential Information that are no less restrictive than the obligations set forth in Article XI.

(b) In respect of each audit of the Auditee's books and records: (i) the Auditee may be audited only [**], (ii) no records for any given year for an Auditee may be audited more than [**]; provided that the Auditee's records shall still be made available if such records impact another financial year which is being audited, and (iii) the Audit Rights Holder shall only be entitled to audit books and records of an Auditee from the [**] Calendar Years prior to the Calendar Year in which the audit request is made.

(c) In order to initiate an audit for a particular Calendar Year, the Audit Rights Holder must provide written notice to the Auditee. The Audit Rights Holder exercising its audit rights shall provide the Auditee with notice of [**] proposed dates of the audit not less than [**] days prior to the first proposed date. The Auditee will reasonably accommodate the scheduling of such audit. The Auditee shall provide such Audit Team(s) with full and complete access to the applicable books and records and otherwise reasonably cooperate with such audit.

(d) The audit report and basis for any determination by an Audit Team shall be made available first for review and comment by the Auditee, and the Auditee shall have the right, at its expense, to request a further determination by such Audit Team as to matters which the Auditee disputes (to be completed no more than [**] days after the first determination is provided to such Auditee and to be limited to the disputed matters). Such Audit Team shall not disclose to the Audit Rights Holder any information relating to the business of the Auditee except that which should properly have been contained in any report required hereunder or otherwise required to be disclosed to the Audit Rights Holder to the extent necessary to verify the payments required to be made pursuant to the terms of this Agreement.

(e) If the audit shows any under-reporting or underpayment, or overcharging by any Party, that under-reporting, underpayment or overcharging shall be reported to the Audit Rights Holder and the underpaying or overcharging Party shall remit such underpayment or reimburse such overcompensation (together with interest at the rate set forth in Section 9.13) to the underpaid or overcharged Party within [**] days after receiving the audit report. Further, if the audit for an annual period shows an under-reporting or underpayment or an overcharge by any Party for that period in excess of [**] percent ([**]%) of the amounts properly determined, the underpaying or overcharging Party, as the case may be, shall reimburse the applicable underpaid or overcharged Audit Rights Holder conducting the audit, for its respective audit fees and reasonable Out-of-Pocket Costs in connection with said audit, which reimbursement shall be made within [**] days after receiving appropriate invoices and other support for such audit-related costs.

(f) For the purposes of the audit rights described herein, an individual Party subject to an audit in any given year will be referred to as the "Auditee" and the other Party who has certain and respective rights to audit the books and records of the Auditee will be referred to as the "Audit Rights Holder."

Section 9.11 Tax Matters.

(a) The royalties, milestones and other amounts payable by a Party to the other Party pursuant to this Agreement ("Payments") shall not be reduced on account of any taxes unless required by Law. The receiving Party alone shall be responsible for paying any and all taxes (other than withholding taxes required by Law to be deducted and paid on the receiving Party's behalf by the paying Party) levied on account of, or measured in whole or in part by reference to, any Payments it receives. The Parties will cooperate in good faith to obtain the benefit of any relevant tax treaties to minimize as far as reasonably possible any taxes which may be levied on any Payments. The paying Party shall deduct or withhold from the Payments any taxes that it is required by Law to deduct or withhold. If the receiving Party is entitled under any applicable tax treaty or any Law to a reduction of the rate of, or the elimination of, applicable withholding tax, it may deliver to the paying Party or the appropriate governmental authority (with the assistance of the paying Party to the extent that this is reasonably required and is expressly requested in writing) the prescribed forms necessary to reduce the applicable rate of withholding or to relieve the paying Party of its obligation to withhold tax, and the paying Party shall apply the reduced rate of withholding tax, or dispense with withholding tax, as the case may be; provided that the paying Party has received evidence of the receiving Party's delivery of all applicable forms (and, if necessary, its receipt of appropriate governmental authorization) at least [**] days prior to the time that the Payment is due. If, in accordance with the foregoing, the paying Party withholds any amount, it shall make timely payment to the proper taxing authority of the withheld amount, and send to the receiving Party proof of such payment within [**] days following that latter payment.

(b) Notwithstanding the foregoing, if the rights and obligations of the paying Party hereunder are assigned to an Affiliate or Third Party outside of the United States or Switzerland pursuant to Section 15.4, and if such Affiliate or Third Party shall be required by Law to withhold any additional taxes from or in respect of any sum payable under this Agreement as a result of such assignment, then any such sum payable under this Agreement shall be increased to take into account the additional taxes withheld as may be necessary so that, after making all required withholdings, the receiving Party receives an amount equal to the sum it would have received had no such assignment been made; provided, however, that, if the rights and obligations of the paying Party hereunder are assigned to an Affiliate or Third Party outside of the United States or Switzerland pursuant to Section 15.4 and if at the time of such assignment such Affiliate or Third Party is not required by Law to withhold any additional taxes as a result of such assignment, the paying Party shall not be required to increase any such sum payable under this Agreement in the event of a change in Law. In addition, if the rights and obligations of the receiving Party hereunder are assigned to an Affiliate or Third Party pursuant to Section 15.4, the paying Party shall not have an obligation to pay an additional sum pursuant to this Section 9.11(b) to the extent that the additional sum would not have been due pursuant to this Section 9.11(b) if the rights and obligations of the receiving Party hereunder had not been assigned to an Affiliate or Third Party pursuant to Section 15.4.

Section 9.12 Currency Exchange.

(a) Unless otherwise expressly stated in this Agreement, all amounts specified in, and all payments made under, this Agreement shall be in United States Dollars. If any currency conversion shall be required in connection with the calculation of amounts payable under this Agreement, such conversion shall be made using the average of the buying and selling exchange rate for conversion of the applicable foreign currency into United States Dollars, quoted for current transactions reported in The Wall Street Journal (U.S., Eastern Edition) for the last [**] Business Days of the Calendar Quarter to which such payment pertains.

(b) Where royalty amounts are due for Net Sales in a country where, for reasons of currency, tax or other regulations, transfer of foreign currency out of such country is prohibited, the Commercializing Party has the right to place royalties due to the other Party in a bank account in such country in the name of and under the sole control of such other Party; provided, however, that the bank selected be reasonably acceptable to such other Party and that the Commercializing Party inform such other Party of the location, account number, amount and currency of money deposited therein. After such other Party has been so notified, those monies shall be considered as royalties duly paid to such Party and will be completely controlled by such Party.

(c) When in any country in the Territory applicable Law prohibits both the transmittal and the deposit of royalties on sales in such country, royalty payments due on Net Sales shall be suspended for as long as such prohibition is in effect and as soon as such prohibition ceases to be in effect, all royalties that the Commercializing Party would have been under an obligation to transmit or deposit but for the prohibition shall forthwith be deposited or transmitted, to the extent allowable.

Section 9.13 Late Payments. The paying Party shall pay interest to the receiving Party on the aggregate amount of any payments that are not paid on or before the date such payments are due under this Agreement at a rate per annum equal to the lesser of the [**] month LIBOR plus [**] percent ([**]%), as reported by The Wall Street Journal, or the highest rate permitted by applicable Law, calculated on the number of days such payments are paid after the date such payments are due; provided that, with respect to any disputed payments, no interest payment shall be due until such dispute is resolved and the interest which shall be payable thereon shall be based on the finally-resolved amount of such payment, calculated from the original date on which the disputed payment was due through the date on which payment is actually made.

## Article X
## Intellectual Property Ownership, Protection and Related Matters

Section 10.1 Ownership of Inventions.

(a) Non-Collaboration Know-How. Any Know-How developed or generated by Celgene or Agios prior to or outside the Collaboration shall remain the sole property of such Party.

(b) Sole Inventions. All Collaboration Know-How developed or generated solely by employees, agents and consultants of a Party shall be owned exclusively by such Party.

(c) Joint Inventions. All Collaboration Know-How developed or generated jointly by employees, agents and consultants of Celgene, on the one hand, and employees, agents and consultants of Agios, on the other hand ("Joint Inventions" and, any Patent Rights Covering

such Joint Inventions, "Joint Patents") shall be owned jointly on the basis of each Party having an undivided interest without a duty to account to the other Party and shall be deemed to be Controlled by each Party. Each Party shall have the right to use such Joint Inventions, or license such Joint Inventions to its Affiliates or any Third Party, or sell or otherwise transfer its interest in such Joint Inventions to its Affiliates or a Third Party, in each case without the consent of the other Party (and, to the extent that applicable Law requires the consent of the other Party, this Section 10.1(c) shall constitute such consent), so long as such use, sale, license or transfer is subject to Section 8.8 and the licenses granted pursuant to this Agreement and is otherwise consistent with this Agreement.

(d) Notice. Each Party agrees to provide regular [**] written reports disclosing to the other Party all Collaboration Intellectual Property developed or generated by employees, agents and consultants of such Party and all Agios Intellectual Property and Celgene Intellectual Property that becomes subject to this Agreement, which disclosures may be made in connection with the updates made in accordance with Sections 3.1(b) and 3.8(c).

(e) Inventorship. The determination of inventorship shall be made in accordance with United States patent laws. In the event of a dispute regarding inventorship, if the Parties are unable to resolve the dispute, the Parties shall jointly engage [**] to resolve such dispute. The decision of such [**] shall be binding on the Parties with respect to the issue of inventorship.

(f) Further Actions and Assignments. Each Party shall take all further actions and execute all assignments requested by the other Party and reasonably necessary or desirable to vest in the other Party the ownership rights set forth in this Article X.

Section 10.2 Prosecution of Patent Rights. Subject to the terms and conditions of the Existing Third Party Agreements to the extent such agreement applies to the Agios Patent Rights or Agios Collaboration Patent Rights, the following provisions shall apply with respect to the Agios Patent Rights, Celgene Patent Rights and Collaboration Patent Rights:

(a) Agios Patent Rights Prosecuted by Agios. Subject to the provisions of Section 10.2(f), prior to the exercise of the Celgene Program Option by Celgene (or, if applicable, the effective date of Celgene's license to Agios Intellectual Property and Agios Collaboration Intellectual Property under Section 8.2), Agios shall have the initial right and option to Prosecute the Agios Patent Rights and Agios Collaboration Patent Rights (excluding Joint Patents). Following the Option Exercise Date (or, if applicable, the effective date of Celgene's license to Agios Intellectual Property and Agios Collaboration Intellectual Property under Section 8.2), Agios shall have the initial right and option to Prosecute the Agios Patent Rights and Agios Collaboration Patent Rights (excluding Joint Patents) with respect to which Celgene does not have the initial right to Prosecute pursuant to Section 10.2(b). In the event that Agios declines to Prosecute such Patent Rights that relate to a Licensed Program or Celgene Reverted Program, it shall give Celgene reasonable notice to this effect, sufficiently in advance to permit Celgene to undertake such Prosecution in such country without a loss of rights, and thereafter Celgene may, upon written notice to Agios, Prosecute such Patent Rights in Agios' name.

(b) Agios Patent Rights Prosecuted by Celgene. Following the Option Exercise Date (or, if applicable, the effective date of Celgene's license to Agios Intellectual Property and Agios Collaboration Intellectual Property under Section 8.2), Celgene shall have the initial right and option to Prosecute any Agios Patent Right or Agios Collaboration Patent Right (excluding Joint Patents) that are Core Patent Rights and that Cover a Licensed Compound or Licensed Product (and the applicable Program, including, with respect to Split Programs, Patent Rights for the US Territory, but excluding Buy-In Compounds or Buy-In Products and the applicable Buy-In Program for which Agios is the Commercializing Party) or a Celgene Reverted Compound or Celgene Reverted Product (and the applicable Program); provided that, with respect to Split Programs, Celgene's right to Prosecute shall apply to [**] Split Program, beginning with the [**] Split Program (*i.e.*, the [**] Split Program, [**] Split Program, etc.). In the event that Celgene declines to Prosecute such Patent Rights, it shall give Agios reasonable notice to this effect, sufficiently in advance to permit Agios to undertake such Prosecution in such country without a loss of rights, and thereafter Agios may, upon written notice to Celgene, Prosecute such Patent Rights in Agios' name.

(c) Celgene Patent Rights. Celgene shall have the sole right and option to Prosecute the Celgene Patent Rights and the Celgene Collaboration Patent Rights (excluding Joint Patents). Except with respect to the Celgene Collaboration Patent Rights that are exclusively licensed to Agios under Section 8.2, Celgene's Prosecution shall not be subject to the diligence and cooperation provisions of Section 10.2(f) below. Following the effective date of Agios' license to Celgene Collaboration Intellectual Property under Section 8.2, if Celgene declines to Prosecute any Celgene Collaboration Patent Rights exclusively licensed to Agios pursuant to Section 8.2, Celgene shall give Agios reasonable notice to this effect, sufficiently in advance to permit Agios to undertake such Prosecution for such Celgene Collaboration Patent Rights in such country without a loss of rights, and thereafter Agios may, upon written notice to Celgene, Prosecute such Patent Rights in Celgene's name.

(d) Joint Patents. The Parties, acting by Mutual Consent, shall determine which Party shall have the initial right and option to Prosecute Joint Patents; provided that (i) if the Parties cannot agree by Mutual Consent, (x) Agios, prior to the Option Exercise Date (or, if applicable, the effective date of Celgene's license to Agios Intellectual Property and Agios Collaboration Intellectual Property under Section 8.2), shall have such initial right and option with respect to Joint Patents that relate to a Discovery Program, and Agios shall have the initial right and option with respect to Joint Patents that relate to Buy-In Programs for which Agios is the Commercializing Party, and (y) Celgene, following the Option Exercise Date (or, if applicable, the effective date of Celgene's license to Agios Intellectual Property and Agios Collaboration Intellectual Property under Section 8.2), shall have the initial right and option with respect to Joint Patents that are Core Patent Rights and that Cover a Licensed Compound or Licensed Product (and the applicable Program, including, with respect to Split Programs, Patent Rights for the US Territory, but excluding Buy-In Compounds or Buy-In Products and the applicable Buy-In Program for which Agios is the Commercializing Party) or a Celgene Reverted Compound or Celgene Reverted Product (and the applicable Celgene Reverted Program); provided that, with respect to Split Programs, Celgene's right to Prosecute shall apply to [**] Split Program, beginning with the [**] Split Program (*i.e.*, the [**] Split Program, [**] Split Program, etc.); provided further that, regardless of whether the Option Exercise Date or effective date of a license has occurred, Celgene shall have the initial right and option with

respect to Joint Patents that claim or embody an improvement to technology claimed or embodied in Celgene Intellectual Property; (ii) in the event that the Party with the initial right to Prosecute declines the option to Prosecute any such Patent Right in any country, such Party shall give the other Party reasonable notice to this effect, sufficiently in advance to permit such other Party to undertake such Prosecution in such country without a loss of rights, and thereafter such other Party may, upon written notice to the first Party, Prosecute such Patent Rights in both Parties' names, with expenses shared as provided in Section 10.2(e); and (iii) in the event that either Party does not want to share in the costs of such Prosecution, such Party shall notify the other Party thereof at least [**] days prior to the date of any applicable filing deadline and shall, and hereby does, assign to the other Party all of its right, title and interest in and to the applicable Joint Patent (and underlying Joint Invention).

(e) Costs and Expenses. Agios shall bear its own costs and expenses in Prosecuting Agios Patent Rights and Agios Collaboration Patent Rights pursuant to Section 10.2(a) and 10.2(b) or Celgene Collaboration Patent Rights pursuant to Section 10.2(c). Celgene shall bear its own costs and expenses in Prosecuting Agios Patent Rights, Agios Collaboration Patent Rights, Celgene Patent Rights and Celgene Collaboration Patent Rights pursuant to Sections 10.2(a), 10.2(b) and 10.2(c). The Parties shall jointly bear all costs and expenses in Prosecuting Joint Patents pursuant to Section 10.2(d), except as provided in clause (iii) of such section.

(f) Diligence and Cooperation.

(i) The Prosecuting Party shall be entitled to use patent counsel selected by it and reasonably acceptable to the non-Prosecuting Party (including in-house patent counsel as well as outside patent counsel) for the Prosecution of the Patents Rights subject to Section 10.2(a), (b), (c), or (d). Each Party agrees to cooperate with the other with respect to the Prosecution of such Patent Rights pursuant to this Section 10.2, including (x) executing all such documents and instruments and performing such acts as may be reasonably necessary in order to permit the other Party to undertake any Prosecution of Patent Rights that such other Party is entitled, and has elected, to Prosecute, as provided for in Sections 10.2(a), 10.2(b), 10.2(c) and 10.2(d), and (y) giving consideration to the proper scope of Patent Rights, including the scope of disclosure of Patent Rights as to Back-Up Compounds. The Prosecuting Party shall:

(A) regularly provide the other Party in advance with reasonable information relating to the Prosecuting Party's Prosecution of Patent Rights hereunder, including by providing copies of substantive communications, notices and actions submitted to or received from the relevant patent authorities and copies of drafts of filings and correspondence that the Prosecuting Party proposes to submit to such patent authorities, each of which shall be provided at least [**] days prior to any filing or response deadlines, or within [**] Business Days of the Prosecuting Party's receipt of any official correspondence if such correspondence only allows for [**] days or less to respond; provided that, if the foregoing time periods are not practicable under the circumstances, the Prosecuting Party shall provide such copies as far in advance as is practicable but with sufficient time for the non-Prosecuting party to provide meaningful input;

(B) consider in good faith and consult with the non-Prosecuting Party regarding its timely comments with respect to the same;

(C) with respect to Patent Rights in the non-Prosecuting Party's portion of the Territory (*i.e.*, the US Territory if the non-Prosecuting Party is Agios, and the ROW Territory if the non-Prosecuting Party is Celgene) Covering Split Compounds or Split Products, (1) if, after taking into account the non-Prosecuting Party's commercial interests in its portion of the Territory, the Prosecuting Party does not intend to incorporate particular comments provided by the non-Prosecuting Party with respect such Patent Rights, notify the non-Prosecuting Party reasonably in advance to allow the Parties to discuss the Prosecuting Party's rationale for not incorporating such comments; and (2) if after such discussion, the non-Prosecuting Party and Prosecuting Party do not agree on a course of action, the matter shall be referred to the JSC for resolution as set forth in Section 10.2(f)(iv);

(D) use Commercially Reasonable Efforts to Prosecute additional claims substantially similar to those suggested by the non-Prosecuting Party, if any, in such jurisdictions of the Territory reasonably requested by the non-Prosecuting Party; and

(E) consult with the non-Prosecuting Party before taking any action that would have a material adverse impact on the scope of claims within the Agios Patent Rights or Collaboration Patent Rights, as applicable.

(ii) To the extent Agios is the Prosecuting Party, the Parties shall determine by Mutual Consent the countries in which Agios shall Prosecute Agios Patent Rights and Agios Collaboration Patent Rights (including Joint Patents), with the understanding that the countries set forth on Schedule 10.2(f) shall generally form the basis for the overall Prosecution strategy for the Agios Patent Rights and Agios Collaboration Patent Rights (including Joint Patents) related to a Licensed Program (including Split Programs) or Celgene Reverted Program; provided that, if the Parties are unable to determine by Mutual Consent the countries in which such filings will be made, Celgene shall have the right to make the final determination of such matter and may exercise the step-in rights available to it under Section 10.2(a) if Agios declines to Prosecute in any such country. Further, Agios shall consult with Celgene well in advance of [**] and [**] deadlines as to additional countries (if any) in which Celgene desires that the Agios Patent Rights and Agios Collaboration Patent Rights be Prosecuted.

(iii) The Prosecuting Party agrees not to abandon the subject matter of a claim in an Agios Patent Right or Agios Collaboration Patent Right or narrow such claim except in response to an office action from the applicable patent office that, in the Prosecuting Party's reasonable judgment after consultation with the non-Prosecuting Party, requires such abandonment or narrowing; provided that, prior to such abandonment or narrowing, if feasible, the Parties will co-operate to file divisional or continuation applications to separate such claim such that Celgene may Prosecute claims to the extent related to Licensed Compounds, Licensed Products, Celgene Reverted Compounds, and Celgene Reverted Products and Agios may Prosecute the remaining claims.

(iv) With respect to Agios Patent Rights and Agios Collaboration Patent Rights (including Joint Patents) related to Split Programs, [**] shall agree upon a strategy (which may be updated from time to time) for Prosecution of such Patent Rights, including [**] to be pursued within such Patent Rights and to [**]; provided that, if the Parties are unable to determine by Mutual Consent the countries in which the Patent Rights shall be Prosecuted, the provisions of Section 10.2(f)(ii) shall apply if Agios is the Prosecuting Party with respect to such Split Program, and Celgene shall have the right to make the final determination of the countries in which to file if Celgene is the Prosecuting Party; provided that, in either case, such Patent Rights shall be prosecuted in the US Territory unless Agios otherwise consents. Thereafter, the Prosecuting Party shall follow such strategy in connection with all Prosecution of Patent Rights related to Split Programs unless [**] approves of a divergence from such strategy. [**] (with escalation through the Executive Officers, as provided in Section 2.8) shall resolve [**] any disputes arising between the non-Prosecuting Party and Prosecuting Party under Section 10.2(f)(i)(C) with respect to Prosecution of Patent Rights in the non-Prosecuting Party's portion of the Territory related to Split Compounds or Split Products, after taking into account the non-Prosecuting Party's [**] in its portion of the Territory, by determining if the non-Prosecuting Party's position should be implemented under the circumstances and instructing the Prosecuting Party to take appropriate action; provided that, if [**] has not yet decided the matter and the deadline for taking an action is within [**] Business Days, the Prosecuting Party shall have the right to take action(s) necessary to preserve the Patent Rights.

(g) Third Party Rights. Agios covenants and agrees that it shall not grant any Third Party any right to control the Prosecution of the Agios Patent Rights or Agios Collaboration Patent Rights or to approve or consult with respect to any Patent Rights licensed to Celgene hereunder, in any case, that is more favorable to the Third Party than the rights granted to Celgene hereunder or that otherwise conflicts with Celgene's rights hereunder.

(h) Existing Third Party Agreements. Each Party acknowledges that, pursuant to the Existing Third Party Agreements, the applicable licensors thereunder Prosecute the Agios Patent Rights covered by such agreements; provided that Agios may have certain rights to assume Prosecution under such agreements and Agios has certain rights to Prosecute "Joint Patent Rights" under the [**] Agreement. Agios agrees to keep Celgene fully informed of these rights, as well as provide to Celgene all information and copies of documents received from the licensors under the Existing Third Party Agreements or their patent counsel relating to the Agios Patent Rights covered by such agreements. To the extent that Agios is permitted to proceed with Prosecution or provide comments or suggestions to patent documents under any Existing Third Party Agreement, then the Agios Patent Rights under such Existing Third Party Agreement shall be treated in the same manner as other Agios Patent Rights under this Section 10.2, and Agios shall exercise all such rights with respect to such Agios Patents Rights pursuant to the instructions of Celgene, if Celgene is given the right to act under this Section 10.2.

Section 10.3 Third Party Infringement. Subject to the terms and conditions of the Existing Third Party Agreements to the extent such agreement applies to the Agios Patent Rights or Agios Collaboration Patent Rights, the following provisions shall apply with respect to the Agios Patent Rights and Collaboration Patent Rights:

(a) Notice. Each Party shall immediately provide the other Party with written notice reasonably detailing any (i) known or alleged infringement of any Agios Patent Rights or Collaboration Patent Rights, or known or alleged misappropriation of any Agios Know-How or

Collaboration Know-How, by a Third Party, (ii) "patent certification" filed in the United States under 21 U.S.C. §355(b)(2) or 21 U.S.C. §355(j)(2) or similar provisions in other jurisdictions, and (iii) any declaratory judgment, opposition, or similar action alleging the invalidity, unenforceability or non-infringement of any such intellectual property rights (collectively "Third-Party Infringement").

(b) Infringement Actions.

(i) As between the Parties, except as provided in Section 10.3(b)(iv), Agios shall have the initial right, but not the obligation, to initiate a suit or take other appropriate action that it believes is reasonably required to protect the Agios Intellectual Property or Agios Collaboration Intellectual Property (excluding Joint Inventions). To the extent that any such suit or action pertains to the infringement, unauthorized use or misappropriation by a Third Party of Agios Intellectual Property or Agios Collaboration Intellectual Property that relates to a Program for which Celgene has a Celgene Program Option that has been exercised or that remains in effect and has not been waived or rejected (or a Program or Celgene Reverted Program with respect to which Celgene has taken an exclusive license under Section 8.2) ("Competitive Infringement"), Agios shall give Celgene advance notice of its intent to file any such suit or take any such action and the reasons therefor, and shall provide Celgene with an opportunity to make suggestions and comments regarding such suit or action. Thereafter, Agios shall keep Celgene promptly informed, and shall from time to time consult with Celgene regarding the status of any such suit or action and shall provide Celgene with copies of all material documents (*e.g.*, complaints, answers, counterclaims, material motions, orders of the court, memoranda of law and legal briefs, interrogatory responses, depositions, material pre-trial filings, expert reports, affidavits filed in court, transcripts of hearings and trial testimony, trial exhibits and notices of appeal) filed in, or otherwise relating to, such suit or action.

(ii) Except as provided in Section 10.3(b)(iv), Celgene shall have the sole right, but not the obligation, to initiate a suit or take other appropriate action that it believes is reasonably required to protect the Celgene Intellectual Property and Celgene Collaboration Intellectual Property (excluding Joint Inventions), without any obligation to consult with Agios. Notwithstanding Section 10.3(e), except with respect to a suit or action described in Section 10.3(b)(iv), all recoveries with respect to any such action, by settlement or otherwise, shall be retained [**] percent ([**]%) by Celgene.

(iii) Except as provided in Section 10.3(b)(iv), the Parties, acting by Mutual Consent, shall determine which Party shall have the initial right, but not the obligation, to initiate a suit or take other appropriate action that the Parties believe is reasonably required to protect the Joint Inventions. Thereafter, the Party authorized to initiate a suit or take other appropriate action shall keep the other Party promptly informed, and shall from time to time consult with the other Party regarding the status of any such suit or action and shall provide the other Party with copies of all material documents (*e.g.*, complaints, answers, counterclaims, material motions, orders of the court, memoranda of law and legal briefs, interrogatory responses, depositions, material pre-trial filings, expert reports, affidavits filed in court, transcripts of hearings and trial testimony, trial exhibits and notices of appeal) filed in, or otherwise relating to, such suit or action.

(iv) On a Program-by-Program, Celgene Reverted Program-by-Celgene Reverted Program, or Agios Reverted Program-by-Agios Reverted Program basis, as applicable, the Lead Party shall have the initial right, but not the obligation, to initiate a suit or take other appropriate action that it believes is reasonably required to protect the Agios Intellectual Property, Agios Collaboration Intellectual Property and Joint Inventions relating to such Program, Celgene Reverted Program, or Agios Reverted Program, as applicable, against Competitive Infringement or to protect the Celgene Collaboration Patent Rights exclusively licensed to Agios under Section 8.2 to the extent related to a Split Program, a Buy-In Program for which Agios is the Commercializing Party, or an Agios Reverted Program against Competitive Infringement. The Lead Party shall give the other Party advance notice of its intent to file any such suit or take any such action and the reasons therefor, and shall provide the other Party with an opportunity to make suggestions and comments regarding such suit or action. Thereafter, the Lead Party shall keep the other Party promptly informed, and shall from time to time consult with the other Party regarding the status of any such suit or action and shall provide the other Party with copies of all material documents (*e.g.*, complaints, answers, counterclaims, material motions, orders of the court, memoranda of law and legal briefs, interrogatory responses, depositions, material pre-trial filings, expert reports, affidavits filed in court, transcripts of hearings and trial testimony, trial exhibits and notices of appeal) filed in, or otherwise relating to, such suit or action. Without limiting the generality of the foregoing, in the case of a Split Program, Agios (as Lead Party in the US Territory) and Celgene (as Lead Party in the ROW Territory) shall discuss in good faith each Party's intended response to a Competitive Infringement.

(c) Step-in Rights. If Agios fails to initiate a suit or take such other appropriate action under Section 10.3(b)(i), the Party authorized to initiate a suit or take such other appropriate action under Section 10.3(b)(iii) or the Lead Party fails to initiate a suit or take such other appropriate action under Section 10.3(b)(iv) above (such Party, the "Responsible Party") within [**] days after becoming aware of the Competitive Infringement, then the other Party may, in its discretion, provide the Responsible Party with written notice of the other Party's intent to initiate a suit or take other appropriate action. If the other Party provides such notice and the Responsible Party fails to initiate a suit or take such other appropriate action within [**] days after receipt of such notice from the other Party, then the Party that is not the Responsible Party shall have the right to initiate a suit or take other appropriate action that it believes is reasonably required to protect the applicable Agios Intellectual Property, Agios Collaboration Intellectual Property, Celgene Collaboration Patent Rights (but only to the extent provided in Section 10.3(b)(iv)) and Joint Inventions related to the applicable Program, Celgene Reverted Program, or Agios Reverted Program, as applicable. The Party that is not the Responsible Party shall give the Responsible Party advance notice of its intent to file any such suit or take any such action and the reasons therefor and shall provide the Responsible Party with an opportunity to make suggestions and comments regarding such suit or action. Thereafter, the Party that is not the Responsible Party shall keep the Responsible Party promptly informed and shall from time to time consult with the Responsible Party regarding the status of any such suit or action and shall provide the Responsible Party with copies of all material documents (*e.g.*, complaints, answers, counterclaims, material motions, orders of the court, memoranda of law and legal briefs, interrogatory responses, depositions, material pre-trial filings, expert reports, affidavits filed in court, transcripts of hearings and trial testimony, trial exhibits and notices of appeal) filed in, or otherwise relating to, such suit or action.

(d) Conduct of Action; Costs. The Party initiating suit shall have the sole and exclusive right to select counsel for any suit initiated by it under this Section 10.3, which counsel must be reasonably acceptable to the other Party. If required under applicable Law in order for such Party to initiate and/or maintain such suit, the other Party shall join as a party to the suit. If requested by the Party initiating suit, the other Party shall provide reasonable assistance to the Party initiating suit in connection therewith at no charge to such Party except that the initiating Party shall reimburse the other Party for Out-of-Pocket Costs incurred in rendering such assistance. The Party initiating suit shall assume and pay all of its own Out-of-Pocket Costs incurred in connection with any litigation or proceedings described in this Section 10.3, including the fees and expenses of the counsel selected by it. The other Party shall have the right to participate and be represented in any such suit by its own counsel at its own expense.

(e) Recoveries. To the extent that any such suit or action pertains to Licensed Compounds or Licensed Products, Celgene Reverted Compounds or Celgene Reverted Products, or Agios Reverted Compounds or Agios Reverted Products (but only, with respect to Agios Reverted Compounds or Agios Reverted Products, to the extent such suit or action pertains to Celgene Collaboration Patent Rights exclusively licensed to Agios as described in Section 10.3(b)(iv)), any recovery obtained as a result of any proceeding described in this Section 10.3 or from any counterclaim or similar claim asserted in a proceeding described in Section 10.4, by settlement or otherwise, shall be applied in the following order of priority:

(i) first, the Party initiating the suit or action shall be reimbursed for all Out-of-Pocket Costs in connection with such proceeding; and

(ii) second, any remainder shall be paid [**] percent ([**]%) to the Party initiating the suit or action, and [**] percent ([**]%) to the other Party.

(f) Existing Third Party Agreements. In the event that (i) a Patent Right covered by one of the Existing Third Party Agreements is at issue in an action under this Section 10.3 or Section 10.4, (ii) Agios has a right to enforce the Agios Patent Rights under such Existing Third Party Agreement, and (iii) Celgene desires to enforce such Patent in accordance with the procedures under this Section 10.3 or Section 10.4, as applicable, then Agios shall either obtain the licensor's consent under the Existing Third Party Agreement so that Celgene may file such an action in its own name or shall undertake such an action on Celgene's behalf.

Section 10.4 Claimed Infringement; Claimed Invalidity.

(a) Infringement of Third Party Rights. Each Party shall promptly notify the other Party in writing of any allegation by a Third Party that the activity of either Party or their Affiliates or Licensee Partners under this Agreement infringes or may infringe the intellectual property rights of such Third Party. Unless otherwise agreed by the Parties, the Lead Party shall have the first right, at its expense, to control the defense of any claim alleging that the Development, Manufacture or Commercialization of any Licensed Product or Licensed Compound in the Territory infringes any such Third Party rights. If the Lead Party fails to proceed in a timely manner with respect to such defense, the other Party shall have the right to control the defense of any such claim. Irrespective of which Party defends the claim, the Parties shall mutually agree on the choice of counsel and shall collaborate on strategic decisions and

their implementation with respect to such activities. Each Party shall have the right to participate in the defense of any such claim with counsel of its own choice at its own expense. Neither Party shall have the right to settle any claim or litigation described in this Section 10.4 without the other Party's prior written consent, which consent shall not be unreasonably withheld or delayed.

(b) Patent Invalidity Claim. If a Third Party at any time asserts a claim that any Agios Patent Right or Agios Collaboration Patent Right (including Joint Patents) is invalid or otherwise unenforceable (an "Invalidity Claim"), whether as a defense in an infringement action brought by Agios or Celgene pursuant to Section 10.3, in a declaratory judgment action or in a Third-Party Infringement claim brought against Agios or Celgene, the Parties shall cooperate with each other in preparing and formulating a response to such Invalidity Claim; provided that, subject to the terms and conditions of the Existing Third Party Agreements to the extent any such agreement applies to such Agios Patent Right or Agios Collaboration Patent Right, the Lead Party shall have the sole right to control the defense and settlement of any such Invalidity Claim primarily involving any Agios Patent Right or Agios Collaboration Patent Right (including Joint Patents), in either case, relating to the Program for which such Party is the Lead Party, and Agios shall have the sole right to control the defense and settlement of any such Invalidity Claim primarily involving any other Agios Patent Right or Agios Collaboration Patent Rights; provided further that the Lead Party shall not settle or compromise any Invalidity Claim without the consent of the other Party.

Section 10.5 Patent Term Extensions. The Parties shall, as necessary and appropriate, use reasonable efforts to agree upon a joint strategy for obtaining, and cooperate with each other in obtaining, patent term extensions for Agios Patent Rights and Agios Collaboration Patent Rights, or at Celgene's election Celgene Patent Rights and Celgene Collaboration Patent Rights, that Cover Licensed Products; provided that, if elections with respect to obtaining such patent term extensions are to be made, Celgene shall have the right to make the election to seek patent term extension, subject to the terms and conditions of the Existing Third Party Agreements to the extent any such agreement applies to such Agios Patent Right or Agios Collaboration Patent Right (except that with respect to a Split Program, Agios shall have the right to make such election in the US Territory). The Parties shall also, as necessary and appropriate, use reasonable efforts to agree upon a joint strategy for obtaining, and cooperate with each other in obtaining, Regulatory Exclusivity regarding any product that the Parties propose to Commercialize as part of the Collaboration under this Agreement.

Section 10.6 Patent Marking. Each Party shall comply with the patent marking statutes in each country in which the Licensed Product is Manufactured or Commercialized by or on behalf of a Party or their respective Affiliates or sublicensees, as applicable, hereunder.

Section 10.7 CREATE Act Application. It is agreed and acknowledged that this Agreement establishes a qualifying collaboration within the scope of the U.S. CREATE Act and, accordingly, shall be deemed to constitute a "Joint Research Agreement" for all purposes under the CREATE Act. Neither Party shall invoke the provisions of the CREATE Act, or file this Agreement, in connection with the prosecution of any patent application claiming, in whole or in part, any CREATE Act invention without the prior written consent of the other Party. In the event that a Party, during the course of prosecuting a patent application claiming a CREATE Act

invention (a "CREATE Act Patent"), deems it necessary to file a terminal disclaimer to overcome an obviousness type double patenting rejection in view of an earlier filed patent held by the other Party (the "Earlier Patent"), then, if the Parties agree, the Parties shall coordinate the filing of such terminal disclaimer in good faith, and, to the extent required under the CREATE Act, both Parties shall agree, in such terminal disclaimer, that they shall not separately enforce the CREATE Act Patent independently from the Earlier Patent. To this end, to the extent required under the CREATE Act, following the filing of such terminal disclaimer, the Parties shall, in good faith, coordinate all enforcement actions with respect to the CREATE Act Patent.

Section 10.8 Challenges to Patent Rights.

(a) Without limiting Celgene's obligations pursuant to Section 8.7(b), if Celgene or any of its Affiliates or any of its sublicensees under the licenses granted to Celgene in this Agreement (i) initiates or requests an interference or opposition proceeding with respect to any Agios Patent Right or Agios Collaboration Patent Right that is directed to a Collaboration Target, Licensed Compound or Licensed Product, (ii) makes, files or maintains any claim, demand, lawsuit, or cause of action to challenge the validity or enforceability of any Agios Patent Right or Agios Collaboration Patent Right that is directed to a Collaboration Target, Licensed Compound or Licensed Product, or (iii) funds or otherwise provides material assistance to any other Person with respect to any of the foregoing (any of the actions described in the foregoing clauses (i), (ii) and (iii), a "Challenge"), and if the outcome of such Challenge is that any claim of an Agios Patent Right or Agios Collaboration Patent Right that Covers a Collaboration Target, Licensed Compound or Licensed Products and that is subject to such Challenge remains valid and enforceable, then (A) Celgene shall [**] Agios in connection with such Challenge, and (B) all royalty amounts payable by Celgene to Agios hereunder with respect to any Licensed Product Covered by any such remaining valid and enforceable claim of a Challenged Agios Patent Right or Agios Collaboration Patent Rights shall [**] of the otherwise applicable royalty amounts payable hereunder.

(b) Without limiting Celgene's obligations pursuant to Section 10.8(a), Celgene shall not, and shall ensure that its Affiliates and its sublicensees under the licenses granted to Celgene in this Agreement do not, use or disclose any Confidential Information of Agios or any nonpublic information regarding the filing, prosecution, maintenance or enforcement of any Agios Patent Rights or Agios Collaboration Patent Rights to which Celgene or any of its Affiliates or sublicensees are or become privy as a consequence of the rights granted to Celgene pursuant to this Article X, in initiating, requesting, making, filing or maintaining, or in funding or otherwise assisting any other Person with respect to, any Challenge.

(c) The provisions of Sections 10.8(a) and 10.8(b) shall apply with respect to Celgene Collaboration Patent Rights exclusively licensed to Agios pursuant to Section 8.2, in each case, substituting "Celgene" for "Agios" and vice versa with respect to all obligations and definitions, and otherwise *mutatis mutandis*.

## Article XI
## Confidentiality

Section 11.1 Confidential Information. All Confidential Information of a Party ("Disclosing Party") shall not be used by the other Party (the "Receiving Party") except in performing its obligations or exercising rights explicitly granted under this Agreement and shall be maintained in confidence by the Receiving Party and shall not otherwise be disclosed by the Receiving Party to any Third Party, without the prior written consent of the Disclosing Party with respect to such Confidential Information, except to the extent that the Confidential Information:

(a) was known by the Receiving Party or its Affiliates prior to its date of disclosure to the Receiving Party; or

(b) is lawfully disclosed to the Receiving Party or its Affiliates by sources other than the Disclosing Party rightfully in possession of the Confidential Information; or

(c) becomes published or generally known to the public through no fault or omission on the part of the Receiving Party, its Affiliates or its sublicensees; or

(d) is independently developed by or for the Receiving Party or its Affiliates without reference to or reliance upon such Confidential Information, as established by written records.

Section 11.2 Permitted Disclosure. The Receiving Party may provide the Disclosing Party's Confidential Information:

(a) to the Receiving Party's respective employees, consultants and advisors, and to the employees, consultants and advisors of such Party's Affiliates, who have a need to know such information and materials for performing obligations or exercising rights expressly granted under this Agreement and have an obligation to treat such information and materials as confidential;

(b) to patent offices in order to seek or obtain Patent Rights or to Regulatory Authorities in order to seek or obtain approval to conduct Clinical Trials or to gain Regulatory Approval with respect to Agreement Compounds as contemplated by this Agreement; provided that such disclosure may be made only following reasonable notice to the Disclosing Party and to the extent reasonably necessary to seek or obtain such Patent Rights or approvals; or

(c) if such disclosure is required by judicial order or applicable Law or to defend or prosecute litigation or arbitration; provided that, prior to such disclosure, to the extent permitted by Law, the Receiving Party promptly notifies the Disclosing Party of such requirement, cooperates with the Disclosing Party to take whatever action it may deem appropriate to protect the confidentiality of the information and furnishes only that portion of the Disclosing Party's Confidential Information that the Receiving Party is legally required to furnish.

Section 11.3 Publicity; Terms of this Agreement; Non-Use of Names.

(a) Except as required by judicial order or applicable Law (in which case, Section 11.3(b) must be complied with) or as explicitly permitted by this Article XI, neither Party shall make any public announcement concerning this Agreement without the prior written consent of the other Party, which consent shall not be unreasonably withheld or delayed. The Party preparing any such public announcement shall provide the other Party with a draft thereof at least [**] Business Days prior to the date on which such Party would like to make the public announcement (or, in extraordinary circumstances, such shorter period as required to comply with applicable Law). Notwithstanding the foregoing, the Parties shall issue a press release, in the form attached as Schedule 11.3, within [**] after the Effective Date. Neither Party shall use the name, trademark, trade name or logo of the other Party or its employees in any publicity or news release relating to this Agreement or its subject matter, without the prior express written permission of the other Party. For purposes of clarity, either Party may issue a press release or public announcement or make such other disclosure relating to this Agreement if the contents of such press release, public announcement or disclosure (x) (i) does not consist of financial information and has previously been made public other than through a breach of this Agreement by the issuing Party or its Affiliates, (ii) is contained in such Party's financial statements prepared in accordance with Accounting Standards, or (iii) is contained in the Redacted Version of this Agreement, and (y) is material to the event or purpose for which the new press release or public announcement is made.

(b) Notwithstanding the terms of this Article XI:

(i) Either Party shall be permitted to disclose the existence and terms of this Agreement to the extent required, in the reasonable opinion of such Party's legal counsel, to comply with applicable Laws, including the rules and regulations promulgated by the Securities and Exchange Commission or any other governmental authority. Notwithstanding the foregoing, before disclosing this Agreement or any of the terms hereof pursuant to this Section 11.3(b), the Parties will coordinate in advance with each other in connection with the redaction of certain provisions of this Agreement with respect to any filings with the Securities and Exchange Commission, London Stock Exchange, the UK Listing Authority, NYSE, the NASDAQ Stock Market or any other stock exchange on which securities issued by a Party or a Party's Affiliate are traded (the "Redacted Version"), and each Party will use commercially reasonable efforts to seek confidential treatment for such terms as may be reasonably requested by the other Party; provided that the Parties will use commercially reasonable efforts to file redacted versions with any governing bodies which are consistent with the Redacted Version.

(ii) Either Party may disclose the existence and terms of this Agreement in confidence:

(A) to (1) its attorneys, professional accountants, and auditors, and (2) bankers or other financial advisors in connection with an initial public offering, other strategic transaction, or corporate valuation for internal purposes; provided that any such disclosure to such professional accountants, auditors, bankers or other financial advisors is under an agreement to keep the terms of confidentiality and non-use no less rigorous than the terms contained in this Agreement and to use such information solely for the applicable purpose permitted pursuant to this Section 11.3(b)(ii)(A);

(B) to each licensor under an Existing Third Party Agreement; provided that such disclosure is under the confidentiality and non-use provisions of such agreement;

(C) to potential acquirers (and their respective attorneys and professional advisors), in connection with a potential merger, acquisition or reorganization; provided that (1) the Party making the disclosure has a bona fide offer from such Third Party for such a transaction, and (2) such disclosure is under an agreement to keep the terms of confidentiality and non-use no less rigorous than the terms contained in this Agreement and to use such information solely for the purpose permitted pursuant to this Section 11.3(b)(ii)(C);

(D) to existing investors, lenders or permitted assignees of such Party (and their respective attorneys and professional advisors); provided that such disclosure is under an agreement to keep the terms of confidentiality and non-use no less rigorous than the terms contained in this Agreement; and

(E) to potential investors, lenders or permitted assignees of such Party, or to potential licensees or sublicensees of such Party (and their respective attorneys and professional advisors); provided that (1) such disclosure shall not be made prior to [**] Business Days prior to the good faith anticipated closing date for the investment, loan, assignment or license, as applicable, and shall be made only if such Party reasonably concludes that such transaction with such disclosee is likely to be consummated; (2) if the disclosee is a Major Pharmaceutical Company or any of its Affiliates, the disclosure shall be limited to the Redacted Version plus such additional terms and conditions reasonably requested by the disclosing Party and consented to by the other Party (for purposes of clarity, the disclosing Party shall not be obligated to disclose the identity of the disclosee in order to request such consent); and (3) such disclosure is under an agreement to keep the terms of confidentiality and non-use no less rigorous than the terms contained in this Agreement. For purposes of this subsection, the term "Major Pharmaceutical Company" means, at a given time, one of the top [**] pharmaceutical companies based on sales of ethical pharmaceuticals for the prior fiscal year as published by Pharmaceutical Executive at the following URL or any subsequent URL: http://pharmexec.findpharma.com/pharmexec/data/articlestandard//pharmexec/352009/621548/article.pdf or, in the event that Pharmaceutical Executive no longer publishes such a list, by a comparable publisher.

(iii) Either Party may issue a press release or make a public disclosure to the extent that such press release or disclosure describes:

(A) clinical or regulatory achievements relating to, in the case of press releases or disclosures by Agios, Agios Reverted Products, Split Products (to the extent relating to the US Territory) and Buy-In Products for which Agios is the Commercializing Party, and, in the case of press releases or disclosures by Celgene, Celgene Reverted Products, Split Products (to the extent relating to the ROW Territory) and any other Licensed Products for which Celgene is the Commercializing Party;

(B) the exercise by Celgene of the Celgene Program Option for any Program, without the disclosure of any financial information without the other Party's prior written consent;

(C) Publications approved in accordance with the provisions of Section 11.4; and

(D) receipt of milestone payments (but not the amount of such payments, except any amount associated with the achievement of any milestone related to a Phase III Study or Regulatory Approval) under Section 9.6, including a brief description of the Development milestone giving rise to such payments;

provided that the Party issuing such a press release or making such a public disclosure shall not refer to the other Party without the other Party's prior written consent; provided further that the Party issuing such a press release or making such a public disclosure shall provide the other Party with a draft thereof at least [**] Business Days prior to the date on which such issuing Party would like to issue such press release or make the public announcement, and such issuing Party shall consider in good faith any comments or concerns of the other Party with respect to such press release or public disclosure. In addition to the foregoing, the Parties shall discuss in good faith the public disclosure of the commencement or "top line" results of Clinical Trials of Licensed Products.

Section 11.4 Publications. The Parties agree that decisions regarding the timing and content of Publications shall be subject to the oversight and approval by Mutual Consent of the JSC and neither Party nor its Affiliates shall have the right to make Publications pertaining to Agreement Compounds (other than Agios Reverted Compounds) or Targets except as provided herein. If a Party or its Affiliates desire to make a Publication, such Party must comply with the following procedure:

(a) The publishing Party shall provide the JSC and the non-publishing Party with an advance copy of the proposed Publication, and the JSC, by Mutual Consent, shall then have [**] days prior to submission for any Publication ([**] days in the case of an abstract or oral presentation) in which to determine whether the Publication meets the Publication Guidelines and may be published and under what conditions, including (i) delaying sufficiently long to permit the timely preparation and filing of a patent application or (ii) specifying changes the JSC reasonably believes are necessary to preserve any Patent Rights or Know-How belonging (whether through ownership or license, including under this Agreement) in whole or in part to the non-publishing Party.

(b) In addition, if the non-publishing Party informs the publishing Party that such Publication, in the non-publishing Party's reasonable judgment, discloses any Confidential Information of the non-publishing Party or could be expected to have a material adverse effect on any Know-How which is Confidential Information of the non-publishing Party, such Confidential Information or Know-How shall be deleted from the Publication.

(c) Each Party shall have the right to present its Publications approved pursuant to this Section 11.4 at scientific conferences, including at any conferences in any country in the world, subject to any conditions imposed by the JSC in its approval.

(d) Notwithstanding the foregoing, the Parties acknowledge that, to the extent that any Publication relates to Agios Intellectual Property that is subject to the Existing Third Party Agreements, the parties to such Existing Third Party Agreements may have retained the right to publish certain information, and nothing in this Section 11.4 is intended to restrict the exercise of such rights; provided that, to the extent that Agios has the right to review and comment on any such publications, Agios shall, to the extent permissible under such Existing Third Party Agreements, exercise such rights after consultation with Celgene.

(e) For purposes of convenience, the JSC may by Mutual Consent delegate its responsibilities under this Section 11.4 to one or more representatives of Agios and Celgene.

Section 11.5 Term. All obligations under this Article XI shall expire [**] years following termination or expiration of this Agreement.

Section 11.6 Return of Confidential Information.

(a) Upon the expiration or termination of this Agreement, the Receiving Party shall return to the Disclosing Party all Confidential Information received by the Receiving Party from the Disclosing Party (and all copies and reproductions thereof). In addition, the Receiving Party shall destroy:

(i) any notes, reports or other documents prepared by the Receiving Party which contain Confidential Information of the Disclosing Party; and

(ii) any Confidential Information of the Disclosing Party (and all copies and reproductions thereof) which is in electronic form or cannot otherwise be returned to the Disclosing Party.

(b) Alternatively, upon written request of the Disclosing Party, the Receiving Party shall destroy all Confidential Information received by the Receiving Party from the Disclosing Party (and all copies and reproductions thereof) and any notes, reports or other documents prepared by the Receiving Party which contain Confidential Information of the Disclosing Party. Any requested destruction of Confidential Information shall be certified in writing to the Disclosing Party by an authorized officer of the Receiving Party supervising such destruction.

(c) Nothing in this Section 11.6 shall require the alteration, modification, deletion or destruction of archival tapes or other electronic back-up media made in the ordinary course of business; provided that the Receiving Party shall continue to be bound by its obligations of confidentiality and other obligations under this Article XI with respect to any Confidential Information contained in such archival tapes or other electronic back-up media.

(d) Notwithstanding the foregoing,

(i) the Receiving Party's legal counsel may retain one copy of the Disclosing Party's Confidential Information solely for the purpose of determining the Receiving Party's continuing obligations under this Article XI; and

(ii) the Receiving Party may retain the Disclosing Party's Confidential Information and its own notes, reports and other documents;

(A) to the extent reasonably required (1) to exercise the rights and licenses of the Receiving Party expressly surviving expiration or termination of this Agreement; or (2) to perform the obligations of the Receiving Party expressly surviving expiration or termination of this Agreement; or

(B) to the extent it is impracticable to do so without incurring disproportionate cost.

Notwithstanding the return or destruction of the Disclosing Party's Confidential Information, the Receiving Party shall continue to be bound by its obligations of confidentiality and other obligations under this Article XI.

## Article XII
## Representations and Warranties

Section 12.1 Mutual Representations. Agios and Celgene each represents, warrants and covenants to the other Party, as of the Effective Date, that:

(a) Authority. It has full corporate right, power and authority to enter into this Agreement and to perform its obligations under this Agreement.

(b) Consents. All necessary consents, approvals and authorizations of all government authorities and other Persons required to be obtained by it as of the Effective Date in connection with the execution, delivery and performance of this Agreement have been or shall be obtained by the Effective Date.

(c) No Conflict. Notwithstanding anything to the contrary in this Agreement, the execution and delivery of this Agreement, the performance of such Party's obligations in the conduct of the Collaboration and the licenses and sublicenses to be granted pursuant to this Agreement (i) do not and will not conflict with or violate any requirement of applicable Laws existing as of the Effective Date and (ii) do not and will not conflict with, violate, breach or constitute a default under any contractual obligations of such Party or any of its Affiliates existing as of the Effective Date.

(d) Enforceability. This Agreement is a legal and valid obligation binding upon it and is enforceable in accordance with its terms.

(e) Employee Obligations. To its knowledge, none of its or its Affiliates' employees who have been, are or will be involved in the Collaboration are, as a result of the nature of such Collaboration to be conducted by the Parties, in violation of any covenant in any contract with a Third Party relating to non-disclosure of proprietary information, non-competition or non-solicitation.

Section 12.2 Additional Agios Representations. Agios represents, warrants and covenants to Celgene, as of the Effective Date, as follows:

(a) Agios possesses sufficient rights to enable Agios to grant all rights and licenses it purports to grant to Celgene with respect to the Agios Intellectual Property under this Agreement.

(b) Agios has not used, and during the Term will not knowingly use, any Know-How in a Discovery Program or Independent Program conducted by Agios that is encumbered by any contractual right of or obligation to a Third Party that conflicts or interferes with any of the rights or licenses granted or to be granted to Celgene hereunder.

(c) The Agios Patent Rights existing as of the Effective Date constitute all of the Patent Rights Controlled by Agios as of such date that are necessary or useful for the Development, Manufacture or Commercialization of Collaboration Compounds, Licensed Compounds and Licensed Product.

(d) Agios has not granted, and during the Term Agios will not grant, any right or license, to any Third Party relating to any of the intellectual property rights it Controls, that conflicts with the rights or licenses granted or to be granted to Celgene hereunder.

(e) There is no pending litigation, and Agios has not received any written notice of any claims or litigation, seeking to invalidate or otherwise challenge the Agios Patent Rights or Agios' rights therein.

(f) There is no pending litigation, and Agios has not received any written notice of any claims or litigation, that alleges that Agios' activities with respect to Collaboration Targets have infringed or misappropriated any intellectual property rights of any Third Party.

(g) [**] practice of the Agios Intellectual Property as contemplated under this Agreement does not (i) infringe any claims of any Patent Rights of any Third Party, or (ii) misappropriate any Know-How of any Third Party.

(h) None of (i) the Agios Patent Rights owned by Agios or both Controlled by and Prosecuted by Agios and (ii) [**], the Agios Patent Rights Controlled but not Prosecuted by Agios are subject to any pending re-examination, opposition, interference or litigation proceedings.

(i) All of (i) the Agios Patent Rights owned by Agios or both Controlled by and Prosecuted by Agios and (ii) [**], the Agios Patent Rights Controlled but not Prosecuted by Agios have been filed and diligently Prosecuted in accordance with all applicable Laws in the Territory and have been maintained, with all applicable fees with respect thereto having been paid.

(j) True and correct copies of the Existing Third Party Agreements have been provided to Celgene, and such agreements are in full force and effect and have not been modified or amended. Neither Agios nor, [**], any licensor under the Existing Third Party Agreements is in default with respect to a material obligation under, and none of such parties has claimed or has grounds upon which to claim that the other party is in default with respect to a material obligation under, the Existing Third Party Agreements.

(k) [**] Agios Patent Rights Controlled by Agios pursuant to the Existing Third Party Agreements were not and are not subject to any restrictions or limitations except as set forth in the Existing Third Party Agreements.

(l) Agios has not waived or allowed to lapse any of its rights under any Existing Third Party Agreement with respect to Collaboration Targets, Collaboration Compounds or Licensed Products, and no such rights have lapsed or otherwise expired or been terminated.

(m) Agios has and, [**] the applicable licensor under each Existing Third Party Agreement has complied with any and all obligations under [**] to perfect rights to the applicable Patent Rights or Know-How licensed thereunder.

(n) Agios has not employed and, to its knowledge, has not used a contractor or consultant that has employed, any individual or entity (i) debarred by the FDA (or subject to a similar sanction of another applicable Regulatory Authority), (ii) who is the subject of an FDA debarment investigation or proceeding (or similar proceeding of another applicable Regulatory Authority), or (iii) has been charged with or convicted under United States Law for conduct relating to the development or approval, or otherwise relating to the regulation of any Licensed Product under the Generic Drug Enforcement Act of 1992, in each case, in the conduct of its activities prior to the Effective Date.

Section 12.3 Additional Celgene Representations. Celgene represents, warrants and covenants to Agios, as of the Effective Date, that, [**] based on Celgene's understanding of the mechanism of action of any therapeutic modality (including any small molecule or biologic) in Celgene's current programs, Celgene has [**] directed to the Development, Manufacture or Commercialization of [**] to a Collaboration Target on the Target List as of the Effective Date, which program is Celgene's program directed to [**].

Section 12.4 Employee Obligations. Agios and Celgene each covenants to the other Party that all of its and its Affiliates' employees, officers, consultants and advisors who have been, are or will be involved in the Collaboration have executed (or, prior to becoming involved in the Collaboration, will have executed agreements) or have existing obligations under Law requiring assignment to such Party of all intellectual property made during the course of and as the result of their association with such Party, and obligating the individual to maintain as confidential such Party's Confidential Information, to the extent required to support such Party's obligations under this Agreement.

Section 12.5 No Warranties. EXCEPT AS OTHERWISE EXPRESSLY SET FORTH HEREIN, THE PARTIES MAKE NO REPRESENTATIONS AND EXTEND NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING ANY REPRESENTATIONS OR WARRANTIES AS TO MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE OR NONINFRINGEMENT.

## Article XIII
## Indemnification

Section 13.1 By Celgene.

(a) Celgene agrees, at Celgene's cost and expense, to defend, indemnify and hold harmless Agios and its Affiliates and their respective directors, officers, employees and agents (the "Agios Indemnified Parties") from and against any losses, costs, damages, fees or expenses arising out of any Third Party claim relating to:

(i) any breach by Celgene of any of its representations, warranties or obligations pursuant to this Agreement;

(ii) the gross negligence or willful misconduct of Celgene;

(iii) the Development, Manufacture, Commercialization, use, sale or other disposition by Celgene, its Affiliates, licensees or sublicensees of any Collaboration Compound, Licensed Compound, Licensed Product, Celgene Reverted Compound or Celgene Reverted Product; and

(iv) the conduct by Celgene, its Affiliates or sublicensees of any Independent Program.

(b) In the event of any such claim against the Agios Indemnified Parties by any Third Party, Agios shall promptly, and in any event within [**] Business Days, notify Celgene in writing of the claim. Celgene shall have the right, exercisable by notice to Agios within [**] Business Days after receipt of notice from Agios of the claim, to assume direction and control of the defense, litigation, settlement, appeal or other disposition of the claim (including the right to settle the claim solely for monetary consideration) with counsel selected by Celgene and reasonably acceptable to Agios; provided that the failure to provide timely notice of a claim by a Third Party shall not limit an Agios Indemnified Party's right for indemnification hereunder except to the extent such failure results in actual prejudice to Celgene. The Agios Indemnified Parties shall cooperate with Celgene and may, at their option and expense, be separately represented in any such action or proceeding. Celgene shall not be liable for any litigation costs or expenses incurred by the Agios Indemnified Parties without Celgene's prior written authorization. In addition, Celgene shall not be responsible for the indemnification or defense of any Agios Indemnified Party to the extent arising from any negligent or intentional acts by any Agios Indemnified Party or the breach by Agios of any representation, obligation or warranty under this Agreement, or any claims compromised or settled without its prior written consent.

Section 13.2 By Agios.

(a) Agios agrees, at Agios' cost and expense, to defend, indemnify and hold harmless Celgene and its Affiliates and their respective directors, officers, employees and agents (the "Celgene Indemnified Parties") from and against any losses, costs, damages, fees or expenses arising out of any Third Party claim relating to:

(i) any breach by Agios of any of its representations, warranties or obligations pursuant to this Agreement;

(ii) the gross negligence or willful misconduct of Agios;

(iii) the Development, Manufacture, Commercialization, use, sale or other disposition by Agios, its Affiliates, licensees (other than Celgene) or sublicensees of any Collaboration Compound, Licensed Compound, Licensed Product, Agios Reverted Compound or Agios Reverted Product; and

(iv) the conduct by Agios, its Affiliates or sublicensees of any Independent Program.

(b) In the event of any such claim against the Celgene Indemnified Parties by any Third Party, Celgene shall promptly, and in any event within [**] Business Days, notify Agios in writing of the claim. Agios shall have the right, exercisable by notice to Celgene within [**] Business Days after receipt of notice from Celgene of the claim, to assume direction and control of the defense, litigation, settlement, appeal or other disposition of the claim (including the right to settle the claim solely for monetary consideration) with counsel selected by Agios and reasonably acceptable to Celgene; provided that the failure to provide timely notice of a claim by a Third Party shall not limit a Celgene Indemnified Party's right for indemnification hereunder except to the extent such failure results in actual prejudice to Agios. The Celgene Indemnified Parties shall cooperate with Agios and may, at their option and expense, be separately represented in any such action or proceeding. Agios shall not be liable for any litigation costs or expenses incurred by the Celgene Indemnified Parties without Agios' prior written authorization. In addition, Agios shall not be responsible for the indemnification or defense of any Celgene Indemnified Party to the extent arising from any negligent or intentional acts by any Celgene Indemnified Party or the breach by Celgene of any representation, obligation or warranty under this Agreement, or any claims compromised or settled without its prior written consent.

Section 13.3 Of [**].

(a) Celgene shall indemnify, defend and hold harmless [**] and its Affiliates and their respective trustees, directors, officers, medical and professional staff, employees, and agents and their respective successors, heirs and assigns (the "[**] Indemnitees"), against any liability, damage, loss or expense (including reasonable attorneys' fees and expenses of litigation) incurred by or imposed upon the [**] Indemnitees or any one of them in connection with any claims, suits, actions, demands or judgments arising out of any theory of liability, including any theory of product liability (including actions in the form of contract, tort, warranty, or strict liability) concerning any product, process or service made, used or sold pursuant to any right or license to the extent sublicensed to Celgene under the [**] Agreement.

(b) Celgene agrees, at its own expense, to provide attorneys reasonably acceptable to [**] to defend against any actions brought or filed against any [**] Indemnitees with respect to the subject of indemnity contained herein, whether or not such actions are rightfully brought; provided, however, that any [**] Indemnitee shall have the right to retain its own counsel, at the expense of Celgene, if representation of such [**] Indemnitee by counsel retained by Celgene would be inappropriate because of actual or potential conflicts of interest of such [**] Indemnitees and any other party represented by such counsel. Celgene agrees to keep [**] informed of the progress in the defense and disposition of such claim and to consult [**] prior to any proposed settlement.

(c) Notwithstanding Celgene's indemnification obligations for the [**] Indemnitees pursuant to Sections 13.3(a) and 13.3(b) above, which indemnification the Parties acknowledge is required pursuant to Section 8.1 of the [**] Agreement, as between Agios and Celgene, the obligation to indemnify the [**] Indemnitees will be allocated between Agios and Celgene in accordance with Sections 13.1 and 13.2.

Section 13.4 Joint Defendants. If a product liability suit is brought against either Party relating in any way to a Collaboration Compound, Licensed Product or Licensed Compound, and it is not clear from the allegations in the complaint or the known facts surrounding the allegations in the complaint as to whether a claim exists for which there is a right of indemnification pursuant to Section 13.1 or 13.2 above, then Celgene shall be responsible for controlling the defense of such suit in the first instance. During such period that Celgene is controlling such defense, with regard to the costs of such defense, including attorneys' fees, Celgene and Agios each shall be responsible for 50% of all such costs. No settlement, consent judgment or other voluntary final disposition of any such suit may be entered into without the prior written consent of Agios, which consent shall not be unreasonably withheld or delayed. If, at any time in the course of such suit, it becomes apparent from discovery or otherwise that a claim exists for which indemnification may be obtained in accordance with Section 13.1 or 13.2, then the indemnification provisions of either Section 13.1 or 13.2, whichever is applicable, shall become applicable and govern further proceedings in the suit, and the Party determined to be responsible shall reimburse the other Party for all prior costs incurred by such other Party for which indemnification should have been obtained in accordance with Section 13.1 or 13.2.

Section 13.5 Limitation of Liability. EXCEPT WITH RESPECT TO A BREACH OF SECTION 8.8 OR ARTICLE XI, OR A PARTY'S LIABILITY PURSUANT TO SECTION 13.1, 13.2, OR 13.3, NEITHER PARTY SHALL BE LIABLE FOR SPECIAL, CONSEQUENTIAL, EXEMPLARY, PUNITIVE, MULTIPLE OR OTHER INDIRECT OR REMOTE DAMAGES, OR FOR LOSS OF PROFITS, LOSS OF DATA OR LOSS OF USE DAMAGES ARISING IN ANY WAY OUT OF THIS AGREEMENT OR THE EXERCISE OF ITS RIGHTS HEREUNDER, WHETHER BASED UPON WARRANTY, CONTRACT, TORT, STRICT LIABILITY OR OTHERWISE, EVEN IF SUCH PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES OR LOSS.

Section 13.6 Insurance. Agios, beginning on [**], and Celgene, beginning upon [**], and, both Parties, thereafter during the Term, shall maintain commercial general liability insurance (including product liability insurance) from a recognized, creditworthy insurance company, with coverage limits of at least $[**] per claim and annual aggregate. Celgene may

elect to self-insure all or parts of the limits described above. Within [**] days following written request from the other Party, each Party shall furnish to the other Party a certificate of insurance evidencing such coverage. If such coverage is modified or cancelled, the insured Party shall notify the other Party and promptly provide such other Party with a new certificate of insurance evidencing that such insured Party's coverage meets the requirements of this Section 13.6.

## Article XIV
## Term and Termination

Section 14.1 Term.

(a) The term of this Agreement (the "Term") shall commence on the Effective Date and shall continue, unless earlier terminated pursuant to Section 14.2, until the following:

(i) expiration of this Agreement in its entirety, which shall occur following the First Commercial Sale of any Royalty-Bearing Product on the expiration of the last-to-expire of all Royalty Terms with respect to all Royalty-Bearing Products;

(ii) expiration of this Agreement on a Royalty-Bearing Product-by-Royalty-Bearing Product and country-by-country basis, which shall occur following the First Commercial Sale of any Royalty-Bearing Product in any country on the expiration of the Royalty Term with respect to such Royalty-Bearing Product in such country; or

(iii) expiration of this Agreement in its entirety, which shall occur upon the expiration of the Option Term (or, if applicable, with respect to any Extended Program, following any Post-Option Extension) if Celgene fails to exercise its Celgene Program Option with respect to at least one nominated Development Candidate, does not select any Picks pursuant to Section 3.7 (or, as applicable, Section 3.3(b)(iii), Section 3.6(c) or Section 15.5), and there are no existing Independent Programs or Celgene Reverted Programs.

(b) Upon the expiration of the Term in accordance with Section 14.1(a)(i) or (ii) above with respect to a Royalty-Bearing Product in a country, all licenses granted by one Party to the other Party under this Agreement for such Royalty-Bearing Product in such country shall become fully paid-up, perpetual, sublicensable, irrevocable, royalty-free licenses.

Section 14.2 Termination.

(a) Termination for Convenience. Celgene shall have the right to terminate this Agreement, in its entirety or on a Program-by-Program basis, for convenience upon ninety (90) days' prior written notice to Agios; provided that Celgene shall not have the right to terminate this Agreement or any Program until six (6) months following the Effective Date; provided further that, if Celgene terminates this Agreement under this Section 14.2(a) with respect to any Independent Program conducted by Agios, such Independent Program shall be deemed an Agios Reverted Program and the rights and obligations under Section 3.12 associated with an Agios Reverted Program shall apply.

(b) Termination for Material Breach or Insolvency.

(i) If either Party (the "Non-Breaching Party") believes that the other Party (the "Breaching Party") is in material breach of this Agreement, then the Non-Breaching Party may deliver written notice of such breach to the Breaching Party. If the Breaching Party fails to cure such breach, or take such steps as would be considered reasonable to effectively cure such breach, within the [**] day period after delivery of such notice, the Non-Breaching Party may terminate this Agreement upon written notice to the Breaching Party, which termination shall apply (i) solely with respect to a Program if such breach is related solely to such Program, or (ii) either on a Program-by-Program basis or to this Agreement in its entirety at the discretion of the Non-Breaching Party if such breach is not related solely to a Program. Notwithstanding the foregoing, if such breach is capable of being cured, but is not reasonably capable of being cured within the [**]-day cure period, if the Breaching Party (A) proposes within such [**]-day period a written plan to cure such breach within a defined time frame extending for a period not to exceed an additional [**] days, and (B) makes good faith efforts to cure such default and to implement such written cure plan, then the Non-Breaching Party may not terminate this Agreement until the earlier of such time as the Breaching Party is no longer diligently pursuing such cure in accordance with such plan or the end of such additional period.

(ii) To the extent permitted by Law, this Agreement may be terminated by either Party upon the filing or institution of bankruptcy, reorganization, liquidation or receivership proceedings, or upon an assignment of a substantial portion of the assets for the benefit of creditors by the other Party; provided, however, that, in the event of any involuntary bankruptcy or receivership proceeding such right to terminate shall only become effective if the Party consents to the involuntary bankruptcy or receivership or such proceeding is not dismissed within ninety (90) days after the filing thereof.

Section 14.3 Effects Of Termination.

(a) Effects of Celgene Termination for Convenience or Agios Termination for Celgene Breach. Upon termination of this Agreement by Celgene under Section 14.2(a) or a termination of this Agreement by Agios under Section 14.2(b), in either case, in whole or with respect to a Terminated Program, the following shall apply:

(i) with respect to licenses,

(A) if the Terminated Program(s) is [**] shall terminate, and [**] shall stay in place, subject to [**] continuing to pay royalties to [**] pursuant to Section 9.7(b)(ii) [**], which royalties shall be reduced by [**] percent ([**]%) of the otherwise applicable royalty;

(B) if the Terminated Program(s) is [**] shall stay in place, subject to [**] continuing to pay royalties to [**] pursuant to Section 9.7(c), which royalties shall be reduced by [**] percent ([**]%) of the otherwise applicable royalty;

(C) if this Agreement is terminated [**] or by [**] shall terminate; and

(D) with respect to any other Terminated Program(s) (other than as set forth in Sections 14.3(a)(i)(A), (B) or (C) above, and other than for [**] with respect to the Terminated Program(s) shall terminate;

(ii) each Party shall be released from its Development, Manufacture and Commercialization obligations with respect to such Terminated Program(s) (except as set forth in Section 14.3(a)(iv)(E) and (F) below with respect to [**] transfer of Manufacturing to [**] hereunder);

(iii) within [**] days after such termination, with respect to Terminated Program(s) that [**], each Party shall provide the other with a report of the costs incurred by such Party that are subject to the Parties' cost-sharing obligations through the effective date of termination for the purpose of calculating a final reconciliation of shared costs with respect to such Terminated Program(s) in accordance with Section 9.4(d); provided, however, that, with respect to Terminated Program(s) that [**] shall remain responsible for its applicable share of the Developments Costs of any Clinical Trials or other Development activities committed by [**] with respect to such Terminated Program(s) prior to the effective date of termination to the extent such Development Costs are within an approved Development Budget under an approved Development Plan in place prior to termination;

(iv) with respect to [**] or with respect to [**], the following shall apply,

(A) within [**] days after such termination, [**] shall provide to [**] a fair and accurate summary report of the status of Development and Commercialization activities conducted by [**] with respect to the Terminated Program(s);

(B) [**] hereby grants to [**], exercisable from and after such termination by [**], a non-exclusive, worldwide, perpetual, royalty-free, fully-paid license, with the right to grant sublicenses, under [**] only to the extent that such [**] is actually used by [**] or its Affiliates in connection with the Terminated Program(s) prior to the date of such termination; provided that the foregoing license under this Section 14.3(a)(iv)(B) shall be exclusive with respect to the applicable Terminated Program only to the extent of claims within the [**] Covering a composition of matter on the Terminated Product in the Terminated Program; provided further that [**] shall be solely responsible for any payments owed by [**] to any Third Party licensors of [**] and shall be responsible for complying with the terms of any license agreements with such Third Party licensors, in either case, directly related to [**] exercise of such license; and, if requested by [**] shall negotiate in good faith with [**] with respect to [**] granting to [**] a royalty-bearing license under [**] and its Affiliates' interest in the [**] only to the extent that such [**] is (x) [**] by [**] or its Affiliates in connection with the Terminated Program(s) prior to the date of such termination and (y) [**] to Develop, Manufacture and/or Commercialize Terminated Products in the Territory;

(C) [**] shall promptly transfer and assign to [**] all of [**] and its Affiliates' rights, title and interests in and to the product trademark(s) (but not any [**] house marks) owned by [**] and solely used for Terminated Products in the Territory;

(D) [**] shall as soon as reasonably practicable transfer and assign to [**] all Regulatory Approvals, the data comprising the Global Safety Database, and other Regulatory Documentation Controlled by [**] which are necessary for the Development, Manufacture and/or Commercialization of Terminated Products in the Territory; provided that [**] may retain a single copy of such items for its records; provided further that, if such approvals, data, or documentation are necessary or useful for the Development, Manufacture and/or Commercialization of a non-Terminated Product, in place of transferring or assigning the foregoing, [**] shall [**] Agios a Right of Reference or Use with respect to such approvals, data, or documentation with respect to such Terminated Products in the Territory;

(E) [**] shall have the option, exercisable within [**] days following the effective date of such termination of this Agreement, to obtain [**] inventory of Terminated Products at a price equal to [**] percent ([**]%) of [**] Manufacturing Costs for such inventory of Terminated Products; provided that, if [**], its Affiliates or sublicensees have outstanding orders, at [**] election, either [**] shall fulfill such orders or, notwithstanding [**] option to purchase inventory, [**] may retain sufficient inventory to fulfill such orders. [**] may exercise such option by written notice to [**] during such [**]-day period; provided that, in the event [**] exercises such right to purchase such inventory, [**] shall grant, and hereby does grant, a royalty-free right and license to any trademarks, names and logos of [**] contained therein for a period of [**] months solely to permit the orderly sale of such inventory, subject to [**] meeting reasonable quality control standards imposed by [**] on the use of such trademarks, names and logos, which shall be consistent with the standards used by [**] prior to such termination;

(F) to the extent that [**] is responsible for Manufacturing any Terminated Product(s) immediately prior to such termination, at [**] written request:

(1) in exchange for a payment equal to [**] percent ([**]%) of [**] Manufacturing Costs, [**] shall use Commercially Reasonable Efforts to supply [**] and its Affiliates with comparable quantities of such Terminated Product(s) in the form, formulation and presentation as were being Developed or Commercialized immediately prior to termination until the earlier of [**] months after the effective date of the termination and establishment by [**] of an alternative supply for such Terminated Product(s);

(2) in the event [**] was utilizing a Third Party manufacturer to Manufacture any Terminated Product(s), to the extent permitted by the terms of such contract, [**] shall promptly assign to [**] the manufacturing agreements with such Third Party with respect to such Terminated Product(s); and

(3) [**] shall transfer, or have transferred, to [**] or its designee, pursuant to a technology transfer plan to be mutually agreed by the Parties, all Manufacturing Technology Controlled by [**] within [**] that is both [**] to Manufacture such Terminated Product(s) as Manufactured by or on behalf of [**] and its Affiliates prior to termination and [**] in support of Development or Commercialization of such Terminated Product(s) (or is in the process of being incorporated), and [**] shall provide reasonable assistance in connection with the transfer of such Manufacturing Technology to [**] or its designee, all of which shall be transferred or provided at [**] Costs;

(v) notwithstanding anything to the contrary in Section 8.8, each Party shall have the right to pursue the Development, Manufacture and Commercialization of products directed to the same Target(s) as the Terminated Product(s), regardless of whether the applicable termination occurred during or after [**]; and

(vi) the provisions of ARTICLE X (other than Section 10.1) shall be terminated with respect to such Terminated Program(s), and [**] shall, if applicable, provide reasonable assistance to [**] and cooperation in connection with the transition of Prosecution and enforcement responsibilities to [**] with respect to [**] and [**] solely related to such Terminated Program(s), including execution of such documents as may be necessary to effect such transition.

(b) Effects of Celgene Termination for Agios Breach. Upon any termination of this Agreement by Celgene in whole or with respect to a Terminated Program under Section 14.2(b):

(i) [**] shall continue in full force in perpetuity;

(ii) all future royalties payable by Celgene under this Agreement with respect to such Terminated Program(s) shall be reduced by [**] percent ([**]%) of the otherwise applicable royalty, and all future milestones payable by Celgene under Article IX with respect to such Terminated Program(s) shall be reduced by [**] percent ([**]%) of the otherwise applicable payment amounts; provided that, if the termination of this Agreement or with respect to a Terminated Program is as a result of Agios' breach of Section 8.8, all future milestones payable by Celgene under Article IX shall terminate;

(iii) if such termination [**], the following will apply:

(A) [**] shall apply;

(B) [**] shall continue under their terms, and [**] shall have the right immediately on such termination to [**];

(C) if [**], then (1) [**] shall become effective and shall continue in full force in perpetuity; (2) all future royalties payable by Celgene under this Agreement with respect to such a Program shall be reduced by [**] percent ([**]%) of the otherwise applicable royalty; and (3) all future milestone payments payable by Celgene under this Agreement with respect to each such Program shall be reduced by [**] percent ([**]%) of the otherwise applicable payment amounts; provided that, if the termination of this Agreement or with respect to a Terminated Program is as a result of Agios' breach of Section 8.8, all future milestones payable by Celgene shall terminate;

(iv) [**] with respect to the Terminated Program(s) shall terminate; provided that, if this Agreement is terminated [**], then [**] shall be deemed to include [**] and, therefore, [**] shall also terminate;

(v) if the Terminated Program(s) is [**], [**], which royalties shall be reduced by [**] percent ([**]%) of the otherwise applicable royalty;

(vi) each Party shall be released from its Development, Manufacture and Commercialization obligations with respect to such Terminated Program(s) (except as set forth in clause (viii) below with respect to [**] transfer of Manufacturing to [**] hereunder);

(vii) with respect to Terminated Program(s) that [**], each Party shall provide the other with a report of the costs incurred by such Party that are subject to the Parties' cost-sharing obligations through the effective date of termination for the purpose of calculating a final reconciliation of shared costs with respect to such Terminated Program(s) in accordance with Section 9.4(d); provided, however, that, with respect to Terminated Program(s) that [**] shall remain responsible for its applicable share of the Developments Costs of any Clinical Trials or other Development activities committed by [**] with respect to such Terminated Program(s) prior to the effective date of termination to the extent such Development Costs are within an approved Development Budget under an approved Development Plan in place prior to termination; and

(viii) with respect to a Terminated Program(s) that [**], the following shall apply [**]:

(A) within [**] days after such termination, [**] shall provide to Celgene a fair and accurate summary report of the status of Development and Commercialization activities conducted by [**] with respect to the Terminated Program(s);

(B) [**] shall continue in full force in perpetuity and [**]; provided that [**] shall be solely responsible for any payments owed by [**] to any [**] or [**] and shall be responsible for complying with the terms of any license agreements with such [**], in either case, directly related to [**] of such license; and

(C) the provisions of Section 14.3(a)(iv)(C), (D), (E), and (F), shall apply with respect to the Terminated Program(s) [**], in each case, substituting "[**]" for "[**]" and vice versa with respect to all obligations and definitions, and otherwise *mutatis mutandis*.

(ix) notwithstanding anything to the contrary in Section 8.8, [**] shall have the right to pursue the Development, Manufacture and Commercialization of products directed to the same Target(s) as the Terminated Product(s), regardless of whether the applicable termination occurred during or after [**]; and

(x) the provisions of ARTICLE X (other than Section 10.1) shall be terminated with respect to such Terminated Program(s) and [**] shall, if applicable, provide reasonable assistance to [**] and cooperation in connection with the transition of Prosecution and enforcement responsibilities to [**] with respect to [**] and [**] solely related to such Terminated Program(s), including execution of such documents as may be necessary to effect such transition.

(c) Sell-Down. Unless Agios exercises its option under Section [**], if Celgene, its Affiliates or sublicensees at termination of this Agreement possess Licensed Product, have started the manufacture thereof or have accepted orders therefor, Celgene, its Affiliates or sublicensees shall have the right, for up to [**] following the date of termination, to

sell their inventories thereof, complete the manufacture thereof and Commercialize such fully-manufactured Licensed Product, in order to fulfill such accepted orders or distribute such fully-manufactured Licensed Product, subject to the obligation of Celgene to pay Agios any and all payments as provided in this Agreement.

(d) Survival. Upon any termination or expiration of this Agreement, unless otherwise specified in this Agreement and except for any rights or obligations that have accrued prior to the effective date of termination or expiration, all rights and obligations of each Party under this Agreement shall terminate in whole or with respect to Terminated Programs, as the case may be; provided, however, that Sections 3.12, 3.14(b), 8.9, 8.10, 8.11, 9.7(f)(iii), 9.9, 9.10, 10.1, 12.5 and 14.1(b), this Section 14.3 and Articles IX (to the extent any amounts are due but unpaid), XI, XIII and XV, as well as any other provision which by its terms or by the context thereof is intended to survive, shall survive any such termination or expiration of this Agreement.

(e) Equitable Relief. Termination of this Agreement shall be in addition to, and shall not prejudice, the Parties' remedies at law or in equity, including the Parties' ability to receive legal damages and/or equitable relief with respect to any breach of this Agreement, regardless of whether or not such breach was the reason for the termination.

(f) Accrued Liabilities. Except as otherwise specifically provided herein, termination of this Agreement shall not relieve the Parties of any liability or obligation which accrued hereunder prior to the effective date of such termination, nor preclude either Party from pursuing all rights and remedies it may have hereunder or at law or in equity with respect to any breach of this Agreement nor prejudice either Party's right to obtain performance of any obligation. In addition, termination of this Agreement shall not terminate provisions which provide by their respective terms for obligations or undertakings following the expiration of the term of this Agreement.

## Article XV
## Miscellaneous

Section 15.1 Dispute Resolution. Except for any disagreements that are within the authority of any Committee as provided in Article II (which disagreements shall be resolved in accordance with Section 2.8 or Section 2.9, as applicable), the Parties agree that any disputes arising with respect to the interpretation, enforcement, termination or invalidity of this Agreement (each, a "Dispute") shall first be presented to the Parties' respective Executive Officers for resolution. If the Parties are unable to resolve a given dispute pursuant to this Section 15.1 after in-person discussions between the Executive Officers within [**] Business Days after referring such dispute to the Executive Officers, either Party may, at its sole discretion, seek resolution of such matter in accordance with Section 15.2.

Section 15.2 Submission to Court for Resolution. Subject to Section 15.1, the Parties hereby irrevocably and unconditionally consent to the exclusive jurisdiction of the courts located in the Southern District of New York for any action, suit or proceeding (other than appeals therefrom) arising out of or relating to this Agreement, and agree not to commence any action, suit or proceeding (other than appeals therefrom) related thereto except in such courts. The Parties further hereby irrevocably and unconditionally waive any objection to the laying of venue

of any action, suit or proceeding (other than appeals therefrom) arising out of or relating to this Agreement in the courts of New York, and hereby further irrevocably and unconditionally waive and agree not to plead or claim in any such court that any such action, suit or proceeding brought in any such court has been brought in an inconvenient forum. Each Party further agrees that service of any process, summons, notice or document by registered mail to its address set forth in Section 15.7 shall be effective service of process for any action, suit or proceeding brought against it under this Agreement in any such court.

Section 15.3 Governing Law. This Agreement and all questions regarding its validity or interpretation, or the performance or breach of this Agreement, shall be governed by and construed and enforced in accordance with the laws of the State of New York, without reference to conflicts of laws principles.

Section 15.4 Assignment.

(a) Neither Party may assign this Agreement, in whole or in part, without the consent of the other Party, except that either Party may assign this Agreement, in whole or in part, without the consent of the other Party, (i) to any Affiliate of such Party, or (ii) to its successor in interest, whether by way of merger, acquisition, sale of all or substantially all of its business or assets to which this Agreement pertains, or otherwise; provided that, except pursuant to clause (i) or clause (ii), Agios shall not have the right under this sentence to assign individual Discovery Programs during the Discovery Term, and neither Party shall have the right to assign individual Independent Programs conducted by such Party unless and until the Buy-In Party's Buy-In Right with respect to such Independent Program has expired; provided further that the assigning Party provides the other Party with written notice of such assignment (which notice must be at least [**] Business Days in advance of any such assignment pursuant to clause (ii)) and such assignee agrees in writing to be bound by the terms and conditions of this Agreement. The terms of this Agreement shall be binding upon and shall inure to the benefit of the successors, heirs, administrators and permitted assigns of the Parties. Any purported assignment in violation of this Section 15.4 shall be null and void.

(b) Each Party agrees that in the event that a Party (the "Acquired Party") is acquired (whether by way of merger, acquisition, sale of all or substantially all of its business or assets to which this Agreement pertains, or otherwise) (an "Acquisition") by a Third Party (the "Acquirer"), (i) the non-Acquired Party shall not obtain any rights or access under this Agreement to any Know-How or Patent Rights Controlled by such Acquirer which were not already within Agios Intellectual Property (if the Acquired Party is Agios) or Celgene Intellectual Property (if the Acquired Party is Celgene) immediately prior to the consummation of such Acquisition; and (ii) the provisions of Section 8.8 shall not apply to any activity otherwise prohibited therein if a Party's involvement in such prohibited activity results from the Acquirer's activities but only if (A) such Acquirer, prior to such acquisition or merger, was already engaged in such prohibited activity (the "Third Party Activity"), and (B) no Celgene Intellectual Property, Agios Intellectual Property, or Collaboration Intellectual Property is used in connection with such Third Party Activity.

(c) Each Party agrees that in the event that a Party acquires (whether by way of merger, acquisition, sale of all or substantially all of its business or assets to which this Agreement pertains, or otherwise) a Third Party (the "Acquired Third Party"), the provisions of Section 8.8 shall not apply to any activity otherwise prohibited therein if a Party's involvement in such prohibited activity results from such acquisition, but only if (i) such Acquired Third Party, prior to such acquisition, was already engaged in such prohibited activity (the "Acquired Party Activity"), and (ii) the Party acquiring such Acquired Third Party shall, within [**] days after the date of the consummation of such acquisition, notify the other Party of such acquisition and comply with the other provisions of this Section 15.4(c). Following consummation of such an acquisition, the acquiring Party shall, at its option, either (A) use good faith efforts to identify a Third Party purchaser to whom such Party will divest its interest in the Acquired Party Activity and to enter into a definitive agreement with such Third Party for such divestiture as soon as reasonably practicable under the circumstances, but such divestiture must be completed no later than [**] months after the closing of such Party's acquisition of the Acquired Party Activity, or (B) promptly discontinue such Acquired Party Activity; provided that notwithstanding which option is chosen, such divesture or discontinuation must be accomplished no later than [**] months after the closing of such Party's acquisition of the Acquired Party Activity. During the time period following the consummation of an acquisition covered by this Section 15.4(c) through the divestiture or discontinuation of the Acquired Party Activity, the acquiring Party shall not use any Celgene Intellectual Property, Agios Intellectual Property, or Collaboration Intellectual Property in connection with such Acquired Party Activities. So long as the acquiring Party divests of, or discontinues, the Acquired Party Activity in accordance with this Section 15.4(c), such acquisition shall not be deemed a violation of Section 8.8.

Section 15.5 Certain Matters Relating to Change of Control. In the event that either Party is subject to a Change of Control, such Party shall notify the other Party at least [**]Business Days prior to the consummation of such Change of Control (or such lesser period of time as is practicable under the circumstances), and shall thereafter provide written notice to the other Party promptly following consummation of such Change of Control.

(a) Upon consummation of such Change of Control of Agios, the following shall occur:

(i) At Celgene's written election within [**] days following consummation of such Change of Control of Agios ("Celgene Election Period"), the Option Term shall be deemed to have expired and the process for identifying Validated Programs pursuant to Section 3.7 shall apply. If Celgene does not elect to exercise such right and the Option Term stays in effect, then, until the expiration of the Option Term (or, if applicable, any Post-Option Extension), Agios shall maintain its corporate form as a separate entity from its acquirer.

(ii) The provisions of this Section 15.5(a)(ii) shall apply if the Change of Control is consummated on or prior to [**] months following the Effective Date and if Celgene elects to have the Option Term expire as a result of the Change of Control. Notwithstanding Section 3.7 or 9.3(b), all the Validated Programs shall be deemed Picks of Celgene, and Celgene shall not owe to Agios any Validated Program Discovery Costs. Furthermore, with respect to such Picked Validated Programs, all royalty obligations under Section 9.7 shall be reduced by [**] percent ([**]%), and all milestones pursuant to Section 9.6 shall terminate. In addition, the Discovery Programs directed at [**] (unless they have become

Licensed Programs) shall be included within Celgene's Picks whether they are Validated Programs or not. Agios shall transfer to Celgene all information and materials concerning such Programs in the manner set forth in Section 3.15(c).

(iii) The provisions of this Section 15.5(a)(iii) shall apply if the Change of Control is consummated more than [**] months after the Effective Date but during the Option Term and if Celgene elects to have the Option Term expire as a result of the Change of Control. Notwithstanding Section 3.7, the Parties shall alternate turns selecting Validated Programs, with [**] being entitled to the [**] and [**] being entitled to the [**], and then repeating such picking order until all Validated Programs have been selected. Notwithstanding Section 9.3(b), Celgene shall not owe to Agios any Validated Program Discovery Costs. Furthermore, with respect to such Picked Validated Programs, all milestones pursuant to Section 9.6, other than the milestones pursuant to Sections 9.6(a)(3) and 9.6(a)(4), shall terminate, but royalty obligations under Section 9.7 shall not be changed. In addition, the Discovery Programs directed at [**] (unless they have become Licensed Programs) shall be included within the Parties' Picks whether they are Validated Programs or not. Agios shall transfer to Celgene all information and materials concerning such Programs in the manner set forth in Section 3.15(c).

(iv) If Celgene elects to have the Option Term expire as a result of the Change of Control, with respect to all Discovery Programs that have reached the DC Selection Stage, notwithstanding anything in Section 3.6(b) to the contrary, at Celgene's election, Celgene may either continue the process for exercise of the Celgene Program Option pursuant to Section 3.6(b) with respect to all such Discovery Programs, or Celgene may exercise the Celgene Program Option with respect to all such Discovery Programs within the Celgene Election Period; provided that, in each case, Agios shall continue to have a right to retain US Territory rights with respect to one [**] Licensed Programs in accordance with Section 3.10; provided further that, if Celgene elects to exercise the Celgene Program Option early pursuant to this Section 15.5(a)(iv):

(A) within [**] days following such election by Celgene, Agios will identify the Discovery Programs that are between DC Selection Stage and IND Acceptance as of the consummation of the Change of Control, in order based on the anticipated date of filing of an IND for such Discovery Program (as contemplated under the applicable Discovery Plans), and, in accordance with Section 3.10, Agios will designate the Discovery Program(s), if applicable, with respect to which Agios elects to retain its US Territory rights (including the right to make an Agios Deferral);

(B) the terms of Sections 15.5(a)(v)(A), (B), (C), (D) and (F) below shall apply (to the extent applicable to any Co-Commercialized Program or Split Program following such early exercise by Celgene of the Celgene Program Option pursuant to this Section 15.5(a)(iv)); and

(C) Celgene shall not be required to pay Agios the IND Amount with respect to such Discovery Program.

(v) If Celgene elects to have the Option Term expire as a result of the Change of Control, then, at Celgene's written election during the Celgene Election Period, with respect to Programs that have already become Licensed Programs prior to the consummation of such Change of Control:

(A) Celgene shall be entitled to assume all Development, Manufacturing, and Commercialization responsibilities with respect to Co-Commercialized Products;

(B) Agios' right to participate in the Commercialization of Co-Commercialized Products, as described in Section 6.3, shall cease;

(C) at Celgene's election, all Committees overseeing any Buy-In Program with respect to which Celgene is the Commercializing Party or any Co-Commercialized Program shall disband, and all decisions allocated to such Committees shall be decisions of Celgene, including decisions requiring Mutual Consent;

(D) with respect to the [**] Split Program only:

(1) if any dispute arises at the JDC with respect to any changes to the Development Plan (including the Development Budget) or any Development activities conducted by a Party under such Split Program (including clinical Manufacturing activities), and such dispute is not resolved at the JDC or JSC level or by the Executive Officers pursuant to Section 2.8, [**] shall have final decision-making authority with respect to such dispute, including with respect to matters otherwise requiring Mutual Consent; provided that [**] shall exercise any such final decision-making authority in a manner consistent with a commitment of Commercially Reasonable Efforts to the Development and Commercialization of Split Product under such Split Program in the US Territory. [**] shall have such final decision-making authority for such [**] Split Program until (x) FDA approval of the first SPA for the first pivotal trial for such [**] Split Program, if the JDC decides to pursue a SPA, or (y) JDC approval of the protocol design for the first pivotal trial for such [**] Split Program, if the JDC decides not to pursue a SPA; and

(2) Celgene shall pay Agios [**] percent ([**]%) of all Development Costs associated with any Phase I Studies incurred by Agios after the consummation of such Change of Control;

(E) with respect to each Buy-In Program for which Celgene is the Buy-In Party, Celgene shall have the right to elect during the Celgene Election Period to either (1) continue to pay its [**] percent ([**]%) share of Development Costs under such Buy-In Program, in which event royalty payments under Section 9.7(c) for Buy-In Products under such Buy-In Program shall continue to be payable by Agios; or (2) discontinue paying its [**] percent ([**]%) share of Development Costs under such Buy-In Program, in which event royalty payments under Section 9.7(c) for Buy-In Products under such Buy-In Program shall be reduced by [**] percent ([**]%); and

(F) except as otherwise provided in this Section 15.5(a), all other financial obligations for any Licensed Programs, including milestone payments, royalty payments, and sharing of Global Development Costs for Split Programs, shall remain in place.

(vi) The obligation to pay the milestone under Section 9.6(b) shall terminate.

Agios shall transfer to Celgene all information and materials concerning such Programs in the manner set forth in Section 3.15(c).

(b) Upon consummation of such Change of Control of Celgene, at the written election of Celgene's acquirer within [**] days following the consummation of such Change of Control, the Option Term shall be deemed to have expired and the process for identifying Validated Programs pursuant to Section 3.7 shall apply. If Celgene's acquirer elects to have the Option Term expire as a result of the Change of Control, the following shall apply:

(i) Notwithstanding Section 3.7, the Parties shall alternate turns selecting Validated Programs, with [**] being entitled to the [**] and [**] being entitled to the [**], and then repeating such picking order until all Validated Programs have been selected. Celgene shall pay Validated Program Discovery Costs as required by Section 9.3(b). In addition, the Discovery Programs directed at [**] (unless they have become Licensed Programs) shall be included within the Parties' Picks whether they are Validated Programs or not. Agios shall transfer to Celgene all information and materials concerning such Programs in the manner set forth in Section 3.15(c).

(ii) At Celgene's written election during such [**]-day period, with respect to Programs that have already become Licensed Programs prior to the consummation of such Change of Control, Agios' right to participate in the Commercialization of Co-Commercialized Products, as described in Section 6.3, shall cease. With respect to each Buy-In Program for which Agios is the Buy-In Party, Agios shall have the right to elect within [**] days following the election by Celgene's acquirer under this Section 15.5(b) to have the Option Term expire, to either (1) continue to pay its [**] percent ([**]%) share of Development Costs under such Buy-In Program, in which event royalty payments under Section 9.7(c) for Buy-In Products under such Buy-In Program shall continue to be payable by Celgene; or (2) discontinue paying its [**] percent ([**]%) share of Development Costs under such Buy-In Program, in which event royalty payments under Section 9.7(c) for Buy-In Products under such Buy-In Program shall be reduced by [**] percent ([**]%).

(c) For purposes of this Section 15.5, "Change of Control" of a Party means any of the following, in a single transaction or a series of transactions: (i) the sale or disposition of all or substantially all of the assets of such Party to a Third Party, (ii) the direct or indirect acquisition by a Third Party (other than (A) an employee benefit plan (or related trust) sponsored or maintained by such Party or any of its Affiliates, and (B) in the case of Agios, any of its current shareholders and their respective Affiliates in a bona fide financing transaction) of beneficial ownership of more than fifty percent (50%) of the then-outstanding common shares or voting power of such Party, or (iii) the merger or consolidation of such Party with or into a Third Party, unless, following such merger or consolidation, the stockholders of such Party immediately prior to such merger or consolidation beneficially own directly or indirectly more than fifty percent (50%) of the then-outstanding common shares or voting power of the entity resulting from such merger or consolidation.

Section 15.6 Force Majeure. If the performance of any part of this Agreement by a Party is prevented, restricted, interfered with or delayed by an occurrence beyond the control of such Party (and which did not occur as a result of such Party's financial condition, negligence or fault), including fire, earthquake, flood, embargo, power shortage or failure, acts of war or terrorism, insurrection, riot, lockout or other labor disturbance, governmental acts or orders or restrictions, acts of God (for the purposes of this Agreement, a "*force majeure* event"), such Party shall, upon giving written notice to the other Party, be excused from such performance to the extent of such prevention, restriction, interference or delay; provided that the affected Party shall use its Commercially Reasonable Efforts to avoid or remove such causes of non-performance and shall continue performance with the utmost dispatch whenever such causes are removed.

Section 15.7 Notices. Unless otherwise agreed by the Parties or specified in this Agreement, all notices required or permitted to be given under this Agreement shall be in writing and shall be sufficient if: (a) personally delivered; (b) sent by registered or certified mail (return receipt requested and postage prepaid); (c) sent by express courier service providing evidence of receipt and postage prepaid where applicable; or (d) sent by facsimile transmission (receipt verified and a copy promptly sent by another permissible method of providing notice described in clauses (a), (b) or (c) above), to address for a Party set forth below, or such other address for a Party as may be specified in writing by like notice:

To Agios:

Agios Pharmaceuticals, Inc.
38 Sidney Street
Cambridge, MA 02139
Attention: J. Duncan Higgons
Telephone: (617) 649-8634
Facsimile: (617) 649-8618

With a copy to:

WilmerHale LLP
60 State Street
Boston, MA 02109
Attention: Steven D. Singer, Esq.
Telephone: (617) 526-6000
Facsimile: (617) 526-5000

To Celgene:

Celgene Corporation
86 Morris Avenue
Summit, NJ 07901
Attention: George S. Golumbeski
Telephone: (908) 673-9043
Facsimile: (908) 673-2769

With a copy to:

Celgene Corporation
86 Morris Avenue
Summit, NJ 07901
Attention: Legal Department
Telephone: (908) 673-9000
Facsimile: (908) 673-2771

Any such notices shall be effective upon receipt by the Party to whom it is addressed.

Section 15.8 Waiver. Except as otherwise expressly provided in this Agreement, any term of this Agreement may be waived only by a written instrument executed by a duly authorized representative of the Party waiving compliance. The delay or failure of either Party at any time to require performance of any provision of this Agreement shall in no manner affect such Party's rights at a later time to thereafter enforce such provision. No waiver by either Party of any condition or term in any one or more instances shall be construed as a further or continuing waiver of such condition or term or of another condition or term.

Section 15.9 Severability. If any provision of this Agreement should be held invalid, illegal or unenforceable in any jurisdiction, the Parties shall negotiate in good faith a valid, legal and enforceable substitute provision that most nearly reflects the original intent of the Parties and all other provisions of this Agreement shall remain in full force and effect in such jurisdiction and shall be liberally construed in order to carry out the intentions of the Parties hereto as nearly as may be possible. If the Parties cannot agree upon a substitute provision, the invalid, illegal or unenforceable provision of this Agreement shall not affect the validity of this Agreement as a whole, unless the invalid, illegal or unenforceable provision is of such essential importance to this Agreement that it is to be reasonably assumed that the Parties would not have entered into this Agreement without the invalid, illegal or unenforceable provision.

Section 15.10 Entire Agreement. This Agreement (including the Schedules and Exhibits attached hereto) constitutes the entire agreement between the Parties relating to its subject matter, and supersedes all prior and contemporaneous agreements, representations or understandings, either written or oral, between the Parties with respect to such subject matter. There are no covenants, promises, agreements, warranties, representations, conditions or understandings, either oral or written, between the Parties other than as set forth herein and therein.

Section 15.11 Modification. No modification, amendment or addition to this Agreement, or any provision hereof, shall be effective unless reduced to writing and signed by a duly authorized representative of each Party. No provision of this Agreement shall be varied, contradicted or explained by any oral agreement, course of dealing or performance or any other matter not set forth in an agreement in writing and signed by a duly authorized representative of each Party.

Section 15.12 Independent Contractors; No Intended Third Party Beneficiaries. Nothing contained in this Agreement is intended or shall be deemed or construed to create any relationship of employer and employee, agent and principal, partnership or joint venture between the Parties. Each Party is an independent contractor. Neither Party shall assume, either directly or indirectly, any liability of or for the other Party. Neither Party shall have any express or implied right or authority to assume or create any obligations on behalf of, or in the name of, the other Party, nor to bind the other Party to any contract, agreement or undertaking with any Third Party. There are no express or implied third party beneficiaries hereunder, (a) except for the indemnitees identified in Sections 13.1, 13.2 and 13.3, and (b) except that [**] are intended third-party beneficiaries of certain provisions of this Agreement, as specifically referred to herein.

Section 15.13 Interpretation; Construction. The captions to the several Articles and Sections of this Agreement are included only for convenience of reference and shall not in any way affect the construction of, or be taken into consideration in interpreting, this Agreement. In this Agreement, unless the context requires otherwise, (a) the word “including” shall be deemed to be followed by the phrase “without limitation” or like expression; (b) references to the singular shall include the plural and vice versa; (c) references to masculine, feminine and neuter

pronouns and expressions shall be interchangeable; (d) the words “herein” or “hereunder” relate to this Agreement; (e) “or” is disjunctive but not necessarily exclusive; (f) the word “will” shall be construed to have the same meaning and effect as the word “shall”; and (g) all references to “dollars” or “$” herein shall mean U.S. Dollars. Each Party represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting hereof. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption will apply against the Party which drafted such terms and provisions.

Section 15.14 Performance by Affiliates. To the extent that this Agreement imposes obligations on Affiliates of a Party, such Party agrees to cause its Affiliates to perform such obligations.

Section 15.15 Counterparts. This Agreement may be executed in two (2) counterparts, each of which shall be deemed an original, and both of which together shall constitute one and the same instrument.

[*Remainder of page intentionally left blank*]

IN WITNESS WHEREOF, the Parties have executed this Discovery and Development Collaboration and License Agreement as of the Effective Date.

AGIOS PHARMACEUTICALS, INC.

By: /s/ David Schenkein
Name: David Schenkein
Title: CEO, Agios

CELGENE CORPORATION

By: /s/ Sol J. Barer
Name: Sol J. Barer
Title: Chair/CEO

Exhibit A

Certain Financial Definitions

"Accounting Standards" means (a) GAAP (United States Generally Accepted Accounting Principles); or (b) IFRS (International Financial Reporting Standards), in either case, consistently applied.

"Annual Net Sales" means, with respect to each Royalty-Bearing Product, the aggregate Net Sales of such Royalty-Bearing Product by the Commercializing Party or its Affiliates or sublicensees in any Calendar Year or, in the first and last years of the term of this Agreement, the portion of such Calendar Year during which this Agreement is in effect.

"Development Costs" means the costs and expenses that are actually incurred by or on behalf of a Party and specifically identifiable or specifically allocable to the Development of Collaboration Compounds, Licensed Compounds and Licensed Products. Development Costs shall not include costs associated with Phase IV Studies. "Development Costs" shall include:

(a) the FTE costs (determined by multiplying the number of FTE hours of service spent by the FTE Rate) of the relevant Party or its Affiliates with respect to such Development;

(b) all Out-of-Pocket Costs incurred by the Parties or their Affiliates, including payments made to Third Parties with respect to such Development (except to the extent that such costs have been included in FTE costs);

(c) Regulatory Expenses other than Regulatory Expenses included within Manufacturing Scale-Up Costs;

(d) the cost of contract research organizations (CROs); and

(e) Manufacturing Costs for clinical supply, including:

(i) costs of packaging of drug products and distribution of drug products used in Clinical Trials;

(ii) expenses incurred to purchase or package comparator drugs;

(iii) costs and expenses of disposal of clinical samples; and

(iv) costs and expenses incurred in scaling up Manufacturing activities related to pre-clinical or clinical supply, including formulation development activities;

all of such costs, as determined from the books and records of the applicable Party and its Affiliates maintained in accordance with the Accounting Standards. Notwithstanding anything in this definition to the contrary, only those Development Costs that are contemplated by, and materially consistent with, the Development Plan and Development Budget for the applicable Collaboration Compound, Licensed Compound or Licensed Product shall be chargeable as Development Costs.

"Field-Based Costs" means all Agios' costs associated with the Commercialization Activities related to Co-Commercialized Products in the US Territory allocated to Agios under the applicable Commercialization Plan, including, if applicable, sales representatives and training of the sales representatives, sales meetings, details, sales call reporting, work on managed care accounts, costs related to customer service and other sales and customer service related expenses; provided that the Commercialization Plan shall set forth the rate at which the Field-Based Costs of Agios will be reimbursed. If Agios' personnel allocated to the Commercialization Activities sells products other than Co-Commercialized Products, only that portion of such personnel's efforts that are related to the Co-Commercialized Products in the US Territory shall be included as Field-Based Costs hereunder.

"FTE" means a full-time equivalent person year (consisting of a total of [**] hours per year) of scientific, technical or commercialization work undertaken by a Party's employees.

"FTE Rate" means $[**] per FTE for the period commencing on the Effective Date and ending December 31, 2011. On January 1, 2012 and on January 1st of each subsequent Calendar Year, the foregoing rate shall be increased for the Calendar Year then commencing by the percentage increase, if any, in the Consumer Price Index ("CPI") as of December 31 of the then most recently completed Calendar Year with respect to the level of the CPI on December 31, 2010. As used in this definition, Consumer Price Index or CPI means the Consumer Price Index – Urban Wage Earners and Clerical Workers, US City Average, All Items, 1982-84 = 100, published by the United States Department of Labor, Bureau of Labor Statistics (or its successor equivalent index).

"Global Development Costs" means, with respect to a Split Product, all Development Costs other than Territory-Specific Development Costs.

"Global Study" means any study that is "used" in both the US Territory and the ROW Territory, with "used" meaning that it will be submitted to the relevant Regulatory Authorities in the United States and the ROW Territory, other than studies submitted solely to meet safety reporting obligations.

"Manufacturing Costs" means, with respect to Collaboration Compounds, Licensed Compounds or Licensed Products, the reasonable FTE costs and Out-of-Pocket Costs of a Party or any of its Affiliates or sublicensees incurred in Manufacturing such Collaboration Compounds, Licensed Compounds or Licensed Products, including Manufacturing Scale-Up Costs and including:

(a) to the extent that any such Collaboration Compound, Licensed Compound or Licensed Product is manufactured by a Party or any of its Affiliates or sublicensees, direct material and direct labor costs, plus manufacturing overhead attributable to such Collaboration Compound, Licensed Compound or Licensed Product (including facility start-up costs, all directly incurred manufacturing variances, and a reasonable allocation of related manufacturing administrative and facilities costs (including depreciation) and a reasonable allocation of the

costs of failed batches to be further described in the applicable supply agreement, to be provided for such Collaboration Compound, Licensed Compound or Licensed Product, but excluding costs associated with excess capacity), all determined in accordance with the books and records of the applicable Party or its Affiliates or sublicensees maintained in accordance with the Accounting Standards, consistently applied; and

(b) to the extent that any such Collaboration Compound, Licensed Compound or Licensed Product is manufactured by a Third Party manufacturer, the Out-of-Pocket Costs paid by a Party or any of its Affiliates or sublicensees to the Third Party for the manufacture, supply, packaging and labeling of such Collaboration Compound, Licensed Compound or Licensed Product, and any reasonable Out-of-Pocket Costs and direct labor costs actually incurred by such Party or any of its Affiliates or sublicensees in managing or overseeing the Third Party relationship, determined in accordance with the books and records of the applicable Party or its Affiliates or sublicensees maintained in accordance with the Accounting Standards, consistently applied.

"Manufacturing Scale-Up Costs" means the reasonable FTE costs and Out-of-Pocket Costs of a Party or any of its Affiliates or sublicensees incurred in scaling up Manufacturing activities related to Licensed Compounds or Licensed Products for commercial supply, including (a) costs for process development work, analytical method optimization, and process validation, (b) costs for complete technology transfer to a commercial site (including costs for Manufacturing of demonstration batches on a suitable scale), and (c) Regulatory Expenses associated with such Manufacturing activities.

"Net Sales" means, with respect to any Royalty-Bearing Product, gross amounts invoiced by the Commercializing Party, its Affiliates or its sublicensees to Third Parties (that are not sublicensees) for the sale or other commercial disposition of such Royalty-Bearing Product anywhere within the Territory, including sales to wholesale distributors, less deductions from such amounts calculated in accordance with the Accounting Standards so as to arrive at "net sales" under the Accounting Standards, and further reduced by write-offs of accounts receivables or increased for collection of accounts that were previously written off.

Net Sales, and any and all set-offs against gross amounts invoiced, shall be determined from books and records maintained in accordance with the Accounting Standards, consistently applied throughout the organization and across all products of the entity whose sales of any Royalty-Bearing Product are giving rise to Net Sales. Sales or other commercial dispositions of Royalty-Bearing Products between the Commercializing Party and its Affiliates and its sublicensees, and Royalty-Bearing Products provided to Third Parties without charge, in connection with research and development, clinical trials, compassionate use, humanitarian and charitable donations, or indigent programs or for use as samples shall be excluded from the computation of Net Sales, and no payments will be payable on such sales or such other commercial dispositions, except where such an Affiliate or sublicensee is an end user of the Royalty-Bearing Product.

If a Royalty-Bearing Product is sold or otherwise commercially disposed of for consideration other than cash or in a transaction that is not at arm's length between the buyer and the seller, then the gross amount to be included in the calculation of Net Sales shall be the

amount that would have been invoiced had the transaction been conducted at arm's length and for cash. Such amount that would have been invoiced shall be determined, wherever possible, by reference to the average selling price of the relevant Royalty-Bearing Product in arm's length transactions in the relevant country.

Notwithstanding the foregoing, in the event a Royalty-Bearing Product is sold as a Combination Product, Net Sales shall be calculated by multiplying the Net Sales of the Combination Product by the fraction A/(A+B), where A is the gross invoice price of the Royalty-Bearing Product if sold separately in a country and B is the gross invoice price of the other product(s) included in the Combination Product if sold separately in such country. If no such separate sales are made by the Commercializing Party, its Affiliates or sublicensees in a country, Net Sales of the Combination Product shall be calculated in a manner to be negotiated and agreed upon by the Parties, reasonably and in good faith, prior to any sale of such Combination Product, which shall be based upon the relative value of the active components of such Combination Product.

As used in this definition, "Combination Product" means any product that comprises a Royalty-Bearing Product sold in conjunction with another active component so as to be a combination product (whether packaged together or in the same therapeutic formulation). Pharmaceutical dosage form vehicles, adjuvants and excipients shall be deemed not to be "active ingredients."

"Out-of-Pocket Costs" means, with respect to certain activities hereunder, direct expenses paid or payable by either Party or its Affiliates to Third Parties (other than employees of such Party or its Affiliates) that are specifically identifiable and incurred to conduct such activities for a Program hereunder and have been recorded in accordance with the Accounting Standards.

"Regulatory Expenses" means, with respect to a Collaboration Compound, Licensed Compound or Licensed Product, all Out-of-Pocket Costs incurred by or on behalf of a Party in connection with the preparation and filing of regulatory submissions for such Collaboration Compound, Licensed Compound or Licensed Product and obtaining of Regulatory Approvals and any applicable governmental price and reimbursement approvals.

"Territory-Specific Development Costs" means, with respect to a Split Product, any Development Costs that are incurred in connection with obtaining Regulatory Approval or Commercialization specifically related only to the US Territory (in which event such costs shall be the responsibility of Agios) or to the ROW Territory (in which event such costs shall be the responsibility of Celgene).

Schedule 1.1

Baseline Activity

Screening Hits:

[**]

Active compound: [**]

Schedule 1.6

Agios Patent Rights
(as of the Effective Date)

| Matter # | Appln No. | Filing Date | Subject | Application Title |
|---|---|---|---|---|

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of 5 pages were omitted. [**]

Schedule 1.53

Existing Third Party Agreements

[**]

Agios has disclosed to Celgene that Agios intends to allocate a portion of the total consideration paid by Celgene pursuant to Section 9.1 and Section 9.2 of this Agreement to the foregoing agreements, as follows:

[**]

Schedule 1.65

IND Study Criteria

IND-Enabling Studies to include:

[**]

Schedule 1.91

Phase I MAD Protocol Criteria

Protocol shall be designed to evaluate [**].

The primary endpoints will be [**].

The study design, endpoints, and evaluation will be modified as mandated by the FDA.

The study may be conducted at [**].

Schedule 1.93

Phase I Report Criteria

[**]

Schedule 1.105

Publication Guidelines

Unless the JSC by Mutual Consent agrees otherwise, the Parties agree as follows:

[**]

Schedule 1.119

Target List

| *Target*[*1] | *Isoforms/Mutation Status* | *Name* | *UniProt identifier* |
|---|---|---|---|

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of three pages were omitted.

[**]

Schedule 1.128

Validation Criteria

Target Validation (biology)

[**].

Validated Target:

A validated Target will satisfy criteria for Target validation above [**].

Schedule 3.5(a)

Target Inclusion Criteria

Available data from published literature or generated in the course of research activities in the Collaboration links a particular Target to [**].

Schedule 3.5(b)

Certain Rationale for Target/Program Exclusion

For purposes of illustration only and without limitation, the following may be presented as rationale for removing a Collaboration Target from the Target List:

[**]

Schedule 3.6(b)

Clinical Candidate Guidelines

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of three pages were omitted. [**]

Back-Up Compounds: [**].

Schedule 10.2(f)

Countries for Filing Agios Collaboration Patent Rights

[**].

Schedule 11.3

Press Release

**CELGENE CORPORATION AND AGIOS PHARMACEUTICALS ANNOUNCE GLOBAL STRATEGIC COLLABORATION TO ADVANCE UNIQUE SCIENCE OF CANCER METABOLISM**

*—Partnership leverages transformational science at Agios and translational capabilities of Celgene to target areas of significant unmet medical need—*

SUMMIT, N.J. & CAMBRIDGE, Mass.—April 15, 2010—(BUSINESS WIRE)—Celgene Corporation (NASDAQ: CELG) and Agios Pharmaceuticals Inc., a privately-held biotechnology company, today announced the formation of a global strategic collaboration focused on targeting cancer metabolism. The goal of the collaboration is to discover, develop, and deliver novel disease-altering therapies in oncology based on the transformational science of Agios' innovative cancer metabolism research platform. This platform is based on the concept that targeting key metabolic enzymes unique to rapidly proliferating cancer cells can "starve" the cancer.

Under the terms of the agreement, Agios will receive a $130 million upfront payment, including an equity investment. In return, Celgene receives an initial period of exclusivity during which it has the option to develop any drugs resulting from the Agios cancer metabolism research platform, In addition, Celgene may extend this exclusivity period through additional funding. If successful, Agios would receive substantial regulatory, clinical and commercial milestones.

"Agios' approach is unique and groundbreaking. We look for early opportunities in the IDH1 and PKM2 programs and see exceptional value in new targets Agios is uniquely positioned to prosecute," said Thomas Daniel, M.D., President of Research for Celgene. "We believe the strategic alliance with Agios can expand our deep and diverse pipeline of innovative programs focused on changing treatment paradigms in serious and debilitating diseases."

Agios will lead discovery and early translational development for all cancer metabolism programs. Celgene has an exclusive option to license any resulting clinical candidates at the end of Phase I, and will lead and fund global development and commercialization of licensed programs. On each program, Agios may receive up to $120 million in milestones as well as royalties on sales, and may also participate in the development and commercialization of certain products in the US.

"We are thrilled to establish this alliance with Celgene, a pre-eminent global biopharmaceutical company, that shares our passion and commitment to discovering breakthrough medicines that may improve the lives of cancer patients worldwide," said David Schenkein, M.D., Chief Executive Officer of Agios. "This transformational alliance provides Agios with the long-term resources and flexibility to extend our leadership position in the cancer metabolism field and to advance our capabilities and programs as an integrated, independent company."

**About Cancer Metabolism**

Cancer metabolism is a new and exciting field of biology that provides an innovative approach to treating cancer. Cancer cell metabolism is marked by profound changes in nutrient requirements and usage to ensure cell proliferation and survival. Research in the field has demonstrated that cancer cells become addicted to certain fuel sources and metabolic pathways. Identifying and disrupting certain enzymes in these metabolic pathways provides a powerful intervention point for discovery and development of cancer therapeutics.

**About Agios Pharmaceuticals**

Agios Pharmaceuticals, a private, independent biopharmaceutical company, is dedicated to the discovery and development of novel therapeutics in the emerging field of cancer metabolism. To support and drive these efforts, Agios has built a robust platform integrating biology, metabolomics, biochemistry and informatics to enable target and biomarker identification.

To date, Agios has put in place a world-class scientific team, built the largest research laboratory dedicated to cancer metabolism and created an emerging compound development pipeline of novel cancer therapeutics. The Company's founders and scientific advisors represent the core thought leaders in the field of cancer metabolism, responsible for key advances, insights and discoveries in the field. Agios Pharmaceuticals is located in Cambridge, Massachusetts. The company is financed by Third Rock, Flagship, ARCH Venture Partners. For more information, please visit the company's website at www.agios.com.

**About Celgene**

Celgene Corporation is an integrated global biopharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through gene and protein regulation. For more information, please visit the Company's website at www.celgene.com.

**Forward-Looking Statements**

*This release contains certain forward-looking statements which involve known and unknown risks, delays, uncertainties and other factors not under the Company's control. The Company's actual results, performance, or achievements could be materially different from those projected by these forward-looking statements. The factors that could cause actual results, performance, or achievements to differ from the forward-looking statements are discussed in the Company's filings with the Securities and Exchange Commission, such as the Company's Form 10-K, 10-Q and 8-K reports. Given these risks and uncertainties, you are cautioned not to place undue reliance on the forward-looking statements.*

**Contact:**
Celgene Corporation

David W. Gryska, 908-673-9059
Senior Vice President and
Chief Financial Officer

or

Tim Smith, 908-673-9951
Director
Investor Relations

Agios Pharmaceuticals
Yates Public Relations
Kathryn Morris
845-635-9828

###

# FIRST AMENDMENT
# TO
# DISCOVERY AND DEVELOPMENT
# COLLABORATION AND LICENSE AGREEMENT

This First Amendment to the Discovery and Development Collaboration and License Agreement (the "First Amendment") is entered into as of October 3rd, 2011 (the "Amendment Effective Date") by and between Agios Pharmaceuticals, Inc. ("Agios") and Celgene Corporation ("Celgene"). Agios and Celgene may each be referred to herein individually as a "Party" and collectively as the "Parties."

## INTRODUCTION

1. Celgene and Agios are parties to that certain Discovery and Development Collaboration and License Agreement, dated as of April 14, 2010 (the "Agreement").

2. Pursuant to the Agreement, the Parties have engaged in the Development of Collaboration Compounds against Collaboration Targets.

3. The Parties wish to amend the Agreement with respect to the use of PKR as a Target and to provide for certain rights for Agios to investigate PKR outside of the Collaboration.

NOW, THEREFORE, in consideration of the covenants and agreements contained herein, and for other valuable consideration, the receipt and adequacy of which are hereby acknowledged, Agios and Celgene agree as follows:

1. **Definitions.** Capitalized terms used in this First Amendment and not otherwise defined herein shall have the meanings set forth in the Agreement.

2. **Amendments.** The Agreement is amended as follows:

(a) **Additional Defined Terms.** Article I of the Agreement is hereby amended by adding the following additional defined terms to such Article in the sections set forth below:

Section 1.6A "Agios Final PKR Compounds" means the compounds designated by Agios pursuant to Section 3.17(c)(ii).

Section 1.6B "Agios Initial PKR Compounds" means the specific chemical entities set forth on Schedule 1.6A attached hereto.

Section 1.6C "Agios PKR Program" means the Development (excluding screening of PKR with Collaboration Compounds), Manufacture and Commercialization by Agios and its Affiliates and, subject to Section 3.17(c), licensees and sublicensees, of compounds that [**] to PKR (including the Agios Final PKR Compound).

Section 1.10A "Amendment Effective Date" means, October 3rd, 2011, which is the effective date of that certain First Amendment to the Discovery and Development Collaboration and License Agreement between the Parties.

Section 1.100B "PKR" means [**].

(b) Amendment of [**] Definition. Section 1.100 of the Agreement is hereby amended and restated in its entirety to read as follows:

Section 1.100 "[**]" means [**]. Notwithstanding the foregoing, [**] shall not be included within, or be deemed to constitute a part of, [**].

(c) Agios PKR Program. Article III of the Agreement is hereby amended to include a new Section 3.17, as follows:

Section 3.17 Agios PKR Program.

(a) Generally. Celgene acknowledges that Agios intends to undertake the Agios PKR Program, either alone or in collaboration with one or more Affiliates and, subject to Section 3.17(c), Third Parties, and that activities undertaken pursuant to the Agios PKR Program for non-Oncology Indications that consist of [**] treating hereditary non-spherocytic haemolytic anemia [**] (the "PKR Indications") shall not constitute activities of the Collaboration, and Celgene shall have no rights with respect to (i) the Agios PKR Program except for those provided in Section 3.17(b) or (ii) any products containing the Agios Final PKR Compound as an active ingredient. The foregoing sentence shall not be construed as granting Agios any rights to use Licensed Compounds and/or Licensed Products in any products containing the Agios Final PKR Compound. Agios agrees that it shall not screen PKR with Collaboration Compounds. Without limiting the generality of the foregoing, the Agios PKR Program shall not be deemed to constitute an Agios Reverted Program or an Independent Program. Agios acknowledges that its activities pursuant to the Agios PKR Program shall continue to be subject to the terms and conditions of Article I, Sections 8.8 (except, under Sections 8.8(a)(ii) and (d), with respect to the PKR Indications), 12.5, 13.2, 13.5, 14.2(b), and 14.3(d)-(f) the Agreement. Solely for purposes of Agios' obligations under Section 8.8 with respect to the Agios PKR Program, [**] shall continue to be deemed [**], except, under Sections 8.8(a)(ii) and (d), with respect to the PKR Indications. Agios shall have no rights to, and shall not, use any intellectual property rights of Celgene (including any Celgene Collaboration Intellectual Property or Celgene Intellectual Property) in connection with the Agios PKR Program. For the avoidance of doubt, none of the licenses granted to Agios by Celgene under Article VIII shall include any licenses with respect to the Agios PKR Program, Agios Final PKR Compounds or Agios Initial PKR Compounds.

(b) Compounds Under the Agios PKR Program. Celgene acknowledges that Agios may (i) chemically modify the Agios Initial PKR Compounds set forth on Schedule 1.6A, or (ii) Develop (excluding screening of PKR with Collaboration Compounds), Manufacture and Commercialize other chemical entities against PKR, under the Agios PKR Program**.** Celgene acknowledges and agrees that Agios shall have the right to maintain the Agios Initial PKR Compounds set forth on Schedule 1.6A and a maximum of [**] chemically modified compounds under Section 3.17(b)(i), until expiration of the Designation Period (as defined below)**.** Prior to the Designation Period, on a rolling basis, but in no event less than [**], excluding the Agios Initial PKR Compounds set forth on Schedule 1.6A and the [**]-chemically modified compounds under Section 3.17(b)(i), the chemically modified compounds under Section 3.17(b)(i) shall be deemed Collaboration Compounds and shall be subject to the terms and conditions of the Agreement, including any exclusive licenses granted to Celgene pursuant to Article VII**.** Agios shall provide the JDC with any available information and data, including, *in vitro* and *in vivo* results, generated under the Agios PKR Program with respect to such chemically modified compounds that are deemed Collaboration Compounds and such information and data shall be deemed Collaboration Know-How.

(c) Agios Initial PKR Compounds and Agios Final PKR Compounds.

(i) As of the Amendment Effective Date, Schedule 1.6A sets forth one (1) compound as a lead candidate and [**] compounds as back-up candidates, which shall cease to constitute Agreement Compounds and the Compound List for the Discovery Program related to [**] is hereby deemed amended to exclude the Agios Initial PKR Compounds set forth on Schedule 1.6A.

(ii) Upon the earlier of [**] or at any time prior to [**] of [**] of the Agios Initial PKR Compounds and [**]-chemically modified compounds under Section 3.17(b)(i), with notice to Celgene, Agios shall designate [**] compounds as the Agios Final PKR Compounds (the "Designation Period")**.** For the avoidance of doubt, the Agios Final PKR Compounds designated under this subsection shall not be deemed an Agreement Compound**.** Upon expiration of the Designation Period, excluding the Agios Final PKR Compounds, all compounds from the Agios Initial PKR Compounds and all remaining chemically modified compounds under Section 3.17(b)(i) (including the [**]-chemically modified compounds), shall be deemed Collaboration Compounds and shall be subject to the terms and conditions of the Agreement, including any exclusive licenses granted to Celgene pursuant to Article VIII and Schedule 1.6A shall be updated accordingly**.** Agios shall provide any available information and data, including, *in vitro* and *in vivo* results, generated

under the Agios PKR Program, excluding the Agios Final PKR Compounds, with respect to such Agios Initial PKR Compounds and all remaining chemically modified compounds under Section 3.17(b)(i) (including the [**]-chemically modified compounds) and such information and data shall be deemed Collaboration Know-How.

(d) Third Party Licensees. Subject to the following right of first negotiation, Agios shall have the right to conduct the Agios PKR Program in collaboration with a Third Party, and shall have the right to grant licenses in connection therewith**.** For a period beginning on the Amendment Effective Date and ending on NDA approval of a chemical entity against PKR, under the Agios PKR Program, (the "ROFN Period"), if Agios or its Affiliates intend to enter into negotiations with Third Parties with respect to the Agios PKR Program, whether as part of a collaboration, license or otherwise (other than in connection with a Change of Control), Agios shall first so notify Celgene and Celgene shall have the right to, by notice to Agios within [**] days, to negotiate exclusively with Agios with respect to the Agios PKR Program**.** If Celgene provides such notice within such period, Agios and Celgene shall enter into good faith negotiations for a period of up to [**] days thereafter with respect to the Agios PKR Program**.** Agios and its Affiliates shall not negotiate with or grant any rights to any Third Party with respect to the Agios PKR Program during such negotiation period**.** In the event the Parties reach agreement during such [**]-day period (or such longer period as the Parties may agree upon), then the Agios PKR Program shall be subject to the agreement reached by the Parties. If the Parties do not reach agreement with respect to the Agios PKR Program during such [**]-day period (or such longer period as the Parties may agree upon), Agios shall be free during the next [**] months after the expiration of the foregoing [**]-day (or, if applicable, longer) negotiation period to commence negotiations with Third Parties and enter into collaboration and license agreements with such Third Parties with respect to the Agios PKR Program; provided that, if Agios does not enter into a collaboration, license or otherwise prior to the expiration of such [**]-month period, the Agios PKR Program shall again be subject to the provisions of this Section 3.17(d). With respect to the conduct of the Agios PKR Program, such Third Parties shall be subject to the terms and conditions of this First Amendment (including the provisions of Section 8.8 of the Agreement) to the same extent as Agios. For purposes of clarity, the right of first negotiation set forth above shall not apply to the use of Third Party Contractors by Agios or its Affiliates; provided that Agios shall be liable for any failure by its Affiliates and Third Party Contractors to comply with all relevant restrictions, limitations and obligations in this First Amendment.

(e) Patent Rights. All Agios Patent Rights and Collaboration Patent Rights shall continue to be subject to the terms and conditions of Article X of this Agreement (except, under Section 10.2(g), with respect to Agios Patent Rights and Agios Collaboration Patent Rights that are directed solely to the Agios Final PKR Compounds); provided that Agios shall have the final say in the prosecution and enforcement of Agios Patent Rights and Agios Collaboration Patent Rights are directed solely to the Agios Final PKR Compounds.

(d) Schedules. The Agreement is hereby amended by adding a new Schedule 1.6A in the form attached hereto as Annex A.

3. **Acknowledgements.** For purposes of clarity, the Parties acknowledge that (i) PKR shall be deemed to be removed from the Target List as of the Amendment Effective Date, and (ii) PKR shall not be deemed to constitute an Agios Reverted Target or an Independent Target. Notwithstanding the foregoing, the Agios PKR Program shall be subject to the terms and conditions of this First Amendment and Article I, Sections 8.8 (except, under Sections 8.8(a)(ii) and (d), with respect to the PKR Indications), 12.5, 13.2, 13.5, 14.2(b), and 14.3(d)-(f) the Agreement.

4. **Incorporation.** Article 15 of the Agreement is hereby incorporated *mutatis mutandis* into this First Amendment.

5. **Effect on Agreement.** Except as specifically amended by this First Amendment, the Agreement will remain in full force and effect and is hereby ratified and confirmed**.** To the extent a conflict arises between the terms of the Agreement and this First Amendment, the terms of this First Amendment shall prevail but only to the extent necessary to accomplish their intended purpose.

[*Remainder of Page Intentionally Left Blank*]

IN WITNESS WHEREOF, the Parties have executed this First Amendment as of the Amendment Effective Date.

AGIOS PHARMACEUTICALS, INC.

By: /s/ David Schenkein
Title: CEO

CELGENE CORPORATION

By: /s/ Robert J. Hugin
Title: CEO

CELGENE LEGAL

/s/ John [illegible]

Annex A

Schedule 1.6A to the Discovery and Development Collaboration and License Agreement

Agios Initial PKR Compounds: [**]

**SECOND AMENDMENT**
**TO**
**DISCOVERY AND DEVELOPMENT**
**COLLABORATION AND LICENSE AGREEMENT**

This Second Amendment to the Discovery and Development Collaboration and License Agreement (the "Second Amendment") is entered into as of October 3rd, 2011 (the "Second Amendment Effective Date") by and between Agios Pharmaceuticals, Inc. ("Agios") and Celgene Corporation ("Celgene"). Agios and Celgene may each be referred to herein individually as a "Party" and collectively as the "Parties." Capitalized terms used in this Second Amendment and not otherwise defined herein shall have the meanings set forth in the Agreement.

**INTRODUCTION**

1. Celgene and Agios are parties to that certain Discovery and Development Collaboration and License Agreement, dated April 14, 2010 and amended October 3rd, 2011 (the "Agreement").

2. Pursuant to the Agreement, the Parties have engaged in a collaboration that applies Agios' expertise and technology to the discovery and validation of novel targets, primarily cancer metabolism targets, and the discovery and development of associated therapeutics, primarily in the Oncology Field, and provides for the development and commercialization of such therapeutics.

3. The Parties wish to amend the Agreement in order to extend the term of the Initial Phase and amend the terms of the First Extension Phase.

NOW, THEREFORE, in consideration of the covenants and agreements contained herein, and for other valuable consideration, the receipt and adequacy of which are hereby acknowledged, Agios and Celgene agree as follows:

1. **Amendment and Restatement of Section 3.3.** Section 3.3 of the Agreement is hereby amended and restated in its entirety to read as follows:

Section 3.3 Option Term.

(a) Initial Phase. Except as otherwise set forth in Section 3.3(b)(iii) below, the initial phase of the Collaboration shall commence on the Effective Date and end four (4) years following the Effective Date (the "Initial Phase").

(b) First Extension Phase.

(i) Celgene shall have the right to elect to extend the Option Term following the Initial Phase ("First Extension Option") for a period (the "First Extension Phase") ending upon the earlier of:

(A) the date following the Effective Date on which (1) FPD of [**] Collaboration Compounds has occurred and (2) the JRC has confirmed the nomination of an additional Development Candidate (the "Second Extension Option Trigger Event"); and

(B) [**] following the end of the Initial Phase.

(ii) Celgene may exercise the First Extension Option by (x) providing written notice to Agios of such election; and (y) paying to Agios [**] Dollars (US$[**]). If Celgene elects to exercise such option, such notice and payment shall be made as follows:

(A) Unless Section 3.3(b)(ii)(B) or 3.3(b)(ii)(C) below applies, if Celgene elects the First Extension Option, Celgene must provide such exercise notice [**] months prior to the end of the initial Phase and must pay such $[**] within [**] days following the end of the Initial Phase.

(B) If Agios has not nominated [**] Development Candidates that are confirmed by the JRC at least [**] months prior to the end of the Initial Phase but [**] Development Candidates are so confirmed prior to the end of the Initial Phase, then, if Celgene elects the First Extension Option, Celgene must provide such exercise notice within [**] months following such confirmation of [**] Development Candidates and must pay such $[**] within [**] days following the later of (1) delivery of such notice and (2) the end of the Initial Phase.

(C) If Celgene elects to have Agios continue Development of the Development Candidates into the Extended Initial Phase in accordance with Section 3.3(b)(iii), then, if Celgene elects the First Extension Option, Celgene must provide such exercise notice on or prior to the date that is [**] days following the end of the Extended Initial Phase and must pay such $[**] days following delivery of such notice.

(iii) Notwithstanding anything in this Section 3.3 to the contrary, if Agios believes that Agios will not be able to nominate at least [**] Development Candidates that meet the Clinical Candidate Guidelines by the end of the Initial Phase, Agios shall notify Celgene thereof (to the extent practicable, by no later than [**] months prior to the end of the Initial Phase). If the JRC has not confirmed at least [**] Development Candidates nominated by Agios that meet the Clinical Candidate Criteria within the Initial Phase, then Celgene shall have the right to either exercise its First Extension Option as provided in Section 3.3(b)(ii)(A) or to have Agios continue Development following the end of the Initial Phase. If Celgene elects to have Agios continue Development, the Initial Phase shall

be extended until the earlier of (x) [**] following the end of the original [**]-year Initial Phase and (y) such time as the JRC has confirmed the nomination of at least [**] Development Candidates that meet the Clinical Candidate Guidelines following the Effective Date (the "Extended Initial Phase").

(A) If Celgene elected to have Agios continue Development through the Extended Initial Phase and the JRC confirms [**] Development Candidates nominated by Agios that meet the Clinical Candidate Guidelines by the end of the Extended Initial Phase, Celgene shall have the right to elect, in its sole discretion (to be exercised in accordance with Section 3.3(b)(ii)(C)), to extend the Option Term following such Extended Initial Phase until the end of the period set forth in Section 3.3(b)(iii)(D). If Celgene does not elect to extend the Option Term through such period, the Option Term shall expire at the end of such Extended Initial Phase and the picking mechanism set forth in Section 3.7 shall apply with respect to Validated Programs at such time.

(B) If the JRC confirms [**] nominated by Agios that meets the Clinical Candidate Guidelines by the end of the Extended Initial Phase, but fails to confirm the nomination of [**] by the end of the Extended Initial Phase, Celgene shall have the right, in its sole discretion (to be exercised in accordance with Section 3.3(b)(ii)(C)), to extend the Option Term following such Extended Initial Phase until the end of the period set forth in Section 3.3(b)(iii)(D). If Celgene does not elect to extend the Option Term through such period, the Option Term shall expire at the end of such Extended Initial Phase and the picking mechanism set forth in Section 3.7 shall apply with respect to Validated Programs at such time; provided, however, that, notwithstanding anything in Section 3.7, 9.3(b) or 9.6(a) to the contrary, (1) [**] shall be entitled to the [**] Picks (including, if such Program has not reached the DC Selection Stage, [**]), and the Parties shall then alternate turns (with [**] having the first turn) selecting [**] until all Validated Programs have been selected; (2) Celgene shall not be obligated to pay any Validated Program Discovery Costs with respect to Celgene's Picked Validated Program(s); and (3) Celgene shall be obligated to pay to Agios royalties as set forth in Section 9.7(d) but shall not be obligated to pay to Agios any of the milestone payments set forth in Section 9.6(a), in each case, with respect to Licensed Compounds and Licensed Products under Celgene's Picked Validated Program(s).

(C) If the JRC fails to confirm the nomination of any Development Candidate by the end of the Extended Initial Phase, Celgene shall have the right, in its sole discretion (to be exercised in accordance with Section 3.3(b)(ii)(C)), to extend the Option Term following such Extended Initial Phase until the end of the period set forth in Section 3.3(b)(iii)(D). If Celgene does not elect to extend the Option

Term through such period, the Option Term shall expire at the end of such Extended Initial Phase and the picking mechanism set forth in Section 3.7 shall apply with respect to Validated Programs at such time; provided, however, that, notwithstanding anything in Section 3.7, 9.3(b) or 9.6(a) to the contrary, (1) Celgene shall have the right to select all Validated Programs remaining in the Collaboration at such time (including, if such Program has not reached the DC Selection Stage, [**]); (2) Celgene shall not be obligated to pay any Validated Program Discovery Costs with respect to Celgene's Picked Validated Program(s); and (3) Celgene shall be obligated to pay to Agios royalties as set forth in Section 9.7(d) but shall not be obligated to pay to Agios any of the milestone payments set forth in Section 9.6(a), in each case, with respect to Licensed Compounds and Licensed Products under such Picked Validated Program(s).

(D) If Celgene elects to extend the Option Term following such Extended Initial Phase pursuant to Section 3.3(b)(iii)(A), 3.3(b)(iii)(B), or 3.3(b)(iii)(C), such First Extension Phase shall extend until the earlier of (1) the Second Extension Option Trigger Event and (2) [**] following the end of the Extended Initial Phase, and, in such event, such period shall be deemed the "First Extension Period."

(E) For purposes of clarity, if the JRC confirms [**] Development Candidates nominated by Agios in the same Calendar Year prior to the end of the Extended Initial Phase, Agios shall be deemed to have met its obligation under this Section 3.3(b)(iii) to nominate at least [**] Development Candidates that the JRC confirms meet the Clinical Candidate Guidelines by the end of the Extended Initial Phase irrespective of whether Celgene defers (or has the right to defer) making the DC Commitment with respect to [**] pursuant to Section 3.6(d) below. In addition, if, during the Initial Phase (or, if applicable, the Extended Initial Phase):

(1) Celgene elects to unilaterally remove a Target from the Target List pursuant to Section 3.5(b) after a Development Candidate directed to such Target had been nominated by Agios and the JRC has not determined that such Development Candidate does not meet the Clinical Candidate Guidelines (as described in Section 3.6(b)(v)),

(2) Celgene elects to unilaterally remove a Target from the Target List within the [**] period prior to when a Development Candidate directed to such Target would have been nominated by Agios (as contemplated under the Discovery Plan); provided that the lead optimization chemical series in the Discovery Program related to such Target has demonstrated [**],

(3) Celgene decides to exercise its Celgene Program Option or to take a license early pursuant to Section 3.6(c) or Section 15.5, as applicable, to a Discovery Program under which a Development Candidate had been nominated by Agios prior to such early exercise,

(4) Celgene exercises its right pursuant to Section 14.2(a) to terminate for convenience any Discovery Program under which a Development Candidate had been nominated by Agios prior to such termination and the JRC has not determined that such Development Candidate does not meet the Clinical Candidate Guidelines (as described in Section 3.6(b)(v)), or

(5) Celgene terminates a Discovery Program for convenience within the [**] period prior to when a Development Candidate would have been nominated by Agios under such Discovery Program (as contemplated under the Discovery Plan); provided that the lead optimization chemical series in the Discovery Program related to such Target has demonstrated [**], then, in each of the foregoing cases, such nominated (or would-be nominated, as applicable) Development Candidate shall be counted as a Development Candidate that has been confirmed by the JRC as meeting the Clinical Candidate Guidelines for purposes of determining whether Agios has met its obligation under this Section 3.3(b) to nominate at least [**] Development Candidates that the JRC confirms meet the Clinical Candidate Guidelines.

(c) Second Extension Option. Celgene shall have the right to elect to extend the Option Term beyond the First Extension Phase ("Second Extension Option") for an additional [**] months following the end of the First Extension Phase ("Second Extension Phase"). Celgene may exercise the Second Extension Option by (i) providing written notice to Agios of such election, and (ii) paying to Agios [**] Dollars (US$[**]) within [**] days following the end of the First Extension Phase**.** Such written notice shall be provided at least [**] months prior to the end of the First Extension Phase (or within [**] days following the Second Extension Option Trigger Event, as applicable); provided that, if the Parties enter into the Extended Initial Phase and such Extended Initial Phase continues until [**] following the end of the original Initial Phase, then such notice need not be provided until at least [**] months prior to the end of the First Extension Phase.

(d) Option Term. The "Option Term" shall refer to the period commencing on the Effective Date and ending upon the earliest of (i) the expiration of the Initial Phase (or Extended Initial Phase, if applicable), if Celgene does not exercise the First Extension Option; (ii) the expiration of the First Extension Phase, if Celgene exercises the First Extension Option but does not exercise the Second Extension Option; and (iii) the expiration

of the Second Extension Phase, if Celgene exercises the Second Extension Option; provided that, notwithstanding the foregoing, if on the date of the events described in the foregoing clauses (i), (ii), and (iii), DC Selection Stage for a Development Candidate has been reached pursuant to Section 3.6(b)(ii) during the Option Term and the Celgene Program Option for such Development Candidate has not expired or been rejected, waived or not exercised within the applicable exercise period, then Celgene's right to exercise such Celgene Program Option will continue for such Development Candidate (and associated Discovery Program) beyond the end of the Option Term as set forth in Section 3.6 until such Celgene Program Option has been exercised or been rejected or waived (such extended period, the "Post-Option Extension," and the Discovery Program associated with such Development Candidate, the "Extended Program"). For purposes of clarity, except as provided in the proviso in the prior sentence or in Section 3.3(b)(iii), if Celgene does not provide written notice of election to Agios in a timely manner, the Option Term shall expire as of the end of the then-current Initial Phase (or Extended Initial Phase, if applicable), First Extension Phase or Second Extension Phase, as the case may be.

2. **Second Amendment Payment.** Article IX of the Agreement is hereby amended to include a new Section 9.1A as follows:

Section 9.1A Second Amendment Payment. In consideration of Agios' performance of its obligation under the Collaboration during the period commencing three (3) years following the Effective Date and ending four (4) years following the Effective Date pursuant to the Second Amendment to this Agreement, Celgene shall make a nonrefundable payment to Agios of Twenty Million Dollars (US$20,000,000) within [**] days following the effective date of the Second Amendment to this Agreement.

3. **Incorporation.** Article 15 of the Agreement is hereby incorporated *mutatis mutandis* into this Amendment.

4. **Effect on Agreement.** Except as specifically amended by this Second Amendment, the Agreement will remain in full force and effect and is hereby ratified and confirmed**.** To the extent a conflict arises between the terms of the Agreement and this Second Amendment, the terms of this Second Amendment shall prevail but only to the extent necessary to accomplish their intended purpose.

**[*Remainder of Page Intentionally Left Blank*]**

IN WITNESS WHEREOF, the Parties have executed this Second Amendment as of the Second Amendment Effective Date.

AGIOS PHARMACEUTICALS, INC.

By: /s/ David Schenkein
Title: CEO

CELGENE CORPORATION

By: /s/ Robert J. Hugin
Title: CEO

CELGENE CORPORATION

By: /s/ Robert J. Hugin
Title: CEO

CELGENE LEGAL

/s/ John [illegible]

**Exhibit 21.1**

Subsidiaries

| Entity | State of Incorporation or Organization |
| --- | --- |
| Agios Securities Corporation | Massachusetts |

**Exhibit 23.1**

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” and to the use of our report dated March 23, 2013 in the Registration Statement (Form S-1) and related Prospectus of Agios Pharmaceuticals, Inc. dated , 2013.

Boston, Massachusetts
, 2013

WILMERHALE

**R. Lee Schindler**

+1 617 526 6904 (t)
+1 617 526 5000 (f)
lee.schindler@wilmerhale.com

May 23, 2013

**CONFIDENTIAL SUBMISSION**

**VIA EDGAR**

U.S. Securities and Exchange Commission
Division of Corporate Finance
100 F Street, N.E.
Washington D.C. 20549

Re: Confidential Submission of Draft Form S-1 by Agios Pharmaceuticals, Inc.

Ladies and Gentlemen:

On behalf of Agios Pharmaceuticals, Inc. (the "Company"), we confidentially submit a draft Registration Statement on Form S-1 (the "Registration Statement") of the Company pursuant to Title I, Section 106 under the Jumpstart Our Business Startups Act of 2012 for non-public review by the Staff of the U.S. Securities and Exchange Commission (the "Staff") prior to the public filing of the Registration Statement.

Should members of the Staff have any questions or comments concerning this submission, please contact me at (617) 526-6904.

Best regards,

/s/ Lee Schindler

Lee Schindler

Enclosure