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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended June 30, 2018

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission file number 001-36014

AGIOS PHARMACEUTICALS, INC.
(Exact Name of Registrant as Specified in Its Charter)

Delaware	**26-0662915**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
88 Sidney Street, Cambridge, Massachusetts	**02139**
(Address of Principal Executive Offices)	**(Zip Code)**

(617) 649-8600
(Registrant's Telephone Number, Including Area Code)

(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

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

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

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

Number of shares of the registrant's Common Stock, $0.001 par value, outstanding on July 30, 2018: 57,992,576

AGIOS PHARMACEUTICALS, INC.

FORM 10-Q

FOR THE THREE AND SIX MONTHS ENDED JUNE 30, 2018

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements (Unaudited)

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Balance Sheets
(in thousands, except share and per share data)
(Unaudited)

	June 30, 2018	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 210,323	$ 102,724
Marketable securities	506,582	321,212
Collaboration receivable – related party	19,326	2,448
Collaboration receivable – other	440	—
Royalty receivable – related party	1,573	1,222
Prepaid expenses and other current assets	15,538	17,655
Total current assets	753,782	445,261
Marketable securities	219,724	143,814
Property and equipment, net	24,134	24,431
Other non-current assets	595	891
Total assets	$ 998,235	$ 614,397
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 17,320	$ 22,767
Accrued expenses	25,793	34,031
Deferred revenue – related party	41,132	37,842
Deferred rent	625	301
Total current liabilities	84,870	94,941
Deferred revenue, net of current portion – related party	72,408	125,798
Deferred rent, net of current portion	17,815	18,155
Total liabilities	175,093	238,894
Stockholders' equity:		
Preferred stock, $0.001 par value; 25,000,000 shares authorized; no shares issued or outstanding at June 30, 2018 and December 31, 2017	—	—
Common stock, $0.001 par value; 125,000,000 shares authorized; 57,932,639 and 48,826,153 shares issued and outstanding at June 30, 2018 and December 31, 2017, respectively	58	49
Additional paid-in capital	1,743,657	1,174,904
Accumulated other comprehensive loss	(2,398)	(1,389)
Accumulated deficit	(918,175)	(798,061)
Total stockholders' equity	823,142	375,503
Total liabilities and stockholders' equity	$ 998,235	$ 614,397

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Operations
(in thousands, except share and per share data)
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Collaboration revenue – related party	$ 26,401	$ 11,346	$ 33,746	21,854
Collaboration revenue – other	12,440	—	12,440	—
Royalty revenue – related party	1,573	—	2,990	—
Total revenue	40,414	11,346	49,176	21,854
Operating expenses:				
Research and development (net of $2,489 and $5,265 of cost reimbursement from related party for the three and six months ended June 30, 2017)	86,730	79,816	164,954	142,548
General and administrative	26,633	16,130	51,183	30,953
Total operating expenses	113,363	95,946	216,137	173,501
Loss from operations	(72,949)	(84,600)	(166,961)	(151,647)
Interest income	4,204	1,518	7,391	2,399
Net loss	$ (68,745)	$ (83,082)	$ (159,570)	$ (149,248)
Net loss per share – basic and diluted	$ (1.19)	$ (1.78)	$ (2.81)	$ (3.35)
Weighted-average number of common shares used in computing net loss per share – basic and diluted	57,721,786	46,745,760	56,713,795	44,525,478

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Comprehensive Loss
(in thousands)
(Unaudited)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Net loss	$ (68,745)	$ (83,082)	$ (159,570)	$ (149,248)
Other comprehensive income (loss)				
Unrealized gain (loss) on available-for-sale securities	245	(438)	(1,009)	(337)
Comprehensive loss	$ (68,500)	$ (83,520)	$ (160,579)	$ (149,585)

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Cash Flows
(in thousands)
(Unaudited)

	Six Months Ended June 30,	
	2018	**2017**
Operating activities		
Net loss	$ (159,570)	$ (149,248)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	3,464	3,164
Stock-based compensation expense	30,977	22,921
Net amortization of premium and discounts on investments	(1,291)	94
Loss on disposal of property and equipment	(20)	40
Changes in operating assets and liabilities:		
Collaboration receivable – related party	(16,878)	44
Collaboration receivable – other	(440)	—
Royalty receivable – related party	(351)	—
Tenant improvement and other receivables	—	2,638
Prepaid expenses and other current and non-current assets	2,413	(2,417)
Accounts payable	(6,198)	4,930
Accrued expenses	(7,841)	(2,392)
Deferred revenue – related party	(10,644)	(11,184)
Deferred rent	(16)	(1,653)
Net cash used in operating activities	(166,395)	(133,063)
Investing activities		
Purchases of marketable securities	(592,664)	(468,556)
Proceeds from maturities and sales of marketable securities	331,666	303,711
Purchases of property and equipment	(2,793)	(1,328)
Net cash used in investing activities	(263,791)	(166,173)
Financing activities		
Payment of public offering costs, net of reimbursements	(391)	104
Proceeds from public offering of common stock, net of commissions	516,206	270,250
Net proceeds from stock option exercises and employee stock purchase plan	21,970	6,845
Net cash provided by financing activities	537,785	277,199
Net change in cash and cash equivalents	107,599	(22,037)
Cash and cash equivalents at beginning of the period	102,724	160,754
Cash and cash equivalents at end of the period	$ 210,323	$ 138,717
Supplemental disclosure of non-cash investing and financing transactions		
Additions to property and equipment in accounts payable and accrued expenses	$ 1,365	$ 1,383
Proceeds from stock option exercises in other current assets	$ —	$ 3
Public offering costs in other receivables, net of amounts in accounts payable and accrued expenses	$ —	$ 125

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Notes to Condensed Consolidated Financial Statements
(Unaudited)

1. Overview and Basis of Presentation

References to Agios

Throughout this Quarterly Report on Form 10-Q, "we," "us," and "our," and similar expressions, except where the context requires otherwise, refer to Agios Pharmaceuticals, Inc. and its consolidated subsidiaries, and "our Board of Directors" refers to the board of directors of Agios Pharmaceuticals, Inc.

Overview

We are a biopharmaceutical company committed to the fundamental transformation of patients' lives through scientific leadership in the field of cellular metabolism, with the goal of making transformative, first- or best-in-class medicines. Our therapeutic areas of focus are cancer and rare genetic diseases, or RGDs, which are diseases that are directly caused by changes in genes or chromosomes, often passed from one generation to the next. Most RGDs are often associated with severe or life-threatening features. The incidence of a single RGD can vary widely but is generally very infrequent, usually equal to or less than one per 100,000 births. In both areas of cancer and RGDs, we are seeking to unlock the biology of cellular metabolism as a platform to create transformative therapies. We are located in Cambridge, Massachusetts.

Basis of presentation

The condensed consolidated balance sheet as of June 30, 2018, the condensed consolidated statements of operations and comprehensive loss for the three and six months ended June 30, 2018 and 2017, and cash flows for the six months ended June 30, 2018 and 2017 are unaudited. The unaudited condensed consolidated financial statements have been prepared on the same basis as the annual financial statements and, in the opinion of our management, reflect all adjustments, which include only normal recurring adjustments, necessary to fairly state our financial position as of June 30, 2018, our results of operations for the three and six months ended June 30, 2018 and 2017, and cash flows for the six months ended June 30, 2018 and 2017. The financial data and the other financial information disclosed in these notes to the condensed consolidated financial statements related to the three and six-month period are also unaudited. The results of operations for the three and six months ended June 30, 2018 are not necessarily indicative of the results to be expected for the year ending December 31, 2018 or for any other future annual or interim period. The year-end condensed consolidated balance sheet data was derived from our audited financial statements, but does not include all disclosures required by U.S. generally accepted accounting principles, or U.S. GAAP. Accordingly, the condensed consolidated interim financial statements should be read in conjunction with the audited consolidated financial statements and notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2017 that was filed with the Securities and Exchange Commission, or the SEC, on February 14, 2018.

Our condensed consolidated financial statements include our accounts and the accounts of our wholly owned subsidiaries, Agios Securities Corporation, Agios International Sarl, and Agios Limited. All intercompany transactions have been eliminated in consolidation. The consolidated financial statements have been prepared in conformity with U.S. GAAP.

Liquidity

In January 2018, we completed a public offering of 8,152,986 shares of common stock at an offering price of $67.00 per share. We received net proceeds from this offering of $516.2 million, after deducting underwriting discounts and commissions paid by us.

As of June 30, 2018, we had cash, cash equivalents and marketable securities of $936.6 million. Although we have incurred recurring losses and expect to continue to incur losses for the foreseeable future, we expect our cash, cash equivalents and marketable securities will be sufficient to fund current operations for at least the next twelve months from the issuance date of these financial statements.

2. Summary of Significant Accounting Policies and Recent Accounting Pronouncements

Significant accounting policies

Revenue from Contracts with Customers

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-09, Revenue from Contracts with Customers (Topic 606), which was codified as Accounting Standards Codification 606, Revenue from Contracts with Customers, or ASC 606, and amended through subsequent ASUs. We adopted ASC 606 effective January

1, 2018 using the modified retrospective method. Under this method, we recognized the cumulative effect of the change in the opening balance of accumulated deficit in the current period condensed consolidated balance sheet.

In adopting ASC 606, we applied the practical expedient that permits aggregating the effect of all modifications that occurred prior to January 1, 2018. No other practical expedients were used.

Upon finalization of our assessment, which resulted in changes to our estimates as of December 31, 2017, the impact of the cumulative effect of the accounting changes upon the adoption of the standard (in thousands) is as follows:

	December 31, 2017	Cumulative Effect	January 1, 2018
Deferred revenue – related party, current and net of current portions	$ 163,640	$ (39,456)	$ 124,184
Accumulated deficit	(798,061)	39,456	(758,605)

The following tables summarize the effects of adopting ASC 606 on our unaudited condensed consolidated financial statements (in thousands, except per share data):

Condensed Consolidated Balance Sheets

	June 30, 2018		
	Under Topic 606	Under Topic 605	Effect of Change
Collaboration receivable – related party	$ 19,326	$ 19,326	$ —
Collaboration receivable – other	440	—	440
Deferred revenue – related party	41,132	35,204	5,928
Deferred revenue, net of current portion – related party	72,408	113,516	(41,108)
Accumulated deficit	(918,175)	(953,795)	35,620

Condensed Consolidated Statements of Operations

	Three Months Ended June 30, 2018			Six Months Ended June 30, 2018		
	Under Topic 606	Under Topic 605	Effect of Change	Under Topic 606	Under Topic 605	Effect of Change
Collaboration revenue – related party	$ 26,401	$ 25,982	$ 419	$ 33,746	$ 35,959	$ (2,213)
Collaboration revenue – other	12,440	12,000	440	12,440	12,000	440
Research and development expense	86,730	85,078	1,652	164,954	162,891	2,063
Total operating expenses	113,363	111,711	1,652	216,137	214,074	2,063
Loss from operations	(72,949)	(72,156)	(793)	(166,961)	(163,125)	(3,836)
Net loss	(68,745)	(67,952)	(793)	(159,570)	(155,734)	(3,836)
Net loss per share – basic and diluted	(1.19)	(1.18)	(0.01)	(2.81)	(2.75)	(0.06)

Condensed Consolidated Statements of Comprehensive (Loss) Income

	Three Months Ended June 30, 2018			Six Months Ended June 30, 2018		
	Under Topic 606	Under Topic 605	Effect of Change	Under Topic 606	Under Topic 605	Effect of Change
Net loss	$ (68,745)	$ (67,952)	$ (793)	$ (159,570)	$ (155,734)	$ (3,836)
Comprehensive loss	(68,500)	(67,707)	(793)	(160,579)	(156,743)	(3,836)

Condensed Consolidated Statements of Cash Flows

	Six Months Ended June 30, 2018		
	Under Topic 606	Under Topic 605	Effect of Change
Net loss	$ (159,570)	$ (155,734)	$ (3,836)
Adjustments to reconcile net loss to net cash used in operating activities:			
Collaboration receivable – related party	(16,878)	(16,878)	—
Collaboration receivable – other	(440)	—	(440)
Deferred revenue – related party	(10,644)	(14,920)	4,276

Recent accounting pronouncements

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, or ASU 2016-02, which establishes principles that lessees and lessors shall apply to report useful information to users of financial statements about the amount, timing and uncertainty of cash flows arising from a lease. ASU 2016-02 was codified as ASC 842, *Leases*. Subsequently, the FASB issued ASU 2017-13, *Revenue Recognition (Topic 605), Revenue from Contracts with Customers (Topic 606), Leases (Topic 840), and Leases (Topic 842): Amendments to SEC Paragraphs Pursuant to the Staff Announcement at the July 20, 2017 EITF Meeting and Rescission of Prior SEC Staff Announcements and Observer Comments (SEC Update)*, which codifies recent announcements by the SEC staff; ASU 2018-01, *Leases (Topic 842): Land Easement Practical Expedient for Transition to Topic 842*, which provides a transition practical expedient for existing or expired land easements; ASU 2018-10, *Codification Improvements to Topic 842, Leases*, which provides amendments to further clarify and improve sections of ASU 2016-02; and ASU 2018-11, *Leases (Topic 842): Targeted Improvements*, which provides an additional transition method. These ASUs, collectively with ASU 2016-02, are referred to as the Leases ASUs.

We will adopt ASC 842 effective January 1, 2019. We are currently in the process of evaluating the impact of the guidance on our consolidated financial statements.

Other accounting standards that have been issued by the FASB or other standards-setting bodies that do not require adoption until a future date are not expected to have a material impact on our financial statements upon adoption.

3. Fair Value Measurements

We record cash equivalents and marketable securities at fair value. ASC 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 our 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, directly or indirectly, for substantially the full term of the asset or liability.

Level 3 – Unobservable inputs that reflect our 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 our cash equivalents and marketable securities measured at fair value on a recurring basis as of June 30, 2018 (in thousands):

	Level 1	Level 2	Level 3	Total
Cash equivalents	$ 193,755	$ 16,206	$ —	$ 209,961
Marketable securities:				
Certificates of deposit	—	1,670	—	1,670
U.S. Treasuries	—	258,117	—	258,117
Government securities	—	111,695	—	111,695
Corporate debt securities	—	354,824	—	354,824
Total cash equivalents and marketable securities	$ 193,755	$ 742,512	$ —	$ 936,267

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. After completing our validation procedures, we did not adjust or override any fair value measurements provided by the pricing services as of June 30, 2018.

There have been no changes to the valuation methods during the six months ended June 30, 2018. We evaluate transfers between levels at the end of each reporting period. There were no transfers between Level 1 and Level 2 during the six months ended June 30, 2018. We have no financial assets or liabilities that were classified as Level 3 at any point during the six months ended June 30, 2018.

4. Marketable Securities

Our marketable securities are classified as available-for-sale pursuant to ASC 320, *Investments – Debt and Equity Securities*, and are recorded at fair value, with unrealized gains and losses included as a component of accumulated other comprehensive

loss other comprehensive loss in stockholders' equity and a component of total comprehensive loss in the condensed consolidated statements of comprehensive loss, until realized. 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 three and six months ended June 30, 2018 and 2017 and, as a result, there were no reclassifications of any amounts out of accumulated other comprehensive loss for those periods.

Marketable securities at June 30, 2018 consisted of the following (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
Certificates of deposit	$ 1,440	$ —	$ (6)	$ 1,434
U.S Treasuries	226,668	4	(245)	226,427
Government securities	64,585	—	(148)	64,437
Corporate debt securities	214,677	—	(393)	214,284
Non-current:				
Certificates of deposit	239	—	(3)	236
U.S Treasuries	31,997	—	(307)	31,690
Government securities	47,534	—	(276)	47,258
Corporate debt securities	141,564	—	(1,024)	140,540
Total marketable securities	$ 728,704	$ 4	$ (2,402)	$ 726,306

Marketable securities at December 31, 2017 consisted of the following (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
Certificates of deposit	$ 8,081	$ —	$ (11)	$ 8,070
U.S. Treasuries	113,852	—	(119)	113,733
Government securities	44,421	—	(57)	44,364
Corporate debt securities	155,222	—	(177)	155,045
Non-current:				
Certificates of deposit	960	—	(8)	952
U.S. Treasuries	36,165	—	(311)	35,854
Government securities	23,992	—	(182)	23,810
Corporate debt securities	83,722	—	(524)	83,198
Total marketable securities	$ 466,415	$ —	$ (1,389)	$ 465,026

At June 30, 2018 and December 31, 2017, we held both current and non-current investments. Investments classified as current have maturities of less than one year. Investments classified as non-current are those that: (i) have a maturity of one year to two years, and (ii) we do not intend to liquidate within the next twelve months, although these funds are available for use and therefore classified as available-for-sale.

At June 30, 2018 and December 31, 2017, we held 246 and 240 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 June 30, 2018 and December 31, 2017 was $616.5 million and $439.4 million, respectively. There were no individual securities that were in a significant unrealized loss position as of June 30, 2018 and December 31, 2017. Given our intent and ability to hold such securities until recovery, and the lack of material of change in the credit risk of these investments, we do not consider these marketable securities to be other-than-temporarily impaired as of June 30, 2018 and December 31, 2017.

5. Collaboration and License Agreements

Celgene Corporation

To date, our revenue has primarily been generated from our collaboration agreements with Celgene, or collectively, the Collaboration Agreements. Celgene is a related party through ownership of our common stock. In April 2010, we entered into a discovery and development collaboration and license agreement focused on cancer metabolism, or the 2010 Agreement. The

2010 Agreement was amended in October 2011 and July 2014. In April 2015, we entered into a joint worldwide development and profit share collaboration and license agreement with Celgene, and our wholly owned subsidiary, Agios International Sarl, entered into a collaboration and license agreement with Celgene International II Sarl, or collectively, the AG-881 Agreements, to establish a worldwide collaboration focused on the development and commercialization of AG-881 products. In May 2016, we entered into a master research and collaboration agreement with Celgene, or the 2016 Agreement.

2016 Agreement

In May 2016, we entered into the 2016 Agreement focused on metabolic immuno-oncology, or MIO, a developing field which aims to modulate the activity of relevant immune cells by targeting critical metabolic nodes, thereby, enhancing the immune mediated anti-tumor response. In addition to new programs identified under the 2016 Agreement, both parties also agreed that all future development and commercialization of two remaining cancer metabolism programs discovered under the 2010 Agreement, including AG-270, an inhibitor of methionine adenosyltransferase 2a, will now be governed by the 2016 Agreement.

During the research term of the 2016 Agreement, we plan to conduct research programs focused on discovering compounds that are active against metabolic targets in the immuno-oncology, or IO, field. The initial four-year research term will expire on May 17, 2020, and may be extended for up to two, or in specified cases, up to four additional one-year terms.

For each program under the 2016 Agreement, we may nominate compounds that meet specified criteria as development candidates and, in limited circumstances, Celgene may also nominate compounds as development candidates for each such program. Celgene may designate the applicable program for further development following any such nomination, after which we may conduct, at our expense, additional preclinical and clinical development for such program through the completion of an initial phase 1 dose escalation study.

At the end of the research term, Celgene may designate for continued development up to three research programs for which development candidates have yet to be nominated, which are referred to as continuation programs. We may conduct further research and preclinical and clinical development activities on any continuation program, at our expense, through the completion of an initial phase 1 dose escalation study.

We granted Celgene the right to obtain exclusive options for development and commercialization rights for each program that Celgene has designated for further development, and for each continuation program. Celgene may exercise each such option beginning on the designation of a development candidate for such program (or on the designation of such program as a continuation program) and ending on the earlier of: (i) the end of a specified period after we have furnished Celgene with specified information about the initial phase 1 dose escalation study for such program, or (ii) January 1, 2030. Research programs that have applications in the inflammation or autoimmune, or I&I, field that may result from the 2016 Agreement will also be subject to the exclusive options described above.

We will retain rights to any program that Celgene does not designate for further development or as to which it does not exercise its option.

Under the terms of the 2016 Agreement, following Celgene’s exercise of its option with respect to a program, the parties will enter into either a co-development and co-commercialization agreement if such program is in the IO field, or a license agreement if such program is in the I&I field. Under each co-development and co-commercialization agreement, the two parties will co-develop and co-commercialize licensed products worldwide. Either we or Celgene will lead development and commercialization of licensed products for the United States, and Celgene will lead development and commercialization of licensed products outside of the United States. Depending on the country, the parties will each have the right to provide a portion of field-based marketing activities. Under each license agreement, Celgene will have the sole right to develop and commercialize licensed products worldwide.

Co-development and co-commercialization agreements

Under each co-development and co-commercialization agreement entered into under the 2016 Agreement, the parties will split all post-option exercise worldwide development costs, subject to specified exceptions, as well as any profits from any net sales of, or commercialization losses related to, licensed products in the IO field. Celgene has the option to designate one program in the IO field as the 65/35 program, for which Celgene will be the lead party for the United States and will have a 65% profit or loss share. For programs in the IO field other than the 65/35 program, we and Celgene will alternate, on a program-by-program basis, being the lead party for the United States, with us having the right to be the lead party for the first such program, and each party will have a 50% profit or loss share. The lead party for the United States will book commercial sales of licensed products, if any, in the United States, and Celgene will book commercial sales of licensed products, if any, outside of the United States.

License agreements

Under each license agreement under the 2016 Agreement, Celgene will be responsible for all post-option exercise worldwide development and associated costs, subject to specified exceptions, as well as worldwide commercialization and associated costs, for licensed products in the I&I field.

Financial terms

Under the terms of the 2016 Agreement, we received an initial upfront payment in the amount of $200.0 million. The 2016 Agreement provides specified rights to extend the research term for up to two, or in specified cases, up to four, additional years by paying a $40.0 million per-year extension fee. Celgene will pay an $8.0 million designation fee for each program that Celgene designates for further development and for each continuation program. During the three months ended March 31, 2017, we received $8.0 million from Celgene upon the designation of AG-270 as a development candidate. For each program as to which Celgene exercises its option to develop and commercialize, subject to antitrust clearance, Celgene will pay an option exercise fee of at least $30.0 million for any designated development program and at least $35.0 million for any continuation programs. In certain cases, Celgene may exercise its option to develop and commercialize two early-stage I&I programs, prior to Celgene designating the program for further development, by paying an option exercise fee of $10.0 million.

We are eligible to receive the following milestone-based payments associated with the 2016 Agreement:

Program	Milestone	Amount
65/35 program in IO field	Specified clinical development event	25 million
65/35 program in IO field	Specified regulatory milestone events	Up to $183.8 million
50/50 program in IO field	Specified clinical development event	$20.0 million
50/50 program in IO field	Specified regulatory milestone events	Up to $148.8 million
I&I field	Specified clinical development event	25.0 million
I&I field	Specified regulatory milestone events	Up to $236.3 million
I&I field	Specified commercial milestone events	Up to $125.0 million

Additionally, for each licensed program in the I&I field, we are eligible to receive royalties at tiered, low double-digit percentage rates on Celgene's net sales, if any.

Opt-out right

Under the 2016 Agreement, we may elect to opt out of the cost and profit share under any co-development and co-commercialization agreement, subject to specified exceptions. Upon opting out, Celgene will have the sole right to develop, manufacture and commercialize the applicable licensed products throughout the world, at its cost, and we will undertake transitional activities reasonably necessary to transfer the development, manufacture and commercialization of such licensed products to Celgene, at our expense. Further, in lieu of the profit or loss sharing described above, we would be eligible to receive royalties at tiered, low double-digit percentage rates on Celgene's net sales, if any, of the applicable licensed products. However, we would continue to be eligible to receive the developmental and regulatory milestone-based payments described above.

Term

The term of the 2016 Agreement commenced on May 17, 2016 and, if not terminated earlier, will expire upon the later of the last-to-expire of the research term and all option exercise periods, or, if an option is exercised by Celgene for one or more programs in the collaboration, upon the termination or expiration of the last-to-exist co-development and co-commercialization agreement or license agreement, as applicable, for any such program.

Termination

Subject to specified exceptions, Celgene may terminate the 2016 Agreement in its entirety for any reason by providing us with prior written notice if there are no active co-development and co-commercialization agreements or license agreements in place or on a program-by-program basis if there are no active co-development and co-commercialization agreements or license agreements in place for the terminated program(s). Either party may terminate the 2016 Agreement for the insolvency of the other party. On a program-by-program basis, prior to the exercise of an option, either party may terminate the 2016 Agreement either in its entirety or with respect to one or more programs on prior written notice to the other party in the case of an uncured material breach by the other party that frustrates the fundamental purpose of the 2016 Agreement. Following the exercise of an option for a program, either party may terminate the 2016 Agreement with respect to such program if such party terminates the co-development and co-commercialization agreement or license agreement for such program for an uncured material breach by the other party that frustrates the fundamental purpose of such agreement. Either party may terminate a co-development and co-

commercialization agreement or a license agreement upon the bankruptcy or insolvency of the other party. Either party also has the right to terminate the co-development and co-commercialization agreement or license agreement if the other party or any of its affiliates challenges the validity, scope or enforceability of or otherwise opposes, any patent included within the intellectual property rights licensed to the other party under such agreement.

Exclusivity

While any of Celgene's options remain available under the 2016 Agreement, subject to specified exceptions, we may not directly or indirectly develop, manufacture or commercialize, outside of the 2016 Agreement, any therapeutic modality in the IO or I&I field with specified activity against a metabolic target.

During the term of each co-development and co-commercialization agreement and license agreement, subject to specified exceptions, neither we nor Celgene may directly or indirectly develop, manufacture or commercialize outside of such agreement any therapeutic modality in any field with specified activity against the metabolic target that is the focus of the program licensed under such agreement.

TIBSOVO® Letter Agreement

In May 2016, we entered into a letter agreement with Celgene regarding TIBSOVO®, or the TIBSOVO® Letter Agreement. Under the TIBSOVO® Letter Agreement, the parties agreed to terminate the 2010 Agreement, effective as of August 15, 2016, as to the program directed to the isocitrate dehydrogenase 1, or IDH1, target, for which TIBSOVO® is the lead development candidate. Under the 2010 Agreement, Celgene had held development and commercialization rights to the IDH1 program outside of the United States, and we held such rights inside the United States. As a result of the termination, we obtained global rights to TIBSOVO® and the IDH1 program. Neither party will have any further financial obligation, including royalties or milestone payments, to the other concerning TIBSOVO® or the IDH1 program. Under the terms of the termination, the parties also agreed to conduct specified transitional activities in connection with the termination. In addition, pursuant to the TIBSOVO® Letter Agreement, the parties are released from their exclusivity obligations under the 2010 Agreement with respect to the IDH1 program. The termination does not affect the AG-881 Agreements, which are directed to both the IDH1 target and the isocitrate dehydrogenase 2, or IDH2, target.

AG-881 Agreements

In April 2015, we entered into the AG-881 Agreements. The AG-881 Agreements establish a joint worldwide collaboration focused on the development and commercialization of AG-881 products. Under the terms of the AG-881 Agreements, we received an initial upfront payment of $10.0 million in May 2015 and are eligible to receive milestone-based payments described below. The parties will split all worldwide development costs equally, subject to specified exceptions, as well as any profits from any net sales of, or commercialization losses related to, licensed AG-881 products. Either party may, at its own expense and with the other party's permission, undertake additional development activities outside of the scope of the development plan agreed upon with the other party.

We are eligible to receive up to $70.0 million in potential milestone payments under the AG-881 Agreements. The potential milestone payments are comprised of: (i) a $15.0 million milestone payment for filing of a first new drug application, or NDA, in a major market, and (ii) up to $55.0 million in milestone payments upon achievement of specified regulatory milestone events. We may also receive royalties at tiered, low-double digit to mid-teen percentage rates on net sales if we elect not to participate in the development and commercialization of AG-881.

Termination

Celgene may terminate the AG-881 Agreements in their entirety for any reason upon ninety days written notice to us. Either party may terminate the AG-881 Agreements for the insolvency of the other party. Either party may terminate the AG-881 Agreements in their entirety or with respect to one of the agreements upon prior written notice to the other party in the case of an uncured material breach by the other party that frustrates the fundamental purpose of the AG-881 Agreements. If one of the AG-881 Agreements terminates, the other will terminate automatically.

2010 Agreement

In April 2010, we entered into the 2010 Agreement, which was amended in October 2011 and July 2014. The goal of the collaboration was to discover, develop and commercialize disease-altering therapies in oncology based on our cancer metabolism research platform. We initially led discovery, preclinical and early clinical development for all cancer metabolism programs under the collaboration. The discovery phase of the 2010 Agreement expired in April 2016.

Upon agreement to terminate the 2010 Agreement, effective as of August 15, 2016, as to the program directed to the IDH1 target, for which TIBSOVO® is the lead development candidate, the sole program remaining under the 2010 Agreement is IDHIFA®, a co-commercialized licensed program for which Celgene leads and funds global development and commercialization activities. We have exercised our right to participate in a portion of commercialization activities in the

United States for IDHIFA® in accordance with the applicable commercialization plan. On August 1, 2017, the U.S. Food and Drug Administration, or FDA, granted Celgene approval of IDHIFA® for the treatment of adult patients with relapsed or refractory acute myeloid leukemia, or R/R AML, with an IDH2 mutation as detected by an FDA-approved test.

During the three months ended June 30, 2018, Celgene submitted a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, for IDHIFA® for IDH2 mutant-positive R/R AML. As a result of the filing, we determined that a $15.0 million milestone payment for filing of a first new drug application equivalent in an ex-U.S. country is considered probable of being reached and a significant reversal of revenue would not occur in future periods. Under the remaining terms of the 2010 Agreement, we are eligible to receive up to $95.0 million in potential milestone payments for the IDHIFA® program. The potential milestone payments are comprised of: (i) up to $70.0 million in milestone payments upon achievement of specified ex-U.S. regulatory milestone events, including the aforementioned $15.0 million milestone for the MAA submission, and (ii) a $25.0 million milestone payment upon achievement of a specified ex-U.S. commercial milestone event.

Under the 2010 Agreement, we receive royalties at tiered, low-double digit to mid-teen percentage rates on net sales of IDHIFA®.

Unless terminated earlier by either party, the term of the 2010 Agreement will continue until the expiration of all royalty terms with respect to IDHIFA®. Celgene may terminate this agreement for convenience in its entirety upon ninety days written notice to us. If either party is in material breach and fails to cure such breach within the specified cure period, the other party may terminate the 2010 Agreement in its entirety. Either party may terminate the agreement in the event of specified insolvency events involving the other party.

Accounting analysis and revenue recognition – collaboration revenue

On January 1, 2018 we adopted ASC 606 under the modified retrospective method. Prior to January 1, 2018 we accounted for the Collaboration Agreements under ASC 605-25, *Multiple Element Arrangements.*

Accounting under ASC 606

In adopting ASC 606, we applied the practical expedient that permits aggregating the effect of all modifications that occurred prior to January 1, 2018. No other practical expedients were used. Similar to the accounting under ASC 605-25, the 2016 Agreement was determined to be a modification of the 2010 Agreement and the AG-881 Agreements. In determining the appropriate amount of revenue to be recognized under ASC 606, we performed the following steps: (i) identified the promised goods or services in the contract; (ii) determined whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measured the transaction price, including the constraint on variable consideration; (iv) allocated the transaction price to the performance obligations; and (v) recognized revenue when (or as) we satisfied each performance obligation.

As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price, or SSP, for each performance obligation identified in the contract. We use key assumptions to determine the SSP, which include forecast of revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

The satisfied and unsatisfied performance obligations at the time of the ASC 606 adoption, each of which are considered by us to be distinct within the context of the contract, their SSP, the method of recognizing the allocated consideration, and the period through which they are expected to be recognized are as follows:

Performance Obligations		SSP	No. of Performance Obligation(s)	Recognition Method
Fully satisfied at time of adoption				
Licenses (1)		$86.7 million	4	Fully satisfied; recognized upon adoption of ASC 606
Research and development services (2) (3)		$350.7 million	10	Fully satisfied; recognized upon adoption of ASC 606
Partially satisfied at time of adoption				
Research and development services (2) (3)	$ 266.6	$266.6 million	6	Proportionally as services are delivered over the performance period, expected to be through September 2022 (4)

(1) The SSP was developed by probability weighting multiple cash flow scenarios using the income approach. Our management estimates within the models include the expected, probability-weighted net profits from estimated future sales, an estimate of the direct cost incurred to generate future cash flows, a discount rate and other business forecast factors. There are significant judgments and estimates inherent in the determination of the SSP of these units of accounting. These judgments and estimates include assumptions regarding future operating performance, the timelines of the clinical trials and regulatory approvals, and other factors. If different reasonable assumptions are utilized, the SSP and revenue recognized would vary.

(2) The SSP was developed using our management's best estimate of the cost of obtaining these services at arm's length from a third-party provider.
(3) The SSP was developed using internal full time equivalent costs to support the development services.
(4) We determined that recognizing revenue on a proportional basis using the ratio of effort incurred to date compared to the total estimated effort required to complete the performance obligation best depicts the satisfaction of our obligations under the Collaboration Agreements.

During the three and six months ended June 30, 2018, we recognized the following as collaboration revenue (in thousands):

	Three Months Ended June 30, 2018			Six Months Ended June 30, 2018		
Performance Obligation	**Under Topic 606**	**Under Topic 605**	**Effect of Change**	**Under Topic 606**	**Under Topic 605**	**Effect of Change**
Collaboration revenue - related party						
Licenses	$ 15,000	$ 15,000	$ —	$ 15,000	$ 15,000	$ —
Research and development services	9,830	9,367	463	16,194	18,320	(2,126)
Committee participations	—	44	(44)	—	87	(87)
Reduction of research and development expenses						
Development services	—	1,652	(1,652)	—	2,063	(2,063)

During the three and six months ended June 30, 2018 and 2017, we recognized as collaboration revenue the following non-contingent consideration allocated to each performance obligation (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	**2017**	**2018**	**2017**
Licenses	$ 15,000	$ —	$ 15,000	$ —
On-going research and development services	$ 9,830	$ 10,279	$ 16,194	$ 20,666
Committee participations	—	41	—	83

During the three and six months ended June 30, 2017, we recognized $2.5 million and $5.3 million, respectively, as a reduction of research and development expenses. During the three and six months ended June 30, 2018, we did not recognize any reductions to research and development expenses.

Consideration for development and commercialization services performed by us, that were not considered performance obligations as of the modification dates, are recognized as collaboration revenue or a reduction of research and development expenses in the period in which they are earned. There was no impact from the adoption of ASC 606 on these obligations. For the three and six months ended June 30, 2018 and 2017, we recognized the following collaboration revenue and reduction of research and development expenses related to such expenses (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	**2017**	**2018**	**2017**
Collaboration revenue - related party				
Development activities	$ 590	$ —	$ 590	$ —
Commercialization activities	981	1,026	1,962	1,105
Reduction of research and development expenses				
Research and development activities	—	—	—	14

For the three and six months ended June 30, 2018 and 2017, we recognized the following totals of collaboration revenue and reduction of research and development expenses (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	**2017**	**2018**	**2017**
Collaboration revenue - related party	$ 26,401	$ 11,346	$ 33,746	$ 21,854
Reduction of research and development expenses	—	2,489	—	5,265

The following table presents changes in our contract assets and liabilities during the six months ended June 30, 2018 (in thousands):

	December 31, 2017	Additions	Deductions	June 30, 2018
Contract assets (1)				
Collaboration receivable – related party	$ 2,448	$ 22,838	$ (5,960)	$ 19,326
Royalty receivable – related party	1,222	$ 2,990	$ (2,639)	$ 1,573
Contract liabilities (2)				
Deferred revenue – related party, current and net of current portions	$ 163,640	5,839	(55,939)	113,540

(1) Additions to contract assets relate to amounts billed to Celgene for reimbursable costs incurred by us during the reporting period. Deductions to contract assets relate to collection of receivables during the reporting period.
(2) Additions to contract liabilities relate to consideration from Celgene during the reporting period. Deductions to contract liabilities relate to deferred revenue recognized as revenue during the reporting period and cumulative catch-up adjustment recognized upon adoption of ASC 606 on January 1, 2018.

During the three and six months ended June 30, 2018, we recognized the following as revenue due to changes in the contract liability balances (in thousands):

	June 30, 2018	
	Three Months Ended	Six Months Ended
Amounts included in the contract liability at the beginning of the period	$ 9,932	$ 15,917
Performance obligations satisfied in previous periods	220	543

As of June 30, 2018, the aggregate amount of the transaction price allocated to performance obligations that are partially unsatisfied was $121.8 million.

We consider the total consideration expected to be earned in the next twelve months for services to be performed as current deferred revenue, and consideration that is expected to be earned subsequent to twelve months from the balance sheet date as non-current deferred revenue.

Accounting analysis and revenue recognition – royalty revenue

For arrangements that include sales-based royalties and sales-based milestones and in which the license is deemed to be the predominant item to which the royalties relate, we recognize royalty revenue upon the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

As the underlying performance obligation, or delivery of the license to IDHIFA®, had been satisfied as of June 2014, royalty revenue is recognized as the related sales occur. During the three and six months ended June 30, 2018, we earned $1.6 million and $3.0 million, respectively, in royalty revenue under the 2010 Agreement.

Accounting analysis and revenue recognition – milestone revenue

At each reporting period we evaluate whether milestones are considered probable of being reached and, to the extent that a significant reversal would not occur in future periods, estimate the amount to be included in the transaction price using the most likely amount method. Milestone payments that are not within our control, such as regulatory approvals, are not considered probable of being achieved and are excluded from the transaction price until those approvals are received.

During the three months ended June 30, 2018, Celgene submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive R/R AML. As a result of the filing, we determined that a $15.0 million milestone payment, which is unbilled as of June 30, 2018, for filing of a first new drug application equivalent in an ex-U.S. country is considered probable of being reached and a significant reversal of revenue would not occur in future periods. As the underlying performance obligation, or delivery of the license to IDHIFA, had been satisfied as of June 2014, the milestone payment was recognized in full as collaboration revenue during the three months ended June 30, 2018.

No other milestones were achieved during the three and six months ended June 30, 2018. The next potential milestone expected to be achieved under our collaboration agreements with Celgene is the first regulatory approval in any of China, Japan or a major European country. Achievement of this event will result in milestone payments of $35.0 million under the 2010 Agreement.

CStone Pharmaceuticals

In June 2018, we entered into an exclusive license agreement, or the CStone Agreement, with CStone Pharmaceuticals, or CStone, to grant CStone specified intellectual property licenses to enable CStone to develop and commercialize certain products containing TIBSOVO® in mainland China, Hong Kong, Macau, and Taiwan. We retain development and commercialization rights with respect to TIBSOVO® for the rest of the world. Pursuant to the CStone Agreement, CStone will initially be responsible for the development and commercialization of TIBSOVO® in acute myeloid leukemia, or AML, cholangiocarcinoma, and, at our discretion, brain cancer indications.

Under the terms of the CStone Agreement,we received an initial upfront payment in the amount of $12.0 million and are entitled to receive up to an additional $412.0 million in milestone payments upon the achievement of certain development, regulatory and sales milestone events. Approximately half of the milestone payments are related to the development and commercialization of TIBSOVO® in AML, cholangiocarcinoma and the other half of the milestone payments are related to brain cancer indications, including glioma. We will also be entitled to receive tiered royalties, ranging from 15 to 19 percent, on annual net sales, if any, of TIBSOVO®.

CStone is responsible for all costs it incurs in developing, obtaining regulatory approval of, and commercializing TIBSOVO® in China, Hong Kong, Macau, and Taiwan, as well as certain costs incurred by us.

During the term of the CStone Agreement, each party and its affiliates are prohibited from developing or commercializing any other compound or product that inhibits IDH1 mutations at specified levels of binding, in the case of CStone, anywhere in the world, and in our case, in China, Hong Kong, Macau, and Taiwan.

Termination

Unless earlier terminated, the CStone Agreement will expire upon the expiration of the last royalty term for the last licensed product within the scope of the CStone Agreement. At any time after CStone has obtained regulatory approval in mainland China in R/R AML and the last patient has been enrolled in a specified clinical trial (or, if earlier, at any time that CStone acquires or is acquired by an entity with a competing or restricted product), CStone may terminate the CStone Agreement in its entirety by providing us with prior written notice. Either party may, subject to specified cure periods, terminate the CStone Agreement in the event of the other party's uncured material breach. Either party may terminate the CStone Agreement under specified circumstances relating to the other party's insolvency. We have the right to terminate the CStone Agreement immediately if CStone or its affiliates or sublicensees or subcontractors challenges the validity, patentability, or enforceability of certain patent rights that relate to TIBSOVO® and are owned by or licensed to us or our affiliates.

Accounting analysis and revenue recognition - collaboration revenue

The CStone Agreement was determined to be within the scope of ASC 606. Accordingly, in determining the appropriate amount of revenue to be recognized, we performed the following steps: (i) identified the promised goods or services in the contract; (ii) determined whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measured the transaction price, including the constraint on variable consideration; (iv) allocated the transaction price to the performance obligations; and (v) recognized revenue when (or as) we satisfied each performance obligation.

As part of the accounting for the CStone Agreement, we developed assumptions that require judgment to determine the SSP for each performance obligation identified in the contract. We use key assumptions to determine the SSP, which include forecast of revenues, development timelines, reimbursement rates, discount rates and probabilities of technical and regulatory success.

The satisfied and unsatisfied performance obligations, each of which are considered by us to be distinct within the context of the contract, their SSP, the method of recognizing the allocated consideration, and the period through which they are expected to be recognized are as follows:

Performance Obligations	SSP	No. of Performance Obligation(s)	Recognition Method
License (1)	$ 16.4	1	Fully satisfied; recognized upon execution of CStone Agreement
Development service (2)	1.7	1	Proportionally as services are delivered over the performance period, expected to be through September 2020 (3)

(1) The SSP was developed by probability weighting multiple cash flow scenarios using the income approach. Our management estimates within the models include the expected, probability-weighted net profits from estimated future sales, an estimate of the direct cost incurred to generate future cash flows, a discount rate and other business forecast factors. There are significant judgments and estimates inherent in the determination of the SSP of these units of accounting. These judgments and estimates include assumptions regarding future operating performance, the timelines of the clinical trials and regulatory approvals, and other factors. If different reasonable assumptions are utilized, the SSP and revenue recognized would vary.

(2) The SSP was developed using our management's best estimate of the cost of obtaining these services at arm's length from a third-party provider.

(3) We determined that recognizing revenue on a proportional basis using the ratio of effort incurred to date compared to the total estimated effort required to complete the performance obligation best depicts the satisfaction of our obligations under the CStone Agreement.

During the three and six months ended June 30, 2018, we recognized as collaboration revenue the following non-contingent consideration allocated to each performance obligation (in thousands):

	Under Topic 606	Under Topic 605	Effect of Change
Collaboration revenue			
License	$ 12,440	$ 12,000	$ 440

The following table presents changes in our contract assets during the six months ended June 30, 2018 (in thousands):

	December 31, 2017	Additions	Deductions	June 30, 2018
Contract assets (1)				
Collaboration receivable	$ —	$ 12,440	$ (12,000)	$ 440

(1) Additions to contract assets relate to amounts receivable from CStone. Deductions to contract assets relate to collection of receivables during the reporting period.

As of June 30, 2018, the aggregate amount of the transaction price allocated to performance obligations that are partially unsatisfied was $1.3 million.

Accounting analysis and revenue recognition – royalty revenue

The license was determined to be the predominant item to which sales-based royalties and sales-based milestones relate. As the license was delivered in June 2018, we will recognize royalty revenue when the related sales occur. To date, no royalties have been received under the CStone Agreement.

Accounting analysis and revenue recognition - milestone revenue

At each reporting period we evaluate whether milestones are considered probable of being reached and, to the extent that a significant reversal would not occur in future periods, estimate the amount to be included in the transaction price using the most likely amount method. Milestone payments that are not within our control, such as regulatory approvals, are not considered probable of being achieved and are excluded from the transaction price until those approvals are received.

No milestones were earned during the six months ended June 30, 2018. The next potential milestone expected to be achieved under the CStone Agreement is the dosing of the first patient in a local study in a hematological indication in mainland China. Achievement of this event will result in milestone payments of $5.0 million under the CStone Agreement.

Aurigene Discovery Technologies Limited

In April 2017, we entered into a new global license agreement with Aurigene Discovery Technologies Limited, or Aurigene, to research, develop and commercialize small molecule inhibitors for dihydroorotate dehydrogenase, or DHODH, or the Aurigene Agreement.

Under the terms of the Aurigene Agreement, Aurigene will provide to us exclusive rights to its portfolio of novel small molecules for DHODH. Financial terms of the Aurigene Agreement include a $3.0 million upfront payment and potential future milestone payments of up to $17.0 million if we achieve certain development and regulatory milestones. The next potential milestone expected to be achieved under our collaboration agreements with Aurigene is the initiation of the first phase 1 clinical trial for AG-636, our DHODH inhibitor. Achievement of this event will result in milestone payments owed to Aurigene of $2.0 million.

Aurigene is also eligible to receive low single-digit royalties on net product sales, if any. We will conduct preclinical studies and, if successful, fund further global research and development, as well as regulatory and commercial activities.

The term of the Aurigene Agreement will continue until the earlier of: (a) termination for convenience at our sole discretion upon 90 days prior written notice, (b) termination by either party for material breach, or (c) the expiration of the last-to-expire of all payment obligations hereunder with respect to all licensed products under the Aurigene Agreement.

Accounting analysis

The $3.0 million upfront payment was incurred in May 2017 and recorded as research and development expense. Costs incurred and milestone payments due to Aurigene prior to regulatory approval are recognized as expenses in the period incurred. Payments due to Aurigene upon or subsequent to regulatory approval will be capitalized and amortized over the shorter of the remaining license or product patent life.

6. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	June 30, 2018	December 31, 2017
Accrued compensation	$ 9,135	$ 15,693
Accrued research and development costs	14,568	14,849
Accrued professional fees	1,875	3,140
Accrued other	215	349
Total accrued expenses	$ 25,793	$ 34,031

7. Share-Based Payments

2013 Stock Incentive Plan

In June 2013, our Board of Directors adopted and, in July 2013 our stockholders approved, the 2013 Stock Incentive Plan, or the 2013 Plan. The 2013 Plan became effective upon the closing of our initial public offering and provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units, or RSUs, performance-based stock units, or PSUs, and other stock-based awards. Following the adoption of the 2013 Plan, we granted no further stock options or other awards under the 2007 Stock Incentive Plan, or the 2007 Plan. Any options or awards outstanding under the 2007 Plan at the time of adoption of the 2013 Plan remained outstanding and effective. As of June 30, 2018, the total number of shares reserved under the 2007 Plan and the 2013 Plan are 8,233,462, and we had 1,915,698 shares available for future issuance under the 2013 Plan.

Stock options

The following table presents stock option activity for the six months ended June 30, 2018:

	Number of Stock Options	Weighted-Average Exercise Price
Outstanding at December 31, 2017	5,577,562	$ 49.58
Granted	1,224,670	78.14
Exercised	(869,272)	23.63
Forfeited/Expired	(226,484)	75.98
Outstanding at June 30, 2018	5,706,476	$ 58.62
Exercisable at June 30, 2018	2,778,508	$ 52.30
Vested and expected to vest at June 30, 2018	5,706,476	$ 58.62

At June 30, 2018, the total unrecognized compensation expense related to unvested stock option awards was $119.1 million, which we expect to recognize over a weighted-average period of approximately 2.8 years.

Restricted stock units

The following table presents RSU activity for the six months ended June 30, 2018:

	Number of Stock Units	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2017	125,584	$ 47.46
Granted	388,912	78.73
Vested	(57,250)	41.76
Forfeited	(18,354)	68.53
Unvested shares at June 30, 2018	438,892	$ 75.03

As of June 30, 2018, there was approximately $27.2 million of total unrecognized compensation expense related to RSUs, which we expect to be recognized over a weighted-average period of approximately 2.3 years.

Performance-based stock units

The following table presents PSU activity for the six months ended June 30, 2018:

	Number of Stock Units	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2017	176,186	$ 52.98
Granted	—	—
Vested	—	—
Forfeited	(3,790)	64.44
Unvested shares at June 30, 2018	172,396	$ 52.73

As of June 30, 2018, there was approximately $9.1 million of total unrecognized compensation expense related to PSUs with performance-based vesting criteria that are not considered probable of achievement.

Our wholly owned product, TIBSOVO®, received FDA approval on July 20, 2018 for the treatment of adult patients with R/R AML with a susceptible IDH1 mutation as detected by an FDA-approved test. As a result of the approval, the underlying performance condition associated with the PSUs was met and we expect to recognize approximately $8.0 million of stock compensation expense related to the PSUs for the three months ended September 30, 2018. The remaining $1.1 million of stock compensation expense is expected to be recognized through January 2019 as the time-based vesting criteria related to the PSUs is satisfied.

2013 Employee Stock Purchase Plan

In June 2013, our Board of Directors adopted, and in July 2013 our stockholders approved, the 2013 Employee Stock Purchase Plan, or the 2013 ESPP. We issued 27,377 shares and 33,521 shares during the six months ended June 30, 2018 and 2017, respectively, under the 2013 ESPP. The 2013 ESPP provides participating employees with the opportunity to purchase up to an aggregate of 327,272 shares of our common stock. As of June 30, 2018, we had 186,414 shares available for future issuance under the 2013 ESPP.

Stock-based compensation expense

Stock-based compensation expense by award type included within the condensed consolidated statements of operations is as follows (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Stock options	$ 13,311	$ 11,083	$ 25,783	$ 20,985
Restricted stock units	2,805	875	4,602	1,470
Employee Stock Purchase Plan	339	229	592	466
Total stock-based compensation expense	$ 16,455	$ 12,187	$ 30,977	$ 22,921

Expenses related to equity-based awards were allocated as follows in the condensed consolidated statements of operations (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2018	2017	2018	2017
Research and development expense	$ 9,667	$ 8,190	$ 18,307	$ 15,215
General and administrative expense	6,788	3,997	12,670	7,706
Total stock-based compensation expense	$ 16,455	$ 12,187	$ 30,977	$ 22,921

8. Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted average shares outstanding during the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by adjusting the 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 calculation, stock options, RSUs and ESPP options are considered to be common stock equivalents, while PSUs with vesting conditions that were not met as of June 30, 2018 are not considered to be common stock equivalents.

Since we had a net loss for all periods presented, the effect of all potentially dilutive securities is anti-dilutive. Accordingly, basic and diluted net loss per share was 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:

	Three and Six Months Ended June 30,	
	2018	2017
Stock options	5,706,476	6,066,163
Restricted stock units	438,892	119,350
Employee Stock Purchase Plan options	21,205	18,287
Total common stock equivalents	6,166,573	6,203,800

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

Forward-looking Information

The following discussion of our financial condition and results of operations should be read with our unaudited condensed consolidated financial statements as of June 30, 2018 and for the three and six months ended June 30, 2018 and 2017, and related notes included in Part I. Item 1. of this Quarterly Report on Form 10-Q, as well as the audited consolidated financial statements and notes and Management's Discussion and Analysis of Financial Condition and Results of Operations, included in our Annual Report on Form 10-K for the year ended December 31, 2017 filed with the Securities and Exchange Commission, or SEC, on February 14, 2018. This Management's Discussion and Analysis of Financial Condition and Results of Operations contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on current expectations, estimates, forecasts and projections, and the beliefs and assumptions of our management, and include, without limitation, statements with respect to our expectations regarding our research, development and commercialization plans and prospects, results of operations, general and administrative expenses, research and development expenses, and the sufficiency of our cash for future operations. Words such as "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar statements or variation of these terms or the negative of those terms and similar expressions are intended to identify these forward-looking statements. Readers are cautioned that these forward-looking statements are predictions and are subject to risks, uncertainties and assumptions that are difficult to predict. Therefore, actual results may differ materially and adversely from those expressed in any forward-looking statements. Among the important factors that could cause actual results to differ materially from those indicated by our forward-looking statements are those discussed under the heading "Risk Factors" in Part II, Item 1A. and elsewhere in this report, and in our Annual Report on Form 10-K. We undertake no obligation to revise the forward-looking statements contained herein to reflect events or circumstances after the date hereof or to reflect the occurrence of unanticipated events, except as required by law.

Overview

We are a biopharmaceutical company committed to the fundamental transformation of patients' lives through scientific leadership in the field of cellular metabolism, with the goal of making transformative, first- or best-in-class medicines. Our therapeutic areas of focus are cancer and rare genetic diseases, or RGDs, which are diseases that are directly caused by changes in genes or chromosomes, often passed from one generation to the next. Most RGDs are often associated with severe or life-threatening features. The incidence of a single RGD can vary widely but is generally very infrequent, usually equal to or less than one per 100,000 births. In both areas of cancer and RGDs, we are seeking to unlock the biology of cellular metabolism as a platform to create transformative therapies.

Our first commercial cancer product is IDHIFA®. In August 2017, the U.S. Food and Drug Administration, or FDA, granted our collaboration partner Celgene Corporation, or Celgene, approval of IDHIFA® for the treatment of adult patients with relapsed or refractory acute myeloid leukemia, or R/R AML, and an isocitrate dehydrogenase 2, or IDH2, mutation as detected by an FDA-approved test. IDHIFA®, an oral targeted inhibitor of the mutated IDH2 enzyme, is the first and only FDA-approved therapy for patients with R/R AML and an IDH2 mutation. We are eligible to receive royalties at tiered low-double digit to mid-teen percentage rates on any net sales of IDHIFA® and have exercised our rights to provide up to one-third of the field-based commercialization efforts in the United States. Celgene has submitted a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, for IDHIFA® for IDH2 mutant-positive AML.

Our wholly-owned product, TIBSOVO®, received FDA approval in July 2018 for the treatment of adult patients with R/R AML with a susceptible isocitrate dehydrogenase 1, or IDH1, mutation as detected by an FDA-approved test. We plan to submit an MAA to the EMA for TIBSOVO® for IDH1 mutant-positive R/R AML in the fourth quarter of 2018.

Our most advanced clinical cancer product candidate is AG-881, which is a brain-penetrant pan-IDH mutant inhibitor and is subject to our joint worldwide development and profit share collaboration and license agreement with Celgene. These mutations are found in a wide range of hematological malignancies and solid tumors.

Our next most advanced cancer product candidate is AG-270, an inhibitor of methionine adenosyltransferase 2a, or MAT2A. We submitted an investigational new drug application, or IND, for AG-270 in November 2017, and in December 2017 the FDA concluded that we may proceed with our planned phase 1 dose-escalation trial of AG-270 in multiple tumor types carrying a methylthioadenosine phosphorylase, or MTAP, deletion, which we initiated in March 2018.

Our most advanced preclinical cancer product candidate is AG-636, an inhibitor of the metabolic enzyme dihydroorotate dehydrogenase, or DHODH. We plan to submit an IND for AG-636 for the treatment of hematologic malignancies in the fourth quarter of 2018.

The lead product candidate in our RGD program, mitapivat (AG-348), targets pyruvate kinase-R for the treatment of pyruvate kinase, or PK, deficiency. PK deficiency is a rare genetic disorder that often results in severe hemolytic anemia, jaundice and lifelong conditions associated with chronic anemia and secondary complications due to inherited mutations in the pyruvate kinase enzyme within red blood cells, or RBCs. In April 2018, we initiated ACTIVATE-T, a single arm, global, pivotal trial of mitapivat (AG-348) in approximately 20 regularly transfused patients with PK deficiency. In June 2018, we initiated ACTIVATE, a 1:1 randomized, placebo-controlled, global, pivotal trial of mitapivat (AG-348) in approximately 80 patients with PK deficiency who do not receive regular transfusions. We also expect to initiate a phase 2 proof of concept trial of mitapivat (AG-348) in thalassemia in the fourth quarter of 2018.

In addition to the aforementioned development programs, we are seeking to advance a number of early-stage discovery programs in the areas of cancer metabolism, RGDs and metabolic immuno-oncology, or MIO, a developing field which aims to modulate the activity of relevant immune cells by targeting critical metabolic nodes, thereby, enhancing the immune mediated anti-tumor response.

2016 Agreement

In May 2016, we entered into a master research and collaboration agreement, or the 2016 Agreement, with Celgene, and Celgene RIVOT Ltd., a wholly owned subsidiary of Celgene. The 2016 Agreement focuses on the discovery and development of cancer programs in the field of MIO. In addition to new programs identified under the 2016 Agreement, both parties also agreed that all future development and commercialization of two remaining cancer metabolism programs discovered under the 2010 discovery and development collaboration and license agreement with Celgene, or the 2010 Agreement, including AG-270, will now be governed by the 2016 Agreement.

During the research term of the 2016 Agreement, we plan to conduct research programs focused on discovering compounds that are active against metabolic targets in the immuno-oncology, or IO, field. The initial four-year research term will expire on May 17, 2020, and may be extended for up to two, or in specified cases, up to four additional one-year terms.

For each program under the 2016 Agreement, we may nominate compounds that meet specified criteria as development candidates and, in limited circumstances, Celgene may also nominate compounds as development candidates for each such program. Celgene may designate the applicable program for further development following any such nomination, after which we may conduct, at our expense, additional preclinical and clinical development for such program through the completion of an initial phase 1 dose escalation study.

At the end of the research term, Celgene may designate for continued development up to three research programs for which development candidates have yet to be nominated, which are referred to as continuation programs. We may conduct further research and preclinical and clinical development activities on any continuation program, at our expense, through the completion of an initial phase 1 dose escalation study.

We granted Celgene the right to obtain exclusive options for development and commercialization rights for each program that Celgene has designated for further development, and for each continuation program. Celgene may exercise each such option beginning on the designation of a development candidate for such program (or on the designation of such program as a continuation program) and ending on the earlier of: (i) the end of a specified period after we have furnished Celgene with specified information about the initial phase 1 dose escalation study for such program, or (ii) January 1, 2030. Research programs that have applications in the inflammation or autoimmune, or I&I, field that may result from the 2016 Agreement will also be subject to the exclusive options described above.

We will retain rights to any program that Celgene does not designate for further development or as to which it does not exercise its option.

Under the terms of the 2016 Agreement, following Celgene’s exercise of its option with respect to a program, the parties will enter into either a co-development and co-commercialization agreement if such program is in the IO field, or a license agreement if such program is in the I&I field. Under each co-development and co-commercialization agreement, the two parties will co-develop and co-commercialize licensed products worldwide. Either we or Celgene will lead development and commercialization of licensed products for the United States, and Celgene will lead development and commercialization of licensed products outside of the United States. Depending on the country, the parties will each have the right to provide a portion of field-based marketing activities. Under each license agreement, Celgene will have the sole right to develop and commercialize licensed products worldwide.

TIBSOVO® Letter Agreement

In May 2016, we entered into a letter agreement with Celgene regarding TIBSOVO®, or the TIBSOVO® Letter Agreement. Under the TIBSOVO® Letter Agreement, the parties agreed to terminate the 2010 Agreement, effective as of August 15, 2016, as to the program directed to the IDH1 target, for which TIBSOVO® is the lead development candidate. Under the 2010 Agreement, Celgene had held development and commercialization rights to the IDH1 program outside of the United States, and

we held such rights inside the United States. As a result of the termination, we obtained global rights to TIBSOVO® and the IDH1 program. Neither party will have any further financial obligation, including royalties or milestone payments, to the other concerning TIBSOVO® or the IDH1 program. Under the terms of the termination, the parties also agreed to conduct specified transitional activities in connection with the termination. In addition, pursuant to the TIBSOVO® Letter Agreement, the parties are released from their exclusivity obligations under the 2010 Agreement with respect to the IDH1 program. The termination does not affect the AG-881 Agreements described below, which are directed to both the IDH1 target and the IDH2 target.

AG-881 Agreements

In April 2015, we entered into a joint worldwide development and profit share collaboration and license agreement with Celgene, and our wholly owned subsidiary, Agios International Sarl, entered into a collaboration and license agreement with Celgene International II Sarl. Both of these agreements are collectively referred to as the AG-881 Agreements. The AG-881 Agreements establish a joint worldwide collaboration focused on the development and commercialization of AG-881 products. The parties will split all worldwide development costs equally, subject to specified exceptions, as well as any profits from any net sales of, or commercialization losses related to, licensed AG-881 products. Either party may, at its own expense and with the other party's permission, undertake additional development activities outside of the scope of the development plan agreed upon with the other party.

2010 Agreement

In April 2010, we entered into the 2010 Agreement, which was amended in October 2011 and July 2014. The goal of the collaboration was to discover, develop and commercialize disease-altering therapies in oncology based on our cancer metabolism research platform. We initially led discovery, preclinical and early clinical development for all cancer metabolism programs under the collaboration. The discovery phase of the 2010 Agreement expired in April 2016.

Upon agreement to terminate the 2010 Agreement, effective as of August 15, 2016, as to the program directed to the IDH1 target, for which TIBSOVO® is the lead development candidate, the sole program remaining under the 2010 Agreement is IDHIFA®, a co-commercialized licensed program for which Celgene leads and funds global development and commercialization activities. We have exercised our right to participate in a portion of commercialization activities in the United States for IDHIFA® in accordance with the applicable commercialization plan.

CStone Agreement

In June 2018, we entered into an exclusive license agreement with CStone Pharmaceuticals, or the CStone Agreement, for the development and commercialization of certain products containing TIBSOVO® in mainland China, Hong Kong, Macau, and Taiwan for therapeutic uses in humans, excluding brain cancer, unless later adopted by us in our sole discretion. We retain development and commercialization rights with respect to TIBSOVO® for the rest of the world.

Pursuant to the CStone Agreement, CStone will initially be responsible for the development and commercialization of TIBSOVO® in acute myeloid leukemia, or AML, and cholangiocarcinoma, as well as other indications that the parties mutually agree to in the future. CStone will also be responsible, at our discretion, for the development and commercialization of TIBSOVO® in brain cancer indications. We granted CStone specified intellectual property licenses to enable CStone to perform its obligations and exercise its rights under the CStone Agreement, including license grants to enable CStone to conduct development and commercialization activities pursuant to the terms of the CStone Agreement.

CStone is responsible for all costs it incurs in developing, obtaining regulatory approval of, and commercializing TIBSOVO® in China, Hong Kong, Macau, and Taiwan, as well as certain costs incurred by us.

During the term of the CStone Agreement, each party and its affiliates are prohibited from developing or commercializing any other compound or product that inhibits IDH1 mutations at specified levels of binding, in the case of CStone, anywhere in the world, and in the case of us, in China, Hong Kong, Macau, and Taiwan. Subject to specified exceptions, CStone and its affiliates are also prohibited from developing or commercializing certain other compounds or products that directly or indirectly treat AML, cholangiocarcinoma or, if applicable, glioma in patients that have an IDH1 mutation.

The CStone Agreement contemplates that we will enter into ancillary arrangements with CStone, including clinical and commercial supply agreements and a pharmacovigilance agreement.

Critical Accounting Policies and Estimates

Our critical accounting policies are those policies which require the most significant judgments and estimates in the preparation of our consolidated financial statements. We have determined that our most critical accounting policies are those relating to revenue recognition, accrued research and development expenses, and stock-based compensation. There have been no significant changes to our critical accounting policies discussed in the Annual Report on Form 10-K for the year ended December 31, 2017.

Financial Operations Overview

General

Since inception, our operations have primarily 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 conducting clinical trials. To date, we have financed our operations primarily through funding received from the 2010 Agreement, the AG-881 Agreements, the 2016 Agreement, CStone Agreement, private placements of our preferred stock, our initial public offering of our common stock and concurrent private placement of common stock to an affiliate of Celgene, and our follow-on public offerings.

Additionally, since inception, we have incurred significant operating losses. Our net losses were $159.6 million and $149.2 million for the six months ended June 30, 2018 and 2017, respectively. As of June 30, 2018, we had an accumulated deficit of $918.2 million. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from year to year. We anticipate that our expenses will increase significantly as we continue to advance and expand clinical development activities for our lead programs: IDHIFA®, TIBSOVO®, AG-881, mitapivat (AG-348), AG-270, AG-636; continue to discover and validate novel targets and drug product candidates; expand and protect our intellectual property portfolio; and hire additional commercial, development and scientific personnel.

Revenue

Through June 30, 2018, we have not generated any revenue from product sales. All of our revenue to date has been derived from our collaborations with Celgene and CStone, and royalty revenue on sales of IDHIFA®. In the future, we expect to generate revenue from a combination of product sales, royalties on product sales, cost reimbursements, milestone payments, and upfront payments to the extent we enter into future collaborations or licensing agreements.

Research and development expenses

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, 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 and commercialize these product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from IDHIFA®, TIBSOVO®, AG-881, mitapivat (AG-348), AG-270, AG-636, or any of our other product candidates. This is due to the numerous risks and uncertainties associated with developing medicines, including the uncertainty of:

- establishing an appropriate safety profile with IND, and/or NDA enabling toxicology and clinical studies;
- the successful enrollment in, and completion of, clinical trials;
- the receipt of marketing approvals from applicable regulatory authorities;
- establishing compliant 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
- maintaining an 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 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 both preclinical and clinical activities on our behalf, and the cost of consultants;
- the cost of lab supplies and acquiring, developing and manufacturing preclinical and clinical study materials; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and the maintenance of facilities, insurance and other operating costs.

The following summarizes our most advanced programs:

IDHIFA®

IDHIFA® 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, who have a historically poor prognosis. In August 2017, the FDA granted Celgene approval of IDHIFA® for the treatment of adult patients with R/R AML and an IDH2 mutation as detected by an FDA-approved test. The FDA's approval of IDHIFA® in R/R AML was based on clinical data from an open-label, single-arm, multicenter, two-cohort phase 1/2 clinical trial of adult patients with R/R AML and an IDH2 mutation. In June 2018, Celgene submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive AML.

Celgene maintains worldwide development and commercial rights to IDHIFA® and will fund the future development and commercialization costs related to this program. Under the 2010 Agreement, Celgene is responsible for all development costs for IDHIFA®, and we are eligible to receive up to $95.0 million in milestone payments, which are comprised of: (i) up to $70.0 million in milestone payments upon achievement of specified ex-U.S. regulatory milestone events, including the aforementioned $15.0 million milestone for the MAA submission, and (ii) a $25.0 million milestone payment upon achievement of a specified ex-U.S. commercial milestone event. Additionally, we are eligible to receive tiered royalties on any net sales of IDHIFA®.

We continue to evaluate IDHIFA® in the following clinical trials, which, unless otherwise noted, are led by Celgene:

Phase 1b frontline combination trial (TIBSOVO® also being evaluated)

IDHIFA® is being evaluated in a phase 1b, multicenter, international, open-label clinical trial, conducted by us, to evaluate the safety and clinical activity of IDHIFA® or TIBSOVO® in combination with induction and consolidation therapy in patients with newly diagnosed AML with an IDH2 or IDH1 mutation who are eligible for intensive chemotherapy using a primary endpoint of safety and tolerability of IDHIFA® or TIBSOVO® when administered with induction and consolidation therapy. The trial is currently enrolling patients.

In December 2017, we presented interim data from this trial at American Society of Hematology meeting in Atlanta, Georgia, or ASH 2017.

Phase 1/2 frontline combination trial (TIBSOVO® also being evaluated)

IDHIFA® is being evaluated in a phase 1/2 frontline combination clinical trial of either IDHIFA® or TIBSOVO® in combination with VIDAZA® (azacitidine) in newly diagnosed AML patients not eligible for intensive chemotherapy, with a phase 1 component to determine the safety of the combinations, followed by a phase 2 randomized component evaluating the safety and clinical activity of each investigational combination versus single-agent VIDAZA® using a primary endpoint of overall response rate. The trial has completed the phase 1 component and is currently enrolling in the phase 2 component, which will assess the activity of IDHIFA® in combination with VIDAZA®.

In June 2018, we presented new safety and efficacy data from this ongoing trial at the American Society of Clinical Oncology meeting in Chicago, Illinois, or ASCO 2018.

IDHENTIFY

IDHIFA® is being evaluated in IDHENTIFY, an international phase 3, multi-center, open-label, randomized clinical trial designed to compare the efficacy and safety of IDHIFA® versus conventional care regimens in patients 60 years or older with IDH2 mutant-positive AML that is refractory to or relapsed after second- or third-line therapy. In January 2016, in conjunction with the initiation of the IDHENTIFY clinical trial, we received a milestone payment of $25.0 million from Celgene pursuant to the 2010 Agreement. This trial is currently enrolling patients and we have not yet presented any clinical data from this trial.

Phase 3 frontline combination trial

We plan to support, with Celgene, the initiation of an intergroup sponsored, global, registration-enabling phase 3 trial combining TIBSOVO® or IDHIFA® and standard induction (7+3) and consolidation chemotherapy with a primary endpoint of event-free survival in frontline AML patients with an IDH1 or IDH2 mutation in the fourth quarter of 2018.The trial is expected to enroll approximately 500 patients with an IDH1 mutation and approximately 500 patients with an IDH2 mutation.

TIBSOVO®

TIBSOVO® 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. We hold worldwide development and commercial rights to TIBSOVO® and will fund the future development and commercialization costs related to this

program. Mutations in IDH1 have been identified in difficult to treat hematologic and solid tumor cancers, including AML, chondrosarcoma, cholangiocarcinoma, and glioma, where both the treatment options and prognosis for patients are poor.

In July 2018, the FDA approved TIBSOVO® for the treatment of adult patients with R/R AML and a susceptible IDH1 mutation as detected by an FDA-approved test. The FDA's approval of TIBSOVO® in R/R AML was based on clinical data from a phase 1 open-label, single-arm, multicenter dose-escalation and expansion trial of adult patients with advanced R/R AML and an IDH1 mutation. Four expansion cohorts have been added to the trial. We plan to submit an MAA to the EMA for TIBSOVO® for IDH1 mutant-positive R/R AML in the fourth quarter of 2018.

The FDA granted us fast track designation for TIBSOVO® for treatment of patients with previously treated, unresectable or metastatic cholangiocarcinoma with an IDH1 mutation, and granted orphan drug designation for TIBSOVO® for the treatment of cholangiocarcinoma.

We are evaluating TIBSOVO® in the following clinical trials:

Phase 1b frontline combination trial

As discussed above, TIBSOVO® and IDHIFA® are also being evaluated in a phase 1b, multicenter, international, open-label clinical trial, in combination with induction and consolidation therapy. The trial is currently enrolling patients.

In December 2017, we presented interim data from this trial at ASH 2017.

Phase 1/2 frontline combination trial

As discussed above, TIBSOVO® and IDHIFA® are also being evaluated in a phase 1/2 frontline clinical trial in combination with VIDAZA®, conducted by Celgene. The trial has completed the phase 1 component and is currently enrolling in the phase 2 component, which will assess the activity of IDHIFA® in combination with VIDAZA®.

In June 2018, we presented new safety and efficacy data from this ongoing trial at ASCO 2018.

AGILE

TIBSOVO® is being evaluated in AGILE, a global, registration-enabling phase 3 clinical trial, combining TIBSOVO® and VIDAZA® in newly diagnosed AML patients with an IDH1 mutation who are ineligible for intensive chemotherapy. The trial is enrolling patients and we expect to complete enrollment in 2021.

Phase 3 frontline combination trial

As discussed above, we plan to support, with Celgene, the initiation of an intergroup sponsored, global, registration-enabling phase 3 trial combining TIBSOVO® or IDHIFA® and standard induction (7+3) and consolidation chemotherapy with a primary endpoint of event-free survival in frontline AML patients with an IDH1 or IDH2 mutation in the fourth quarter of 2018.

Phase 1 clinical trial (advanced solid tumors)

TIBSOVO® is being evaluated in a phase 1 multicenter, open-label, dose-escalation and expansion clinical trial, designed to assess its safety, clinical activity and tolerability as a single agent in patients with advanced solid tumors with an IDH1 mutation, including glioma, cholangiocarcinoma, and chondrosarcoma. Enrollment is now complete for four expansion cohorts of 25 patients each in (i) low grade glioma with at least six months of prior scans to assess volumetric changes, (ii) second-line cholangiocarcinoma, (iii) high grade, or metastatic, chondrosarcoma, and (iv) other solid tumors with an IDH1 mutation, who will receive the recommended dose of 500 mg of TIBSOVO® once daily.

In June 2017, we reported updated interim data from the dose escalation and dose expansion cohorts of our ongoing phase 1 clinical trial evaluating TIBSOVO® in patients with IDH1 mutant-positive cholangiocarcinoma at the ASCO 2017. In November 2017, we reported updated interim data from the dose expansion cohort of our ongoing phase 1 clinical trial evaluating TIBSOVO® in patients with progressive low-grade IDH1 mutant-positive glioma at the Society for Neuro-Oncology Annual Meeting in San Francisco, California.

ClarIDHy

TIBSOVO® is being evaluated in ClarIDHy, a registration-enabling phase 3, multicenter, randomized, double-blind, placebo-controlled clinical trial of TIBSOVO® in previously-treated patients with nonresectable or metastatic cholangiocarcinoma with an IDH1 mutation. The trial was initiated in December 2016 and is currently enrolling patients, and we expect to complete enrollment in the first half of 2019.

AG-881: brain penetrant pan-IDH program

AG-881 is an orally available, selective, brain-penetrant, pan-IDH mutant inhibitor, which provides added flexibility to our current portfolio of IDH mutant inhibitors. We are currently focusing our development efforts for AG-881 in glioma.

We and Celgene are jointly collaborating on a worldwide development program for AG-881, wherein we share worldwide development costs, subject to specified exceptions, and profits and Celgene would book any worldwide commercial sales. Either party may, at its own expense and with the other party's permission, undertake additional development activities outside of the scope of the development plan agreed upon with the other party. We will lead commercialization in the United States with both companies sharing equally in field-based commercial activities, and Celgene will lead commercialization outside of the United States with us providing one third of field-based commercial activities in the major European Union markets. Under the AG-881 Agreements, we are eligible to receive up to $70.0 million in potential milestone payments related to AG-881. We may also receive royalties at tiered, low-double digit to mid-teen percentage rates on net sales if we elect not to participate in the development and commercialization of AG-881.

Phase 1 clinical trial (advanced hematologic malignancies)

We are conducting a phase 1 multi-center, open-label clinical trial of AG-881 in patients with advanced IDH1 or IDH2 mutant-positive hematologic malignancies whose cancer has progressed on a prior IDH inhibitor therapy. The goal of this trial is to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and clinical activity of AG-881 in hematologic malignancies.

This trial has completed its dose escalation portion, establishing proof of mechanism as measured by reductions in 2-hydroxygluturate levels, and is now closed for enrollment. No maximum tolerable dose, or MTD, was reached. We have not yet presented any clinical data from this trial. In October 2017, we presented the first preclinical data of AG-881 in IDH mutant-positive hematologic malignancies at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Philadelphia, Pennsylvania.

Phase 1 clinical trial (advanced solid tumors)

We are conducting a phase 1 multi-center, open-label clinical trial of AG-881 in patients with advanced IDH1 or IDH2 mutant-positive solid tumors, including glioma. The goal of this trial is to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and clinical activity of AG-881 in advanced solid tumors. An MTD was established and enrollment in this trial is complete. In June 2018, we presented at the first data from this trial at ASCO 2018.

In the first quarter of 2018, we initiated a perioperative study with TIBSOVO® and AG-881 in low grade glioma to further investigate their effects on brain tumor tissue. Pursuant to the AG-881 Agreements, Celgene has elected not to participate in this clinical trial and, as a result, we will fund the trial ourselves. Celgene will continue to co-fund the ongoing phase 1 trials of AG-881 described above.

Mitapivat (AG-348)

Mitapivat (AG-348) in is an orally available small molecule and a potent activator of the wild-type (normal) and mutated PKR enzyme, which has resulted in restoration of adenosine triphosphate, or ATP, levels and a decrease in 2,3-diphosphoglycerate, or 2,3-DPG, levels in blood sampled from patients with PK deficiency and treated ex-vivo with mitapivat (AG-348). The wild-type PKR activity of mitapivat (AG-348) allowed the study of enzyme activation in healthy volunteers, providing an opportunity to understand the safety, dosing and pharmacodynamic activity of mitapivat (AG-348) prior to entering a proof-of-concept study in patients. We have worldwide development and commercial rights to mitapivat (AG-348) and expect to fund the future development and commercialization costs related to this program. The FDA granted orphan drug designation for mitapivat (AG-348) for treatment of patients with PK deficiency and granted us fast track designation to mitapivat (AG-348) for the treatment of patients with PK deficiency. In December 2016, we announced our decision to advance mitapivat (AG-348) into pivotal development as the first potential disease-modifying treatment for PK deficiency.

We have worldwide development and commercial rights to mitapivat (AG-348) and expect to fund the future development and commercialization costs related to this program.

DRIVE PK

In June 2015, we initiated DRIVE PK, a global phase 2, first-in-patient, open-label safety and efficacy clinical trial of mitapivat (AG-348) in adult, transfusion-independent patients with PK deficiency. In June 2016, we reported the first clinical data from DRIVE PK at EHA 2017, establishing proof of concept for mitapivat (AG-348). The trial reached target enrollment of 52 patients in November 2016, and in December 2017, we reported updated data from the trial at ASH 2017.

ACTIVATE-T/ACTIVATE

In April 2018, we initiated ACTIVATE-T, a single arm, global, pivotal trial of mitapivat (AG-348) in approximately 20 regularly transfused patients with PK deficiency. In June 2018, we initiated ACTIVATE, a 1:1 randomized, placebo-controlled, global, pivotal trial of mitapivat (AG-348) in approximately 80 patients with PK deficiency who do not receive regular transfusions. The primary endpoint of the ACTIVATE-T trial is a greater than 33% reduction in transfusion burden over a six-

month period compared to the patient's transfusion history, and the primary endpoint of the ACTIVATE trial is the proportion of patients who achieve at least a 1.5 g/dL increase in hemoglobin sustained over multiple visits.

In addition to the above ongoing clinical trials of mitapivat (AG-348), we plan to initiate a phase 2 proof of concept trial of mitapivat (AG-348) in thalassemia in the fourth quarter of 2018.

AG-270: Targeting MAT2A for the treatment of MTAP-deleted cancers

AG-270, a MAT2A inhibitor, is our development candidate focused on MTAP-deleted cancer. MTAP is a metabolic gene that is deleted in approximately 15 percent of all cancers. We have shown in preclinical studies that MTAP deletion predicts sensitivity to inhibition of a subset of enzymes involved in the synthesis or utilization of the methyl donor S-adenosylmethionine, or SAM. Among this subset of enzymes, we have targeted MAT2A, the enzyme responsible for the synthesis of SAM in tumor cells.

In March 2018, we initiated a phase 1 dose-escalation trial of AG-270 in multiple tumor types carrying an MTAP deletion. The purpose of this phase 1 multi-center, open-label study is to evaluate the safety, pharmacokinetics, pharmacodynamics and clinical activity of AG-270 in approximately 50 patients with advanced solid tumors or lymphoma with MTAP deletion. AG-270 will be administered as a single agent dosed orally once daily in 28-day cycles. The first part of the study is a dose-escalation phase in which cohorts of patients will receive ascending doses of AG-270 to determine the MTD or optimal dose. The second part of the study is a dose expansion phase where additional patients will receive AG-270 at the MTD or optimal dose to further evaluate its safety, tolerability and clinical activity as a potential dose for future studies.

AG-636: Targeting DHODH for the treatment of hematologic malignancies

In January 2018, we announced that we plan to submit an IND in the fourth quarter of 2018 for AG-636, an inhibitor of DHODH, licensed by us from Aurigene Discovery Technologies Limited, for the treatment of hematologic malignancies. We have discovered a lineage-specific dependence on DHODH in hematologic malignancies, particularly AML and diffuse large B-cell lymphoma. DHODH catalyzes a critical step in the biosynthesis of pyridimidines, which are critical for the production of RNA and DNA. We believe that DHODH inhibition will be differentiated from standard-of-care therapies, both by exhibiting activity in cancers that are resistant to standard-of-care chemotherapeutics and through a mechanism of anti-tumor effect that combines cell growth arrest and cellular differentiation.

Other research and platform programs

Other research and platform programs include activities related to exploratory efforts, target validation and lead optimization for our discovery and follow-on programs, and our proprietary metabolomics platform.

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, business development, commercial, legal and human resources functions. Other significant costs include facility related 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, and commercialization activities, including activities related to the commercialization of TIBSOVO® and the potential commercialization of our other product candidates. 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.

Results of Operations

Comparison of the three months ended June 30, 2018 and 2017

The following table summarizes our results of operations for the three months ended June 30, 2018 and 2017 ($ in thousands):

	Three Months Ended June 30,			
	2018	2017	$ Change	% Change
Collaboration revenue – related party	$ 26,401	$ 11,346	$ 15,055	133 %
Collaboration revenue – other	12,440	—	$ 12,440	N/A
Royalty revenue – related party	1,573	—	$ 1,573	N/A
Total revenue	40,414	11,346	$ 29,068	256 %
Operating expenses:				
Research and development (net of $2,489 of cost reimbursement from related party for the three months ended June 30, 2017)	86,730	79,816	6,914	9 %
General and administrative	26,633	16,130	10,503	65 %
Loss from operations	(72,949)	(84,600)	11,651	(14)%
Interest income	4,204	1,518	2,686	177 %
Net loss	$ (68,745)	$ (83,082)	$ 14,337	(17)%

Revenue. For the three months ended June 30, 2018, we recognized $26.4 million in collaboration revenue from our agreements with Celgene. The amount recognized includes a $15.0 million milestone payment related to Celgene's June 2018 submission of an MAA to the EMA for IDHIFA® for IDH2 mutant-positive R/R AML. Collaboration revenue from our Celgene agreements recognized during the three months ended June 30, 2018 were accounted for under Accounting Standards Codification, or ASC, 606, *Revenue from Contracts with Customers*, or ASC 606, which we adopted as of January 1, 2018. For further discussion regarding adoption of ASC 606, refer to Note 2, *Summary of Significant Accounting Policies*, and Note 5, *Collaboration and License Agreements*, in the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q.

As previously discussed, in June 2018, we entered into the CStone Agreement for the development and commercialization of certain products containing TIBSOVO® in mainland China, Hong Kong, Macau, and Taiwan. Upon execution of the CStone Agreement, we delivered the license to CStone and recognized $12.4 million of consideration as collaboration revenue.

In addition to collaboration revenue, we also recognized $1.6 million in royalty revenue on Celgene's net sales of IDHIFA® under the 2010 Agreement.

For the three months ended June 30, 2017, we recognized $11.3 million in revenue under our collaboration agreements with Celgene.

Research and Development Expense. The increase in research and development expenses for the three months ended June 30, 2018 was primarily attributable to net increases of $6.3 million in external services and $0.6 million in internal expenses; both of these increases are inclusive of cost reimbursements recorded as a reduction of research and development expenses.

We use our employee and infrastructure resources across multiple research and development programs, and we allocate internal employee-related and infrastructure costs, including stock-based compensation and facilities costs, as well as certain third-party costs, net of reimbursements from Celgene, to our research and development programs based on the personnel resources allocated to such program.

Our allocated research and development expenses, by major program, are outlined in the table below ($ in thousands):

	Three Months Ended June 30,			
	2018	2017	$ Change	% Change
IDHIFA® (IDH2 inhibitor)	$ 3,108	$ 1,885	$ 1,223	65 %
TIBSOVO® (IDH1 inhibitor)	$ 34,716	$ 38,883	$ (4,167)	(11)%
Pan-IDH inhibitor (AG-881)	$ 3,797	$ 5,622	$ (1,825)	(32)%
AG-881 reduction of R&D expenses	*$ —*	*$ (2,489)*	*$ 2,489*	*(100)%*
PKR activator (mitapivat (AG-348))	$ 14,604	$ 10,821	$ 3,783	35 %
MTAP-deleted cancers program (AG-270)	$ 5,908	$ 5,084	$ 824	16 %
DHODH inhibitor (AG-636)	$ 3,204	$ —	$ 3,204	N/A
Other research and platform programs	$ 21,393	$ 20,010	$ 1,383	7 %
Total research and development expenses, net	$ 86,730	$ 79,816	$ 6,914	9 %

The changes in research and development expense depicted in the table above were primarily attributable to the following:

- IDHIFA® costs increased as a result of increased internal and external expenses related to our ongoing phase 1b frontline combination trial development work.
- TIBSOVO® costs decreased compared to the prior period as prior period costs included manufacturing expenses associated with our initial commercial inventory of TIBSOVO® as part of our NDA submission in December 2017.
- AG-881 costs decreased as our phase 1 trial in patients with advanced IDH1 or IDH2 mutant-positive hematologic malignancies and our phase 1 trial in IDH1 or IDH2 mutant-positive advanced solid tumors, including glioma, both completed their dose escalation portions.

  Cost reimbursements for AG-881 were recognized as revenue in the current period.
- Mitapivat (AG-348) costs increased as a result of the start-up costs for the ACTIVATE trial, which we initiated in June 2018.
- AG-270 costs increased as we initiated a phase 1 trial in March 2018.
- AG-636 costs increased as we complete IND-enabling studies in anticipation of an IND filing in the fourth quarter of 2018.
- The increase in the costs of other research and platform programs include activities related to exploratory efforts, target validation and lead optimization for our discovery and follow-on programs, and our proprietary metabolomics platform.

General and Administrative Expense. The increase in general and administrative expense was primarily attributable to an increase of $10.1 million related to our growing commercial organization for the launch of TIBSOVO®.

Interest Income. The increase in interest income is attributable to higher investment balances driven by funds received from our January 2018 follow-on public offering, resulting in higher interest earned on investments.

Comparison of the six months ended June 30, 2018 and 2017

The following table summarizes our results of operations for the six months ended June 30, 2018 and 2017 ($ in thousands):

	Six Months Ended June 30,			
($ in thousands)	**2018**	**2017**	**$ Change**	**% Change**
Collaboration revenue – related party	$ 33,746	$ 21,854	$ 11,892	54 %
Collaboration revenue – other	12,440	—	12,440	N/A
Royalty revenue – related party	2,990	—	2,990	N/A
Total revenue	49,176	21,854	27,322	125 %
Operating expenses:				
Research and development (net of $5,265 of cost reimbursement from related party for the six months ended June 30, 2017)	164,954	142,548	22,406	16 %
General and administrative	51,183	30,953	20,230	65 %
Loss from operations	(166,961)	(151,647)	(15,314)	10 %
Interest income	7,391	2,399	4,992	208 %
Net loss	$ (159,570)	$ (149,248)	$ (10,322)	7 %

Revenue. For the six months ended June 30, 2018, we recognized $33.7 million in collaboration revenue from our agreements with Celgene. The amount recognized includes a $15.0 million milestone payment related to Celgene's June 2018 submission of an MAA to the EMA for IDHIFA® for IDH2 mutant-positive R/R AML. Collaboration revenue recognized during the six months ended June 30, 2018 were accounted for under Accounting Standards Codification, or ASC, 606, *Revenue from Contracts with Customers*, or ASC 606, which we adopted as of January 1, 2018. For further discussion regarding adoption of ASC 606, refer to Note 2, *Summary of Significant Accounting Policies*, and Note 5, *Collaboration and License Agreements*, in the Notes to Condensed Consolidated Financial Statements included in Part I, Item 1 of this Quarterly Report on Form 10-Q.

As previously discussed, we also recognized $12.4 million of consideration as revenue under our CStone Agreement.

In addition to collaboration revenue, we also recognized $3.0 million in royalty revenue on Celgene net sales of IDHIFA® under the 2010 Agreement.

For the six months ended June 30, 2017, we recognized $21.9 million in revenue, which includes partial recognition of the development candidate designation payment for AG-270, our program focused on MTAP-deleted cancers, of $1.5 million.

Research and Development Expense. The increase in research and development expenses for the six months ended June 30, 2018 was primarily attributable to net increase of $26.8 million in external services, offset by a $4.4 million decrease in internal expenses. Both of these changes are inclusive of cost reimbursements recorded as a reduction of research and development expenses.

We use our employee and infrastructure resources across multiple research and development programs, and we allocate internal employee-related and infrastructure costs, including stock-based compensation and facilities costs, as well as certain third-party costs, net of reimbursements from Celgene, to our research and development programs based on the personnel resources allocated to such program.

Our allocated research and development expenses, by major program, are outlined in the table below ($ in thousands):

($ in thousands)	Six Months Ended June 30, 2018	2017	$ Change	% Change
IDHIFA® (IDH2 inhibitor)	$ 5,647	$ 3,465	$ 2,182	63 %
IDHIFA® reduction of R&D expenses	*$ —*	*$ (14)*	*$ 14*	*(100)%*
TIBSOVO® (IDH1 inhibitor)	$ 65,223	$ 69,661	$ (4,438)	(6)%
Pan-IDH inhibitor (AG-881)	$ 7,478	$ 11,208	$ (3,730)	(33)%
AG-881 reduction of R&D expenses	*$ —*	*$ (5,251)*	*$ 5,251*	*(100)%*
PKR activator (mitapivat (AG-348))	$ 27,719	$ 18,290	$ 9,429	52 %
MTAP-deleted cancers program (AG-270)	$ 11,936	$ 9,633	$ 2,303	24 %
DHODH inhibitor (AG-636)	$ 6,058	$ —	$ 6,058	100 %
Other research and platform programs	$ 40,893	$ 35,556	$ 5,337	15 %
Total research and development expenses, net	$ 164,954	$ 142,548	$ 22,406	16 %

The changes in research and development expense depicted in the table above were primarily attributable to the following:

- IDHIFA® costs increased as a result of increased internal and external expenses related to our ongoing phase 1b frontline combination trial development work.
- TIBSOVO® costs decreased compared to the prior period as prior period costs included manufacturing expenses associated with our initial commercial inventory of TIBSOVO® as part of our NDA submission in December 2017.
- AG-881 costs decreased as our phase 1 trial in patients with advanced IDH1 or IDH2 mutant-positive hematologic malignancies and our phase 1 trial in IDH1 or IDH2 mutant-positive advanced solid tumors, including glioma, both completed their dose escalation portions.

  Cost reimbursements for AG-881 were recognized as revenue in the current period.
- Mitapivat (AG-348) costs increased as a result of the start-up costs for the ACTIVATE-T trial and the initiation of ACTIVATE in the second quarter of 2018.
- AG-270 costs increased as we initiated a phase 1 trial in March 2018.
- AG-636 costs increased as we complete IND-enabling studies in anticipation of an IND filing in the fourth quarter of 2018.
- The increase in the costs of other research and platform programs include activities related to exploratory efforts, target validation and lead optimization for our discovery and follow-on programs, and our proprietary metabolomics platform.

General and Administrative Expense. The increase in general and administrative expenses was primarily attributable to an increase of $17.3 million related to supporting our growing commercial organization for the launch of TIBSOVO®.

Interest Income. The increase in interest income is attributable to higher investment balances driven by funds received from our January 2018 follow-on public offering, resulting in higher interest earned on investments.

Liquidity and Capital Resources

Sources of liquidity

Since our inception, and through June 30, 2018, we have funded our operations through upfront, milestone, extension, cost reimbursement and royalty payments related to our collaboration agreements, proceeds received from our issuance of preferred stock, our initial public offering and concurrent private placement of common stock to an affiliate of Celgene, and our follow-on public offerings.

In January 2018, we completed a public offering of 8,152,986 shares of common stock at an offering price of $67.00 per share. We received net proceeds from this offering of $516.2 million, after deducting underwriting discounts and commissions paid by us.

In addition to our existing cash, cash equivalents and marketable securities, we are eligible to earn a significant amount of milestone payments, cost reimbursements, and royalty payments under our collaboration agreements with Celgene and CStone, and designation fees, license option fees and extension fees under our collaboration agreements with Celgene. Our ability to earn the milestone payments, cost reimbursements and royalty payments, and the timing of earning these amounts are

dependent upon the timing and outcome of our development, regulatory and commercial activities, and is uncertain at this time. Our right to payments under our collaboration agreements with Celgene and CStone are our only committed potential external source of funds.

Cash flows

The following table provides information regarding our cash flows for the six months ended June 30, 2018 and 2017 (in thousands):

	Six Months Ended June 30, 2018	
	2018	**2017**
Net cash used in operating activities	$ (166,395)	$ (133,063)
Net cash used in investing activities	(263,791)	(166,173)
Net cash provided by financing activities	537,785	277,199
Net change in cash and cash equivalents	$ 107,599	$ (22,037)

Net cash used in operating activities. During the six months ended June 30, 2018, we received $8.9 million in cost reimbursements related to our collaboration agreements with Celgene and $12.0 million under the CStone Agreement. These amounts were offset by increased operating expenses that relate to increases in clinical study costs due to advancements in our most advanced product candidates, commercialization efforts, expanded facilities and increased staffing needs due to our expanding operations.

During the six months ended June 30, 2017, we received $8.1 million in cost reimbursements related to our collaboration agreements with Celgene. These amounts were offset by increased operating expenses which relate to increases in clinical study costs due to advancements in our most advanced product candidates, expanded facilities and increased staffing needs due to our expanding operations.

Net cash used in investing activities. The cash used in investing activities for the six months ended June 30, 2018 and 2017 was primarily the result of higher purchases of marketable securities than proceeds from maturities and sales of marketable securities, and $2.8 million and $1.3 million in purchases of property and equipment, respectively.

Net cash provided by financing activities. The cash provided by financing activities for the six months ended June 30, 2018 was primarily the result of the $516.2 million net proceeds received from our January 2018 follow-on public offering, after underwriting discounts and commissions, as well as proceeds received from stock option exercises and purchases made pursuant to our employee stock purchase plan. The cash provided by financing activities for the six months ended June 30, 2017 was the result of proceeds received from stock option exercises and purchases made pursuant to our employee stock purchase plan.

Funding requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we commercialize TIBSOVO®, and continue the research, development and clinical trials of, and seek additional marketing approvals for, our product candidates. If we obtain additional marketing approval for any of our other product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of Celgene or other collaborators. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations.

We expect that our existing cash, cash equivalents and marketable securities as of June 30, 2018 together with anticipated product and royalty revenue, anticipated interest income and anticipated expense reimbursements under our collaboration agreements, but excluding any additional program-specific milestone payments, will enable us to fund our operating expenses and capital expenditure requirements through at least the end of 2020. 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 collaborations;
- 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 associated with the commercial launch of TIBSOVO® and preparation for the potential commercial launch of one or more of our other product candidates;

- 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.

Until such time, if ever, as we can generate substantial product revenue, 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 collaborations. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. 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 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 or on attractive terms, 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.

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 SEC rules.

Contractual obligations

We have entered into agreements 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. These contractual obligations are cancelable at any time by us, generally upon prior written notice to the vendor.

During the six months ended June 30, 2018, there were no material changes to our contractual obligations and commitments described under Management's Discussion and Analysis of Financial Condition and Results of Operations in the Annual Report on Form 10-K for the year ended December 31, 2017.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates. As of June 30, 2018 and December 31, 2017, we had cash, cash equivalents and marketable securities of $936.6 million and $567.8 million, respectively, consisting primarily of investments in certificates of deposit, U.S. Treasuries, government securities and corporate debt securities. 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, we do not believe an immediate and uniform 100 basis point increase in interest rates would have a material effect on the fair market value of our investment portfolio.

We are also exposed to market risk related to changes in foreign currency exchange rates. We have contracts with CROs located in Asia and Europe that 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 June 30, 2018 and December 31, 2017, we had minimal or no liabilities denominated in foreign currencies.

Item 4. Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of the end of the period covered by this Quarterly Report on Form 10-Q, the effectiveness of our disclosure controls and procedures. Based on that evaluation of our disclosure controls and procedures as of June 30, 2018, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports it

files or submits under the Exchange Act is accumulated and communicated to its management, including its principal executive officer and principal financial officer, or person performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

No change in our internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, occurred during the fiscal quarter ended June 30, 2018 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1A. Risk Factors

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained herein, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of our management 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,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. 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. You should read this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may be materially different from what we expect. The risks described are not the only risks facing our company. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition and/or operating results. 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. These risk factors restate and supersede the risk factors set forth under the heading “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2017.

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 losses were $314.7 million, $198.5 million, and $117.7 million for the years ended December 31, 2017, 2016 and 2015, respectively, and $159.6 million for the six months ended June 30, 2018. As of June 30, 2018, we had an accumulated deficit of $918.2 million. Other than revenue from royalties on sales of IDHIFA®, we have not generated any revenue from product sales. The U.S. Food and Drug Administration, or FDA, approved IDHIFA® in August 2017 for the treatment of adult patients with relapsed or refractory acute myeloid leukemia, or R/R AML, and an IDH2 mutation as detected by an FDA-approved test, and in July 2018 the FDA approved TIBSOVO® for the treatment of adult patients with R/R AML with a susceptible IDH1 mutation as detected by an FDA-approved test. We have not obtained marketing approval for any of our other product candidates, which are in preclinical or clinical development stages. We have financed our operations primarily through private placements of our preferred stock, our initial public offering and the concurrent private placement, our follow-on public offerings and our collaboration agreements with Celgene Corporation and its subsidiaries, or Celgene, focused on cancer metabolism and metabolic immuno-oncology. We have devoted substantially all of our efforts to research and development. Although we may from time to time report profitable results, 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:

- initiate and continue clinical trials for our products and product candidates, including: IDHIFA®, TIBSOVO®, AG-881, mitapivat (AG-348), and AG-270 and AG-636;
- continue our research and preclinical development of our product candidates;
- seek to identify additional product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- establish and maintain a sales, marketing and distribution infrastructure to commercialize any medicines for which we may obtain marketing approval, including IDHIFA® and TIBSOVO®;
- require the manufacture of larger quantities of product candidates for clinical development and, potentially, commercialization;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control and scientific personnel;
- add additional personnel to support our product development and planned future commercialization efforts and our operations;

• add equipment and physical infrastructure to support our research and development; 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 revenue that are significant or large enough to achieve profitability. 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 our 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 our stockholders to lose all or part of their 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 and continue clinical trials of, and seek marketing approvals for, our product candidates. Although Celgene will reimburse us for our co-promotion efforts in the U.S. for IDHIFA® under the 2010 Agreement, if we obtain additional marketing approvals for any of our other product candidates, we expect to incur significant expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of Celgene or other collaborators. For example, in July 2018 the FDA approved TIBSOVO® for the treatment of adult patients with R/R AML with an IDH1 mutation as detected by an FDA approved test, and we have incurred and expect to continue to incur significant expenses related to the commercialization of TIBSOVO®. 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 our existing cash, cash equivalents and marketable securities as of June 30, 2018, together with anticipated product and royalty revenue, anticipated interest income and anticipated expense reimbursements under our collaboration agreements, but excluding any additional program-specific milestone payments, will enable us to fund our operating expenses and capital expenditure requirements through at least the end of 2020. Our estimate as to how long we expect our existing cash and cash equivalents to be available to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. 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, and developments regarding, our collaborations;

• the costs, timing and outcome of regulatory review of our product candidates;

• 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 additional marketing approvals and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Even if we succeed in developing and commercializing one or more of our product candidates, we may never achieve sufficient sales revenue to achieve or maintain profitability. 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, 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 revenue, 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 collaborations, which are limited in scope and duration. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may require us to enter into agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

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.

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 were incorporated 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, undertaking preclinical and clinical studies of our product candidates, and establishing a commercial infrastructure. All of our product candidates are still in preclinical and clinical development, with the exception of IDHIFA® and TIBSOVO®. We have not yet demonstrated our ability to successfully complete any large-scale or pivotal clinical trials or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes about 10 to 15 years to develop one new medicine from the time it is discovered to when it is available for treating patients, assuming that it successfully completes all stages of research and development and achieves marketing approval, all of which is highly uncertain. 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.

We may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors that may adversely affect our ability to successfully commercialize our products and product candidates. We are in the early stages of transitioning from a company with solely a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Risks Related to the Discovery, Development, and Commercialization of our Product Candidates

We do not know whether we will be able to develop any medicines of commercial value, based on our approach to the discovery and development of product candidates that target cellular metabolism.

Our scientific approach focuses on using our proprietary technology to identify key metabolic enzymes in cancer, rare genetic diseases, or RGDs, or other diseased cells in the laboratory and then using these key enzymes to screen for and identify product candidates targeting cellular metabolism. We are also focused on metabolic immuno-oncology, an emerging field of cancer research focused on altering the metabolic state of immune cells to enhance the body's immune response to cancer.

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 RGDs. Any medicines that we develop may not effectively correct metabolic pathways or alter the metabolic state of immune cells. 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. In addition, even if we obtain marketing approval for one of our product candidates, we can provide no assurance that commercialization of such product candidate will be successful.

We may not be successful in our commercialization of TIBSOVO®. If we do not successfully commercialize TIBSOVO® for the treatment of adult patients with R/R AML with a susceptible IDH1 mutation as detected by an FDA approved test, our future prospects may be substantially harmed.

In July 2018, the FDA approved TIBSOVO® for the treatment of adult patients with R/R AML with a susceptible IDH1 mutation as detected by an FDA approved test. We are still evaluating TIBSOVO® in other clinical trials. Our ability to generate product revenue from TIBSOVO® will depend heavily on our successful development and commercialization of the product.

The development and commercialization of TIBSOVO® could be unsuccessful if:

- TIBSOVO® becomes no longer accepted as safe, efficacious, and cost-effective for the treatment of adult patients with R/R AML with a susceptible IDH1 mutation in the medical community and by third-party payors;
- we fail to maintain the necessary financial resources and expertise to manufacture, market and sell TIBSOVO®;
- we fail to continue to develop and implement effective marketing, sales and distribution strategies and opreations for the development and commercialization of TIBSOVO®;
- we fail to continue to develop, validate and maintain a commercially viable manufacturing process for TIBSOVO® that is compliant with current good manufacturing practices;
- we fail to successfully obtain third party reimbursement and generate commercial demand that results in sales of TIBSOVO®;
- we encounter any third party patent interference, derivation, inter partes review, post-grant review, reexamination or patent infringement claims with respect to TIBSOVO®;
- we fail to comply with regulatory and legal requirements applicable to the sale of TIBSOVO®;
- competing drug products are approved for the same indications as TIBSOVO®; or
- TIBSOVO® does not demonstrate acceptable safety and efficacy in current or future clinical trials, or otherwise does not meet applicable regulatory standards for approval in indications other than for the treatment of adult patients with R/R AML with a susceptible IDH1 mutation.

If we experience significant delays or an inability to successfully commercialize TIBSOVO®, our business would be materially harmed.

The failure to maintain the CStone Agreement or the failure of CStone to perform its obligations under the CStone Agreement, could negatively impact our business.

In June 2018, we entered into an exclusive license agreement, or the CStone Agreement, with CStone Pharmaceuticals, or CStone, for the development and commercialization of TIBSOVO®, either as monotherapy or in combination with other therapies, in mainland China, Hong Kong, Macau and Taiwan, or the CStone Territory. Pursuant to the CStone Agreement, CStone will be responsible for the development and commercialization of TIBSOVO® in the CStone Territory. Our ability to generate royalty and milestone revenue under the CStone Agreement is dependent on CStone's performance of its obligations under the agreement. We cannot control the amount and timing of resources that CStone will dedicate to these efforts.

We are subject to a number of other risks associated with our dependence on the CStone Agreement with respect to TIBSOVO® in the CStone Territory, including:

- CStone may fail to comply with applicable regulatory guidelines with respect to developing, manufacturing or commercializing TIBSOVO®, which could adversely impact future development or potential sales of TIBSOVO® in the CStone Territory or elsewhere;
- We and CStone could disagree as to future development plans and CStone may delay, fail to commence or stop future clinical trials or other development;
- There may be disputes between CStone and us, including disagreements regarding the CStone Agreement, that may result in the delay of or failure to achieve developmental, regulatory and sales objectives that would result in milestone or royalty payments, the delay or termination of any future development or commercialization of TIBSOVO® in the CStone Territory, and/or costly litigation or arbitration that diverts our management's attention and resources;
- CStone may fail to provide us with timely and accurate information regarding development, sales and marketing activities or supply forecasts, which could adversely impact our ability to comply with our obligations to CStone, as well as our ability to generate accurate financial forecasts; and
- Business combinations or significant changes in CStone's business strategy may adversely affect CStone's ability or resources available to perform its obligations under the CStone Agreement.

The CStone Agreement is also subject to early termination, including through CStone's right under certain circumstances to terminate upon advance notice to us. If the agreement is terminated early, we may not be able to find another collaborator for the further development and commercialization of TIBSOVO® in the CStone Territory on acceptable terms, or at all, and we may be unable to pursue continued development and commercialization of TIBSOVO® in the CStone Territory on our own.

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 RGDs, as well as in immune cells for the treatment of cancer. 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 RGDs. In addition, our efforts in the emerging field of metabolic immuno-oncology may not be as successful as our efforts to date in cancer metabolism and RGDs. Furthermore, 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 revenue 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 clinical product candidates. Clinical trials of our product candidates may not be successful. If we or our collaborators 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 products and most advanced clinical product candidates, which are IDHIFA®, TIBSOVO® and AG-881 for the treatment of hematological and solid tumors, mitapivat (AG-348) for the treatment of pyruvate kinase, or PK, deficiency, and AG-270 for the treatment of methylthioadenosine phosphorylase, or MTAP, deleted cancers. We have initiated clinical trials for all of these product candidates. The FDA approved IDHIFA® and TIBSOVO for the treatment of adult patients with R/R AML with an IDH2 or IDH1 mutation, respectively. In June 2018, Celgene submitted a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMA, for IDHIFA® for IDH2 mutant-positive R/R AML, and we plan to submit an MAA to the EMA for TIBSOVO® for IDH1 mutant-positive R/R AML in the fourth quarter of 2018. We have not commenced clinical trials for any of our other product candidates. Our ability to generate product revenue will depend heavily on the successful development and eventual commercialization of our product candidates.

The success of TIBSOVO® and our other product candidates will depend on many factors, including the following:

• successful enrollment in, and completion of, clinical trials;

• safety, tolerability and efficacy profiles that are satisfactory to the FDA, the EMA or any comparable foreign regulatory authority for marketing approval;

• timely receipt of marketing approvals from applicable regulatory authorities;

• establishing both clinical and commercial manufacturing capabilities or making arrangements with third-party manufacturers;

• the performance of any collaborators;

• 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;

• continuing acceptable safety profile for the medicines following approval;

• enforcing and defending intellectual property rights and claims; and

• achieving desirable medicinal properties for the intended indications.

Many of these factors are beyond our control, including clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any collaborator. If we or any

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

If clinical trials of products or 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, and any collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Foreign regulatory authorities, such as the EMA, impose similar requirements. We have not previously submitted similar drug approval filings to comparable foreign regulatory authorities for any 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. The FDA has approved IDHIFA® and TIBSOVO® for the treatment of adult patients with R/R AML and an IDH2 or IDH1 mutation, respectively. In June 2018 Celgene submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive AML, and we plan to submit an MAA to the EMA for TIBSOVO® for IDH1 mutant-positive R/R AML in the fourth quarter of 2018. However, we can provide no assurance that we will successfully submit such MAA, or any NDA for any of our other product candidates, or that any MAA or NDA submitted by us or Celgene will receive regulatory approval on the timeframe we expect, or at all.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of our product candidates is susceptible to the risk of failure inherent at any stage of product development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable. For instance, in December 2016, we withdrew our IND for AG-519, our second PKR activator, following verbal notification of a clinical hold from the FDA relating to a previously disclosed case of drug- induced cholestatic hepatitis which occurred in our phase 1 clinical trial of AG-519 in healthy volunteers. Although these decisions and this hepatic adverse event finding do not affect our ongoing clinical trials for mitapivat (AG-348), our first PKR activator, we cannot provide any assurances that there will not be similar or other treatment- related severe adverse events in our other clinical trials of mitapivat (AG-348), that our other trials will not be placed on clinical hold in the future, or that patient recruitment for our other trials will not be adversely impacted.

It is possible that even if one or more of our product candidates has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by our product candidates, or mistakenly believe that our product candidates are toxic or not well-tolerated when that is not in fact the case.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us, or any future collaborators, and impair our ability to generate revenue from product sales, regulatory and commercialization milestones and royalties. Moreover, 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.

Our failure to successfully complete clinical trials of our product candidates and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market any of our product candidates would significantly harm our business.

If we, or any collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of our product candidates, potential clinical development, marketing approval or commercialization of our product candidates could be delayed or prevented.

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, our collaborators or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we or our collaborators 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 or our collaborators may decide, or regulators may require us, to conduct additional clinical trials, including testing in more subjects, 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 RGD programs, may be slower than we anticipate; or participants may drop out of these clinical trials at a higher rate than we anticipate;
- third-party contractors used by us or our collaborators may fail to comply with regulatory requirements or meet their contractual obligations in a timely manner, or at all;
- we or our collaborators 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, institutional review boards, or the data safety monitoring board for such trials may require that we, our collaborators 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 anticipated;
- 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, our collaborators or our investigators, regulators or institutional review boards to suspend or terminate the trials.

Product development costs for us, or any collaborators, will increase if we, or they, experience delays in testing or pursuing marketing approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our product candidates. We do not know whether any preclinical tests or clinical trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we, or any future collaborators, may have the exclusive right to commercialize our product candidates or allow our competitors, or the competitors of any collaborators, to bring products to market before we, or any collaborators, do and impair our ability, or the ability of any collaborators, to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of marketing approval of any of our product candidates.

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 or they are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or analogous regulatory authorities outside the United States. Enrollment may be particularly challenging for some of the orphan diseases we target in our RGD programs. 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.

Utilizing our precision medicine approach, we focus our development activities on genetically or biomarker defined patients most likely to respond to our therapies. As a result, the potential patient populations for our clinical trials are narrowed, and we may experience difficulties in identifying and enrolling a sufficient number of patients in our clinical trials. In particular, the successful completion of our clinical development program for mitapivat (AG-348) for the treatment of PK deficiency is dependent upon our ability to enroll a sufficient number of patients with PK deficiency. PK deficiency is a rare disease with a small patient population. Further, there are only a limited number of specialist physicians that regularly treat patients with PK deficiency and major clinical centers that support PK deficiency are concentrated in a few geographic regions. The small population of patients, the nature of the disease and limited trial sites may make it difficult for us to enroll enough patients to complete our clinical trials for mitapivat (AG-348) for PK deficiency in a timely and cost-effective manner.

In addition, other companies are conducting clinical trials, or may in the future conduct clinical trials, which may have similar eligibility criteria as our current or future clinical trials. For example, Daiichi Sankyo Company, Ltd., with DS-1001b, Bayer AG, or Bayer, with BAY1436032, and Forma Therapeutics Holdings, LLC, with FT-2102, are conducting clinical trials in patients with IDH1 mutant positive-cancers, and Rocket Pharma LTD is in the preclinical stages of development for a gene therapy targeting PK deficiency. As these companies and others initiate and conduct clinical trials, they may compete for eligible patients with our clinical trials of TIBSOVO®, AG-881 or mitapivat (AG-348). Competition for these patients may make it particularly difficult for us to enroll enough patients to complete our clinical trials for TIBSOVO®, AG-881 or mitapivat (AG-348) in a timely and cost-effective manner.

Furthermore, we rely on contract research organizations, or CROs, and clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we have limited influence over their actual performance. 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.

With the exception of IDHIFA® and TIBSOVO®, all of our most advanced product candidates are still in clinical stage 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. Adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us, any future collaborators, an institutional review board or regulatory authorities to interrupt, delay or halt clinical trials of one or more of our product candidates and could result in a more restrictive label, or the delay or denial of marketing approval by the FDA or comparable foreign regulatory authorities. If adverse effects were to arise in patients being treated with any of our product candidates, it could require us to halt, delay or interrupt clinical trials of such product candidate or adversely affect our ability to obtain requisite approvals to advance the development and commercialization of such product candidate. If any of our product candidates is associated with adverse events or undesirable side effects or has properties that are unexpected, we, or any future collaborators, may need to abandon development or limit development of that product candidate 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 earlier stage testing for treating cancer, RGDs or other diseases have later been found to cause side effects that prevented further development of the compound. For instance, in December 2016, we withdrew our IND for AG-519, our second PKR activator, following verbal notification of a clinical hold from the FDA relating to a previously disclosed case of drug-induced cholestatic hepatitis which occurred in our phase 1 clinical trial of AG-519 in healthy volunteers. Although these decisions and this hepatic adverse event finding do not affect our ongoing clinical trials for mitapivat (AG-348), we cannot provide any assurances that there will not be similar or other treatment-related severe adverse events in our other clinical trials for mitapivat (AG-348), that our other trials will not be placed on clinical hold in the future, or that patient recruitment for our other trials will not be adversely impacted.

Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials.

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in future clinical trials. Many companies in the pharmaceutical

and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical

trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we, or future collaborators, believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable foreign regulatory authorities may disagree and may not grant marketing approval of our product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

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.

If we are unable to successfully develop companion diagnostics for our 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 will depend, in part, on our ability to develop companion diagnostics, which are assays or tests to identify an appropriate patient population for these drug candidates. There has been limited success to date industry-wide in developing these types of companion diagnostics. To be successful, we need to address a number of scientific, technical and logistical challenges. 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 rely and expect to continue to rely in part or in whole on third parties for their design and manufacture. We also depend on Celgene and Abbott Laboratories for the development of the FDA approved companion diagnostics for IDHIFA® and TIBSOVO®, respectively, and may in the future depend on Celgene or other third parties for the development of other companion diagnostics for our cancer therapeutic product candidates. If any parties, including without limitation Celgene or us, or any third parties engaged by Celgene or 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 of any of these events, our business would be harmed, possibly materially.

We may be unable to obtain, or may be delayed in obtaining, marketing approval for our product candidates.

It is possible that the FDA or EMA may refuse to accept for substantive review any NDA or MAA that we and/or Celgene submit for our product candidates, including the MAA that Celgene submitted for IDHIFA® and the MAA that we plan to

submit for TIBSOVO® in the fourth quarter of 2018, or may conclude after review of our data that our application is insufficient to obtain marketing approval of our product candidates. If the FDA or EMA does not accept or approve our NDAs or MAAs for any of our product candidates, it may require that we conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data before it will reconsider our applications. Depending on the extent of these or any other FDA- or EMA-required trials or studies, approval of any NDA or MAA that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA or EMA to approve our NDAs or MAAs, as applicable. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us or Celgene from commercializing TIBSOVO® or IDHIFA® in the E.U., or any future product candidate for which we may seek marketing approval, generating revenue and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our development efforts for our product candidates, which could significantly harm our business.

Even if any of our product candidates receives marketing approval, we or others may later discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, which could compromise our ability, or that of any future collaborators, to market the product.

Clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse events could occur:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we, or any future collaborators, may be required to recall the product, change the way the product is administered or conduct additional clinical trials;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication, including, for example, the black box warning for differentiation syndrome on the labels for IDHIFA® and TIBSOVO®;
- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

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.

IDHIFA®, TIBSOVO®, or any of our product candidates that receive marketing approval in the future, 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 revenue 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 approval, availability, market acceptance and reimbursement for the companion diagnostic;
- 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;
- ensuring uninterrupted product supply;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and

• the prevalence and severity of any side effects.

If we are unable to establish and maintain 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 have little 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. Although we have established sales and marketing capabilities to support our co-promotion efforts for IDHIFA® and the commercial launch of TIBSOVO®, we may need to further build our sales and marketing infrastructure to sell , or participate in sales activities with our collaborators for, our other 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 revenue or the profitability of product revenue 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 we and our collaborators will face competition with respect to any product candidates that we or they 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 AML and high risk myelodysplasia. For example, Jazz Pharmaceuticals plc, Abbvie Inc. (in collaboration with Roche Holdings Inc., or Roche) and Bayer are each developing or marketing therapies to treat AML. Some 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 RGDs. 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 most of 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 IDHIFA®, and other of our product candidates, if approved, 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 RGDs. There are a variety of treatment options available, including a number of marketed enzyme replacement therapies, for treating patients with RGDs. 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 RGDs. 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 marketing approval.

There are also a number of product candidates in preclinical or clinical development by third parties to treat cancer and RGDs by targeting cellular metabolism. These companies include large pharmaceutical companies, including AstraZeneca plc, Bayer, Eli Lilly and Company, Roche and its subsidiary Genentech, Inc., GlaxoSmithKline plc, Merck & Co., or Merck, Pfizer, Inc., and Genzyme, a Sanofi company. There are also biotechnology companies of various sizes that are developing therapies to target cellular metabolism, including BioMarin Pharmaceutical Inc., Calithera Biosciences, Inc., or Calithera, Cornerstone Pharmaceuticals, Inc., Daiichi Sankyo Company, Ltd. with its IDH1 mutant inhibitor DS-1001b, and Forma Therapeutics Holdings LLC with its IDH1 mutant inhibitor FT-2102. In addition, there are several companies developing immunotherapies, including metabolic immunotherapies, targeting cancer, including Arcus Biosciences, AstraZeneca PLC, Merck, Bristol-Myers Squibb Company, Calithera, Incyte Corporation, NewLink Genetics Corporation, Novartis, and Rheos Medicines . 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 clinical 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.

If the FDA does not grant our products appropriate periods of data exclusivity before approving generic versions of our products, the sales of our products could be adversely affected.

With FDA approval of an NDA, the product covered by the application is specified as a “reference-listed drug” in the FDA’s publication, “Approved Drug Products with Therapeutic Equivalence Evaluations,” or the Orange Book. Manufacturers may seek approval of generic versions of reference-listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer need not conduct clinical trials. Rather, the applicant generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration and conditions of use or labeling as the reference-listed drug and that the generic version is bioequivalent to the reference-listed drug, meaning it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference-listed drug and companies that produce generic products are generally able to offer them at lower prices. Thus, following the introduction of a generic drug, a significant percentage of the sales of any reference- listed drug may be typically lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference-listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non- patent exclusivity for a new drug containing a new chemical entity. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the reference-listed drug is either invalid or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the reference-listed drug. The FDCA also provides a period of three years of new clinical investigation, data exclusivity in connection with the approval of a supplemental indication for the product for which a clinical trial is essential for approval.

In the event that a generic manufacturer is somehow able to obtain FDA approval without adherence to these periods of data exclusivity, the competition that our approved products may face from generic versions could negatively impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on our investments in those product candidates.

Even if we or any collaborators 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 commercial success of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by third-party payors, including government health administration authorities and private health coverage insurers. If coverage and reimbursement is not available, or reimbursement is available only to limited levels, we, or any future collaborators, may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investments. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug 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, or any future collaborators, might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, possibly for lengthy time periods, which may negatively impact the revenue we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of any future collaborators to recoup our or their investment in one or more product candidates, even if our product candidates obtain marketing approval.

Patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators, to commercialize any of our product candidates will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors. Third-party payors decide which medications they will cover and establish reimbursement levels. The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications, which could affect our ability or that of any future collaborators to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenue. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging the prices charged. We cannot be sure that coverage will be available for any product candidate that we, or any future collaborator, commercialize and, if available, that the reimbursement rates will be adequate.

Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our product candidates for which we, or any future collaborator, obtain marketing approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

We and our collaborators 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 as we or they commercially sell any medicines that we or they may develop. If we or our collaborators cannot successfully defend ourselves or themselves 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;

• reduced resources of our management to pursue our business strategy; 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 as we advance or expand our 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. In addition, if one of our collaboration partners were to become subject to product liability claims or were unable to successfully defend themselves against such claims, any such collaboration partner could be more likely to terminate such relationship with us and therefore substantially limit the commercial potential of our products.

Our internal computer systems, or those of any collaborators or contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to damage from cyber-attacks, computer viruses, worms and other destructive or disruptive software, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. System failures, accidents or security breaches could cause interruptions in our operations, and could result in a material disruption of our clinical and commercialization activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and our product research, development and commercialization efforts could be delayed. In addition, we may not have adequate insurance coverage to provide compensation for any losses associated with such events.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our employees or employees of our vendors to disclose sensitive information in order to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and viruses, and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

Risks Related to Our Dependence on Third Parties

We are reliant on Celgene for the successful development and commercialization of IDHIFA®. If Celgene does not successfully commercialize IDHIFA® for the treatment of adult patients with R/R AML and an IDH2 mutation, our future prospects may be substantially harmed.

In August 2017, the FDA approved IDHIFA® for the treatment of adult patients with R/R AML and an IDH2 mutation, on the basis of an NDA submitted by Celgene. Although IDHIFA® has received FDA approval in R/R AML with an IDH2 mutation, we and Celgene are still evaluating IDHIFA® in other clinical trials. Celgene maintains worldwide development and commercial rights to IDHIFA® and Celgene will fund the development and commercialization costs related to this program, although we have certain co-commercialization and co-promotion rights to IDHIFA®. Under the 2010 Agreement, Celgene is responsible for all development costs for IDHIFA®, and we are eligible to receive up to $95.0 million in milestone payments and a tiered royalty on any net sales of products containing IDHIFA®. Thus, our ability to generate product revenue from IDHIFA® will depend heavily on Celgene's successful development and eventual commercialization of the product.

The development and commercialization of IDHIFA® could be unsuccessful if:

• IDHIFA® becomes no longer accepted as safe, efficacious, and cost-effective for the treatment of adult patients with R/R AML and an IDH2 mutation in the medical community and by third-party payors;

• Celgene fails to continue to apply the necessary financial resources and expertise to manufacturing, marketing and selling IDHIFA®;

• Celgene does not continue to develop and implement effective marketing, sales and distribution strategies and operations for development and commercialization of IDHIFA®;

• Celgene does not continue to develop, validate and maintain a commercially viable manufacturing process for IDHIFA® that is compliant with current good manufacturing practices;

• Celgene does not successfully obtain third party reimbursement and generate commercial demand that results in sales of IDHIFA®;

• Celgene fails to provide us with timely and accurate information regarding development, sales and marketing activities;

• we or Celgene encounter any third party patent interference, derivation, inter partes review, post-grant review, reexamination or patent infringement claims with respect to IDHIFA®;

• Celgene does not comply with regulatory and legal requirements applicable to the sale of IDHIFA®;

• competing drug products are approved for the same indications as IDHIFA®;

• new safety risks are identified;

• IDHIFA® does not demonstrate acceptable safety and efficacy in current or future clinical trials, or otherwise does not meet applicable regulatory standards for approval in indications other than for the treatment of adult patients with R/R AML and an IDH2 mutation;

• Celgene determines to re-prioritize its commercial or development programs and reduce or terminate its efforts on the development or commercialization of IDHIFA®; or

• Celgene does not maintain or defend intellectual property rights associated with IDHIFA®.

If we or Celgene experience significant delays or an inability to successfully commercialize IDHIFA®, our business would be materially harmed.

We depend on our collaborations 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 are party to several collaboration agreements, including the 2010 Agreement, the AG-881 Agreements and the 2016 Agreement with Celgene, and the CStone Agreement. These collaborations involve complex allocations of rights, provide for milestone payments to us based on the achievement of specified clinical development, regulatory and commercial milestones, provide us with royalty-based revenue if certain product candidates are successfully commercialized and provide for cost reimbursements of certain development activities. We cannot predict the success of these collaborations.

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 revenue 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 collaborations with Celgene and CStone, pose the following risks to us:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations. Under the 2010 Agreement, the AG-881 Agreements, programs under a co-development and co-commercialization agreement pursuant to the 2016 Agreement and the CStone Agreement, development and commercialization plans and strategies for licensed programs, such as IDHIFA® or, in the CStone Territory, TIBSOVO®, 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 or CStone, as to which Celgene or CStone, as applicable, may have final decision-making authority. For example, Celgene has elected not to participate in our planned perioperative study of TIBSOVO® and AG-881 in patients with low grade glioma and, pursuant to the AG-881 Agreements, we will fund the trial ourselves.
- 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, under the 2016 Agreement, 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 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, which may result in a need for additional capital to pursue further development or commercialization of the applicable product candidate. For example, under the 2010 Agreement and the 2016 Agreement, 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.
- Collaborators 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, under specified circumstances Celgene has the first right to maintain or defend our intellectual property rights with respect to IDHIFA® under the 2010 Agreement 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 agreements 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 agreements with us, in their entirety or with respect to IDHIFA® under the 2010 Agreement or any program under the 2016 Agreement, upon 90 days' notice and can terminate each entire agreement with us in connection with a material breach of the agreement by us that remains uncured for a period ranging from 60 to 90 days. CStone has the right, under certain circumstances, to terminate the CStone Agreement upon advance notice to us, and may, subject to specified cure periods, terminate the CStone Agreement in the event of our uncured material breach or under specified circumstances relating to our insolvency.
- 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 collaborators 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 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 the 2016 Agreement, we may not directly or indirectly develop, manufacture or commercialize, except pursuant to the agreement, any medicine or product candidate with specified activity against certain metabolic targets except in connection with certain third-party collaborations or with respect to certain targets the rights to which have reverted back to us pursuant to the terms of the 2016 Agreement. Following the discovery phase until termination or expiration of the 2010 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. Following the discovery phase of the 2016 Agreement until termination or expiration of the applicable co-development and co-commercialization agreement or license agreement under the 2016 Agreement, we may not directly or indirectly develop, manufacture or commercialize, outside of the collaboration, any medicine or product candidate with specified activity against the collaboration target that is the subject of such co-development and co-commercialization agreement or license agreement, except in connection with certain third- party collaborations or with respect to certain targets the rights to which have reverted back to us pursuant to the terms of the 2016 Agreement. During the term of the CStone Agreement, we are prohibited from developing or commercializing, in the CStone Territory and in specified indications, other compounds or products that inhibit IDH1 mutations at specified levels of binding.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of 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 rely and expect to continue 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 do not independently conduct clinical trials of any of our product candidates. We rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. In addition 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, some in the event of an uncured material breach and some at any time. If any of our relationships with these third parties terminate, we may not be able

to enter into arrangements with alternative third-parties or to do so on commercially reasonable terms. Switching or adding additional third parties involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays may occur in our product development activities. Although we seek to carefully manage our relationships with our CROs, we could encounter similar challenges or delays in the future and these challenges or delays could have a material adverse impact on our business, financial condition and prospects.

Our reliance on 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 are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, and legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our responsibility to comply with any such standards. We and these third parties are required to comply with current good clinical practices, or cGCP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these cGCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA, or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with cGCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practices, or cGMP, regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register ongoing clinical trials and post the results of

completed clinical trials on a U.S. government-sponsored database, clinicaltrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, third parties on whom we rely may also have relationships with other entities, some of which may be our competitors. In addition, these third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our on-going clinical, nonclinical and preclinical programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may 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. As a result, our results of operations and the commercial prospects for our medicines would be harmed, our costs could increase and our ability to generate revenue could be delayed.

We also rely and expect to continue 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 and clinical testing and expect to continue to do so for late-stage 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 our product candidates for our ongoing preclinical and clinical testing from third-party manufacturers.

Although we have long-term supply agreements in place for commercial supply of TIBSOVO® with third-party manufacturers, we may be unable to establish any further long-term supply 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, environmental and safety and pharmacovigilance reporting.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements on a global basis. 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 substance or drug product. If any one of our current contract manufacturers 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. We do not yet have issued patents for all our most advanced product candidates in all markets we intend to commercialize.

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 have licensed patent rights, and in the future may license additional patent rights, from third parties. These licensed patent rights may be valuable to our business, and 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 that protect our technology or medicines or that 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 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 PTO, 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 or our collaborators 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 PTO. For example, in 2011, The Leonard and Madlyn Abramson Family Cancer Research Institute at the Abramson Cancer Center of the University of Pennsylvania initiated a lawsuit against us, one of our founders, Craig B. Thompson, M.D., and Celgene, alleging misappropriation of intellectual property and, in 2012, the Trustees of the University of Pennsylvania initiated a similar lawsuit against us and Dr. Thompson. Each of these lawsuits was settled in 2012. We are not aware of any other legal proceedings having been filed against us to date. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we or one of our collaborators are found to infringe a third party's intellectual property rights, we or they could be required to obtain a license from such third party to continue developing and marketing our medicines and technology. However, we or our collaborators may not be able to obtain any required license on commercially reasonable terms or at all. Even if we or our collaborators 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 or our collaborators could be forced, including by court order, to cease developing and commercializing the infringing technology or medicine. In addition, we or our collaborators could be found liable for monetary damages. A finding

of infringement could prevent us or our collaborators from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we or our collaborators 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, consultants or advisors are currently or 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, consultants and advisors 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 individuals have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or 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 our 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

Even if we complete necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they 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, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and comparable regulatory authorities in other countries. With the exception of IDHIFA® and TIBSOVO®, we and our collaborators have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. Celgene has submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive AML, and we plan to submit

an MAA to the EMA for TIBSOVO® for IDH1 mutant-positive R/R AML in the fourth quarter of 2018. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. 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 marketing 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 we submit, 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 or our collaborators ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved medicine not commercially viable.

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

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

In order to market and sell our medicines in the E.U. and many other jurisdictions, we or our 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, a product must be approved for reimbursement before the product can be approved for sale in that country. We or our collaborators may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. In particular, although Celgene has submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive AML, and we plan to submit an MAA to the EMA for TIBSOVO® for IDH1 mutant-positive R/R AML in the fourth quarter of 2018, Celgene or we may not be successful in obtaining EMA approval of IDHIFA® or TIBSOVO® , respectively, on a timely basis, or ever. Moreover, 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.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the E.U., commonly referred to as Brexit. On March 29, 2017, the country formally notified the E.U. of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from E.U. directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the E.U. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the E.U. and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or E.U. for our product candidates, which could significantly and materially harm our business.

A fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process, nor does it assure approval of the product candidate by FDA.

In the United States, IDHIFA® and TIBSOVO® received fast track designation for treatment of patients with AML that harbor an IDH2 and IDH1 mutation, respectively. If a drug is intended for the treatment of a serious or life-threatening disease or condition and the drug demonstrates the potential to address unmet medical needs for this disease or condition, the drug sponsor may apply for FDA fast track designation. The FDA has broad discretion whether or not to grant fast track designation, so even if we believe a particular product candidate is eligible for such designation, the FDA may decide not to grant it. Even if our

product candidates receive fast track designation, we may not experience a faster development process, review or approval, if at all, compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

We, or any future collaborators, may not be able to obtain orphan drug designation or orphan drug exclusivity for our drug candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving competing drugs.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same product for that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition. Moreover, even after an orphan drug is approved, the FDA can subsequently approve a different product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, the Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Any product candidate for which we or our collaborators obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to substantial 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 or our collaborators 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 and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and record keeping. 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, including the requirement to implement a risk evaluation and mitigation strategy.

The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose 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. Violations of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

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

• restrictions on such medicine, 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 studies or clinical trials;

• warning letters or untitled letters;

• withdrawal of the medicine from the market;

• refusal to approve pending applications or supplements to approved applications that we submit;

• recall of medicines;

• damage to relationships with any potential collaborators;

• unfavorable press coverage and damage to our reputation;

• 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;

• injunctions or the imposition of civil or criminal penalties; and

• litigation involving patients using our medicines.

Non-compliance with E.U. requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with the E.U. requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Our relationships with healthcare providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, in the event of a violation, 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 will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third-party payors 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 any medicines for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

• the federal 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, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

• the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $10,781.40 to $21,562.80 per false claim;

• the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

• HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

• the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals; and

• analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

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 and may require drug manufacturers

to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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, imprisonment, exclusion of products 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 healthcare 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.

Under the CURES Act and the Trump Administration's regulatory reform initiatives, the FDA's policies, regulations and guidance may be revised or revoked and that could prevent, limit or delay regulatory approval of our product candidates, which would impact our ability to generate revenue.

In December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. An under-staffed FDA could result in delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. Moreover, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This Executive Order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the Executive Order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, President Trump issued an executive order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations, however it is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain marketing approval and commercialize our drug candidates and affect the prices we, or they, 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, among other things, prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any future collaborators, to profitably sell any drugs for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any future collaborators, may receive for any approved drugs.

Among the provisions of the Patient Protection and Affordable Care Act, or ACA, of potential importance to our business and our drug candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and will stay in effect through 2024 unless additional Congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. In May 2017, the U.S. House of Representatives passed legislation known as the American Health Care Act of 2017. Thereafter, the Senate Republicans introduced and then updated a bill to replace the ACA known as the Better Care Reconciliation Act of 2017. The Senate Republicans also introduced legislation to repeal the ACA without companion legislation to replace it, and a "skinny" version of the Better Care Reconciliation Act of 2017. In addition, the Senate considered proposed healthcare reform legislation known as the Graham-Cassidy bill. None of these measures was passed by the U.S. Senate.

The Trump Administration has also taken executive actions to undermine or delay implementation of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Administration announced that it will discontinue the payment of cost-sharing reduction (CSR) payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

More recently, with enactment of the Tax Cuts and Jobs Act of 2017, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA, during the next Congressional session.

We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is highly uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop or commercialize product candidates.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

Moreover, legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical drugs. 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 drug candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any future collaborators to more stringent drug labeling and post-marketing testing and other requirements.

We are subject to U.S. and foreign anti-corruption and anti-money laundering laws with respect to our operations and non-compliance with such laws can subject us to criminal and/or civil liability and harm our business.

We are subject to the U.S. Foreign Corrupt Practices Act of 1977, as amended, or the FCPA, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and possibly other state and national anti-bribery and anti-money laundering laws in countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, third-party intermediaries, joint venture partners and collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or benefits to recipients in the public or private sector. We may have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. In addition, we may engage third party intermediaries to promote our clinical research activities abroad and/or to obtain necessary permits, licenses, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of these third-party intermediaries, our employees, representatives, contractors, partners, and agents, even if we do not explicitly authorize or have actual knowledge of such activities.

Noncompliance with anti-corruption and anti-money laundering laws could subject us to whistleblower complaints, investigations, sanctions, settlements, prosecution, other enforcement actions, disgorgement of profits, significant fines, damages, other civil and criminal penalties or injunctions, suspension and/or debarment from contracting with certain persons, the loss of export privileges, reputational harm, adverse media coverage, and other collateral consequences. If any subpoenas, investigations, or other enforcement actions are launched, or governmental or other sanctions are imposed, or if we do not prevail in any possible civil or criminal litigation, our business, results of operations and financial condition could be materially harmed. In addition, responding to any action will likely result in a materially significant diversion of management's attention and resources and significant defense and compliance costs and other professional fees. In certain cases, enforcement authorities may even cause us to appoint an independent compliance monitor which can result in added costs and administrative burdens.

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.

If we obtain approval to commercialize our product candidates outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

We expect that we will be subject to additional risks in commercializing our product candidates outside the United States, including:

- different regulatory requirements for approval of drugs in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism or natural disasters including earthquakes, typhoons, floods and fires.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain our key executives and scientific leadership and to attract, retain and motivate qualified personnel.

We are highly dependent on the principal members of our management and scientific teams, each of whom is 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.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations, report financial information or data accurately, disclose unauthorized activities to us, or comply with securities laws. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, including for illegal insider trading activities, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

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.

We may engage in acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. Because we have not made any acquisitions to date, our ability to do so successfully is unproven. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies and operations into our existing business in an effective, timely and non-disruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to Our Common Stock and Other Matters

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 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 securities analysts do not publish research or reports about our business or if they publish negative, or inaccurate, evaluations of our stock, the price of our stock and trading volume could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. 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 and trading volume to decline.

An active trading market for our common stock may not be sustained.

Although our common stock is listed on the Nasdaq Global Select Market, an active trading market for our shares may not be sustained. If an active market for our common stock does not continue, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or to sell their shares at all. An inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The price of our common stock is likely to be volatile, which could result in substantial losses for purchasers of our common stock.

The trading price of our common stock has been, and may continue to be, volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. For example, since January 1, 2014 the price of our common stock on the Nasdaq Global Select Market has ranged from $21.70 per share to $138.85 per share. 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. The market price for our common stock may be influenced by many factors, including:

• regulatory actions with respect to our product candidates or our competitors' products and product candidates;

• announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;

• the timing and results of clinical trials of product candidates;

• commencement or termination of collaborations for our development programs;

• failure or discontinuation of any of our development programs;

• results of clinical trials of product candidates 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 develop additional product candidates or products;

• actual or anticipated changes in estimates as to financial results or development timelines;

• announcement or expectation of additional financing efforts;

• sales of our common stock by us, our insiders or other stockholders;

• variations in our financial results, including fluctuations in levels of sales of TIBSOVO® or royalties on sales of IDHIFA®, or results of companies that are perceived to be similar to us;

• changes in estimates or recommendations by securities analysts, if any, that cover our stock;

• 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.

If any of the forgoing matters were to occur, or if our operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. In the past, following periods of volatility in the market price of a company's securities, securities class-action litigation often has been instituted against that company. Such litigation, if instituted against us, could cause us to incur substantial costs to defend such claims and divert management's attention and resources, which could seriously harm our business, financial condition, results of operations and prospects.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Certain stockholders hold a substantial number of shares of our common stock. If such stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our stock incentive plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act of 1933, as amended, or the Securities Act, and, in any event, we have filed a registration statement permitting shares of common stock issued on exercise of options to be freely sold in the public market. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Certain holders of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates. Any sales of securities by these stockholders who have exercised registration rights could have a material adverse effect on the trading price of our common stock.

Our executive officers, directors and principal stockholders maintain the ability to significantly influence all matters submitted to stockholders for approval.

As of June 30, 2018, our executive officers, directors and a small group of stockholders, in the aggregate, beneficially owned shares representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence 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, could significantly influence 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.

Future sales and issuances of our common stock or rights to purchase common stock could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to those of holders of our common stock.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, or the IRC, if a company undergoes an “ownership change,” generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income or taxes may be limited. Our prior equity offerings and other changes in our

stock ownership, some of which are outside of our control, may have resulted or could in the future result in an ownership change. We completed a review of our changes in ownership through December 31, 2017, and determined that we had a qualified ownership change since our last review as of December 31, 2011. We do not expect that this or any previous changes of ownership will result in our net operating loss carryforwards or certain other tax attributes expiring unutilized. Future ownership changes under Section 382 may limit the amount of net operating loss and tax credit carryforwards that we could potentially utilize to reduce future tax liabilities.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revised the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

We are subject to taxation in numerous U.S. states and territories. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the newly enacted federal income tax law, changes in the mix of our profitability from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

We incur costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

We have incurred and will continue to incur significant legal, accounting and other expenses as a public company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly.

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

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 the sole source of gain for our stockholders for the foreseeable future.

Item 6. Exhibits

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
3.1	Restated Certificate of Incorporation	8-K	001-36014	July 30, 2013	3.1	
3.2	Amended and Restated By-Laws	8-K	001-36014	July 30, 2013	3.2	
10.1	First Amendment of Lease, dated April 11, 2018, by and between UP 64 Sidney Street, LLC and Agios Pharmaceuticals. Inc.	8-K	001-36014	April 13, 2018	—	
10.2†	License Agreement, dated June 25, 2018, by and between Agios Pharmaceuticals, Inc. and CStone Pharmaceuticals					X
31.1	Certification of principal executive officer pursuant to Rule 13a 14(a)/15d 14(a) of the Securities Exchange Act of 1934, as amended					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
32.1	Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
32.2	Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					X
101.INS	XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are not embedded within the Inline XBRL document					X
101.SCH	XBRL Taxonomy Extension Schema Document					X
101.CAL	XBRL Taxonomy Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Label Linkbase Document					X
101.PRE	XBRL Taxonomy Presentation Linkbase Document					X

† Confidential treatment requested as to portions of the exhibit. Confidential materials omitted and filed separately with the Securities and Exchange Commission.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

AGIOS PHARMACEUTICALS, INC.

August 2, 2018 By: /s/ David P. Schenkein

David P. Schenkein
President and Chief Executive Officer
(principal executive officer)

August 2, 2018 By: /s/ Andrew Hirsch

Andrew Hirsch
Chief Financial Officer
(principal financial officer)

Confidential Materials omitted and filed separately with the
Securities and Exchange Commission. Double asterisks denote omissions.

LICENSE AGREEMENT

BY AND BETWEEN

AGIOS PHARMACEUTICALS, INC.

AND

CSTONE PHARMACEUTICALS

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LIST OF EXHIBITS

LIST OF SCHEDULES

Schedule 8.04(e) – Milestone Examples

LICENSE AGREEMENT

THIS **LICENSE AGREEMENT** (this "**Agreement**") is made and entered into as of June 25, 2018 ("**Effective Date**") between Agios Pharmaceuticals, Inc., a corporation organized and existing under the laws of Delaware with a principal place of business at 88 Sidney Street, Cambridge, MA 02139 ("**Agios**"), and CStone Pharmaceuticals, a corporation organized and existing under the laws of the Cayman Islands, with a registered address at P.O. Box 31119, Grand Pavilion, Hibiscus Way, 802 West Bay Road, Grand Cayman, KY1-1205, Cayman Islands ("**Licensee**").

Agios and Licensee may be referred to herein individually as a "**Party**" and collectively as the "**Parties**".

RECITALS

WHEREAS, Agios is the owner of, or otherwise controls, the Agios Technology in the Territory (each as defined below);

WHEREAS, Licensee has expertise in the development of biopharmaceutical products and has regulatory and commercial capabilities in the Territory, and is interested in obtaining an exclusive license to Develop and Commercialize the Licensed Products in the Territory (each as defined below); and

WHEREAS, the Parties desire to collaborate to Develop, Manufacture and Commercialize the Licensed Products in the Territory;

NOW THEREFORE, the Parties agree as follows:

I. DEFINITIONS

Section 1.01 "**Accounting Standards**" means United States Generally Accepted Accounting Principles, consistently applied.

Section 1.02 "Affiliate" means, with respect to an entity, any corporation or other business entity controlled by, controlling, or under common control with such entity, with "control" meaning (a) direct or indirect beneficial ownership of at least fifty percent (50%) of the voting stock of, or at least a fifty percent (50%) interest in the income of, the applicable entity (or such lesser percentage that is the maximum allowed to be owned by a foreign entity in a particular jurisdiction and is sufficient to grant the holder of such voting stock or interest the power to direct the management and policies of such entity) or (b) possession, directly or indirectly, of the power to direct the management and policies of an entity, whether through ownership of voting securities, by contract relating to voting rights or corporate governance or otherwise.

Section 1.03 "[**] Trial" means the Global Study identified as [**].

Section 1.04 "Agios Combination Therapy Invention" means any invention (whether patentable or not) conceived or reduced to practice by Agios or any of its Affiliates during the Term, solely or jointly, that (a) [**], (b) [**] that is (A) [**] and (B) [**] and (c) is Controlled [**] by Agios.

Section 1.05 "**Agios Combination Therapy Know-How**" means any Know-How (a) conceived, identified, discovered, authored, developed or reduced to practice by Agios or any of its Affiliates during the Term that comprises, or is necessary for the Development, Manufacture or Commercialization of, any Agios Combination Therapy Invention and (b) Controlled [**] by Agios.

Section 1.06 "**Agios Combination Therapy Patent Rights**" means Patent Rights (a) Covering Agios Combination Therapy Inventions and (b) Controlled [**] by Agios.

Section 1.07 "**Agios Combination Therapy Technology**" means Agios Combination Therapy Inventions, Agios Combination Therapy Know-How and Agios Combination Therapy Patent Rights.

Section 1.08 "Agios Entity" means, as applicable, (a) Agios, (b) any of Agios' Affiliates or (c) any [**] with respect to the Licensed Compound or any Licensed Product (other than any [**]).

Section 1.09 "Agios Know-How" means all Know-How that is both (a) Controlled [**] by Agios and (b) [**] for the Development, Manufacture or Commercialization of any Licensed Product in the Field in the Territory; but excluding [**] and [**]. "Agios Know-How" includes Agios Combination Therapy Inventions and Agios Combination Therapy Know-How to

the extent such Agios Combination Therapy Inventions and Agios Combination Therapy Know-How satisfy the requirements of clauses (a) and (b).

Section 1.10 "Agios Patent Rights" means all Patent Rights that both (a) are Controlled [**] by Agios in the Territory and (b) [**] any Licensed Product, or its Development, Manufacture or Commercialization, in the Field in the Territory; but excluding [**]. Agios Patent Rights as of the Effective Date include those listed in Exhibit A. "Agios Patent Rights" includes Agios Combination Therapy Patent Rights to the extent such Agios Combination Therapy Patent Rights satisfy the requirements of clauses (a) and (b).

Section 1.11 "Agios Regulatory Documents" means Regulatory Documents Controlled by Agios as of the Effective Date or at any time during the Term that relate to the Licensed Compound or a Licensed Product.

Section 1.12 "Agios Technology" means Agios Know-How and Agios Patent Rights.

Section 1.13 "Angiogenesis Inhibitor" means a drug or substance that prevents or inhibits the formation of new blood vessels by blocking one or more vascular endothelial growth factors (VEGFs) or the associated VEGF receptors (VEGFRs).

Section 1.14 "API" means active pharmaceutical ingredient.

Section 1.15 "API Bulk Drug Substance" means the Licensed Compound in bulk [**] intermediate form manufactured for use as an API.

Section 1.16 "Brain Cancer" means any neoplasm originating from cells of the brain.

Section 1.17 "Brightstock" means oral solid dose tablets that contain Bulk Drug Product in sealed unlabeled bottles as set forth in the applicable specifications provided by Agios.

Section 1.18 "**Bulk Drug Product**" means oral solid dose tablets that contain API Bulk Drug Substance in bulk form as set forth in the applicable specifications provided by Agios.

Section 1.19 "Business Day" means a day other than (a) a Saturday or a Sunday or (b) a day on which banking institutions in Boston, Massachusetts, or in Beijing, China, are authorized or required by Law to remain closed.

Section 1.20 "Change in Control" means, as to a Party, the (i) consolidation or merger of such Party with or into any person or entity as a result of which the beneficial owners of the outstanding voting securities or other ownership interests of such Party immediately prior to such transaction have beneficial ownership of fifty percent (50%) or less of the outstanding voting securities or other ownership interests of such surviving person or entity immediately following such transaction, or (ii) sale, transfer or other disposition of all or substantially all of the assets of such Party related to this Agreement, or (iii) acquisition by any person or entity, or group of persons or entities acting in concert, of beneficial ownership of fifty percent (50%) percent or more of the outstanding voting securities or other ownership interests of such Party or the power,

directly or indirectly, to elect a majority of the members of such Party's board of directors or similar governing body, or (iv) acquisition by any person or entity, or group of persons or entities acting in concert, of the power to direct the management or policies of such Party. No initial or subsequent offering by a Party of securities for sale on a public securities exchange shall be considered to be or to involve a Change in Control of such Party unless such offering meets the requirements of clause (iii) of the preceding sentence; *provided, however,* that an acquisition of voting securities by an underwriter in an underwritten public offering for the purpose of effecting a wider distribution of such voting securities shall be deemed not to meet the requirements of clause (iii) of the preceding sentence.

Section 1.21 "Chemotherapy" means cytotoxic anti-cancer drugs that belong to one of the following categories: alkylating agents, antimetabolites, anti-tumor antibiotics, topoisomerase inhibitors, mitotic inhibitors, corticosteroids and proteasome inhibitors. For clarity, chemotherapy does not include targeted cancer therapies that use drugs or substances that block the growth and spread of cancer by interfering with specific targets.

Section 1.22 "**[**] Trial**" means the Global Study identified as [**], which Agios is conducting as of the Effective Date with a Licensed Product in [**].

Section 1.23 "Commercialization" or "Commercialize" means, with respect to a pharmaceutical product (whether in monotherapy or as part of a combination therapy), any and all activities directed to the marketing, promotion, importation, distribution, pricing, Reimbursement Approval, offering for sale, or sale of such pharmaceutical product, and interacting with Regulatory Authorities regarding the foregoing. Commercialization shall exclude Development and Manufacturing.

Section 1.24 "Commercialization Plan" means the annual plan for Commercialization of Licensed Products in the Field in the Territory and the activities to be conducted by Licensee Entities relating thereto, including detailed plans for sales and marketing after launch, sales and marketing budgets, sales forecasts and target numbers regarding reach and frequency of sales performance, market access plans, reimbursement plans and strategies, and plans to address Medical Affairs matters, which plan Licensee shall ensure is consistent with (a) the terms and conditions of this Agreement and (b) the Global Brand Strategy. The Launch Plan will include the first Commercialization Plan for the calendar year in which a Licensed Product is launched.

Section 1.25 "Commercially Reasonable Efforts" means, with respect to the performing Party under this Agreement, the carrying out of obligations of such Party with efforts and resources that are consistent with the efforts and resources typically used by biopharmaceutical companies of similar size and resources as such Party with respect to the Development, Manufacture or Commercialization of products of market potential, profit potential and strategic value and of a stage in Development or product life comparable to that of Licensed Product(s), including the use of reasonably necessary personnel, based on conditions then prevailing and taking into account issues of safety and efficacy, product profile, difficulty in Developing such Licensed Product, competitiveness of alternative Third Party products in the marketplace, the patent or other proprietary position of such Licensed Product, the regulatory

structure involved and the potential profitability of such Licensed Product, as applicable, but [**] under this Agreement.

Section 1.26 "Competing Product" means any compound or product, other than the Licensed Compound or any Licensed Product, that inhibits IDH-1 mutations through direct binding to the mutated IDH-1 protein [**].

Section 1.27 "Confidential Information" means, subject to **Section 12.02(a)-(d)**, Know-How and any technical, scientific, trade, research, manufacturing, business, financial, compliance, marketing, product, supplier, intellectual property or other information that may be disclosed by one Party or any of its Affiliates to the other Party or any of its Affiliates, regardless of whether such information is specifically designated as confidential and regardless of whether such information is in written, oral, electronic, or other form. Notwithstanding the foregoing, subject to **Section 12.02(a)-(d)**, all information that (a) was disclosed prior to the Effective Date by or on behalf of either Party or any of its Affiliates under, and subject to, the Mutual Confidential Agreement dated [**] between CStone Pharmaceutical (Suzhou) Co., Ltd. and Agios Pharmaceuticals, Inc., as amended on [**] ("**Confidentiality Agreement**") and (b) is "Confidential Information" as defined in the Confidentiality Agreement, shall be deemed "Confidential Information" hereunder.

Section 1.28 "**Controlled**" means, subject to **Section 2.06(a)** and **Section 16.02 (Acquisitions)**, with respect to a Party, and any Know-How, Patent Right, Regulatory Documents or other intellectual property right, that such Party or any of its Affiliates has the ability (other than pursuant to a license granted to such Party under this Agreement) to grant to the other Party a license or sublicense to, or other right with respect to, such Know-How, Patent Right, Regulatory Documents or other intellectual property right without violating the terms of any pre-existing agreement or other pre-existing arrangement with any Third Party.

Section 1.29 "**Cost of Goods Sold**" or "**COGS**" means, with respect to particular Ivosidenib Materials, the reasonable internal and Out-of-Pocket Costs of Agios or any of its Affiliates incurred in Manufacturing such Ivosidenib Materials, including:

(a) to the extent that the Ivosidenib Materials are Manufactured by Agios or any of its Affiliates, direct material and direct labor costs, logistics costs, plus manufacturing overhead directly attributable to the Ivosidenib Materials (including facility start-up costs, directly incurred manufacturing variances, warehousing costs, costs to maintain inventory and a reasonable allocation of related manufacturing administrative and facilities costs (including depreciation) and a reasonable allocation of the costs of failed batches and validation batches to be further described in the applicable Supply Agreement, to be provided for the Ivosidenib Materials, but excluding costs associated with excess capacity), all determined in accordance with the books and records of Agios or its applicable Affiliate(s) maintained in accordance with United States Generally Accepted Accounting Principles, consistently applied; and

(b) to the extent that the Ivosidenib Materials are Manufactured by a Third Party manufacturer, the Out-of-Pocket Costs paid by Agios or any of its Affiliates to the Third Party for the Manufacture of the Ivosidenib Materials, plus all reasonably allocated costs of Agios and its

Affiliates as described in the foregoing clause (a) incurred in managing or overseeing the sourcing of such Ivosidenib from such Third Party, determined in accordance with the books and records of Agios or its applicable Affiliate(s) maintained in accordance with United States Generally Accepted Accounting Principles, consistently applied.

Section 1.30 "**Cover**", "**Covering**" or "**Covered**" means, with respect to a product, composition, technology, process or method and a Patent Right, that, in the absence of ownership of, or a license granted under, a claim in such Patent Right, the manufacture, use, offer for sale, sale or importation of such product or composition or the practice of such technology, process or method would infringe such claim (or, in the case of a claim of a pending patent application, would infringe such claim if it were to issue as a claim of an issued patent).

Section 1.31 "CS1001" means Licensee's proprietary anti-PD-L1 monoclonal antibody designated as CS1001, the sequence of which is included in the following patent filings: [**].

Section 1.32 "CS1003" means Licensee's proprietary anti-PD-1 monoclonal antibody designated as CS1003, the sequence of which is included in the following patent filings: [**].

Section 1.33 "**Development**" means Pre-Clinical Research and clinical development activities, including (i) clinical trials of a pharmaceutical compound or product, investigator sponsored trials and registry studies (whether in monotherapy or as part of a combination therapy) and (ii) preparation, submission, review, and development of data or information for the purpose of submission to a Regulatory Authority to obtain authorization to conduct clinical trials or obtain Regulatory Approval of a pharmaceutical product. Development shall include clinical trials initiated prior to or following receipt of Regulatory Approval, but shall exclude Manufacturing and Commercialization.

Section 1.34 "**Development Plan**" means the plan setting out activities to be undertaken in Developing the Licensed Products in the Field in the Territory, together with timelines for such activities, including the proposed clinical trials, registry studies and regulatory plans, as well as outlining the key elements involved in obtaining Regulatory Approval of the Licensed Products in the Field in the Territory, as may be amended from time to time in accordance with **Section 4.01 (Development in the Field in the Territory)**, which plan (a) Licensee shall ensure is at all times consistent with the terms and conditions of this Agreement, (b) Licensee shall ensure is focused on efficiently obtaining Regulatory Approval for Licensed Products (whether in monotherapy or as part of a combination therapy) in each Initial Indication and Additional Indication in each Jurisdiction in the Territory and cannot reasonably be expected to have a material adverse effect on the Development, Manufacture or Commercialization of the Licensed Compound or any Ivosidenib Materials or Licensed Product outside of the Territory and (c) shall include in reasonable detail (i) all Development activities reasonably anticipated to be undertaken by the Licensee Entities, (ii) the endpoints for all clinical trials contemplated by such plan, (iii) identification of the clinical trial(s) that is(are) intended to be a Pivotal Trial(s) and (iv) all regulatory activities and interactions anticipated to be conducted by the Licensee Entities in support of Regulatory Approval of the Licensed Products in the Field in the Territory, including all planned Regulatory Filings to be submitted in connection with such approvals.

Section 1.35 "**Dollars**" **or** "**$**" means the legal tender of the U.S.

Section 1.36 "**Drug Approval Application**" means a New Drug Application as defined in the FD&C Act, or an equivalent application filed with any Regulatory Authority in any country other than the United States.

Section 1.37 "**FDA**" means the U.S. Food and Drug Administration or any successor agency thereto.

Section 1.38 "**FD&C Act**" means the U.S. Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 et seq., as amended from time to time.

Section 1.39 "**Field**" means all therapeutic uses in humans in all indications except Brain Cancer indications. Brain Cancer indications will be included in the Field if and when Agios provides written notice to Licensee to add any Brain Cancer indication to the Field.

Section 1.40 "**Finished Drug Product**" means the finished product formulation of a Licensed Product, containing Bulk Drug Product labeled and packaged in a form ready for administration.

Section 1.41 "**First Commercial Sale**" means, for each Licensed Product in the Field in a Jurisdiction, the first sale for end use or consumption of such Licensed Product in the Field in such Jurisdiction by any Licensee Entity in an arms' length transaction to a Third Party following receipt of applicable Regulatory Approval of such Licensed Product in such Jurisdiction. Sales for test marketing or clinical trial purposes shall not constitute a First Commercial Sale.

Section 1.42 "**Global Brand Strategy**" means the global brand strategy that determines, among other aspects, product positioning, market access strategies, messaging strategies, trademark layout and logos, all as determined by Agios for Licensed Products and updated from time to time and provided to Licensee.

Section 1.43 "**Global Medical Affairs Strategy**" means the global Medical Affairs strategy for Licensed Products, as determined by Agios and updated from time to time and provided to Licensee.

Section 1.44 "**Global Study**" means (a) any clinical trial for any Licensed Product that (i) is conducted, in whole or in part, by any Agios Entity and (ii) includes clinical sites in more than one country or jurisdiction and (b) solely for purposes of **Section 8.03 (Development Costs)**, the [**] Trial.

Section 1.45 "**Good Clinical Practices**" **or** "**GCP**" means the then-current good clinical practice standards, practices, and procedures promulgated or endorsed by any applicable Regulatory Authority as set forth in the guidelines imposed by such Regulatory Authority, as may be updated from time to time.

Section 1.46 "**Good Laboratory Practices**" **or** "**GLP**" means the then-current good laboratory practice standards, practices, and procedures promulgated or endorsed by any applicable Regulatory Authority as set forth in the guidelines imposed by such Regulatory Authority, as may be updated from time to time.

Section 1.47 "**Good Pharmacovigilance Practices**" **or** "**GVP**" means the then-current good pharmacovigilance practice standards, practices, and procedures promulgated or endorsed by any applicable Regulatory Authority as set forth in the guidelines imposed by such Regulatory Authority, as may be updated from time to time.

Section 1.48 "**Governmental Authority**" means any federal, national, multinational, state, provincial, county, city or local government or any court, arbitrational tribunal, administrative agency or commission or government authority acting under the authority of any federal, national, multinational, state, provincial, county, city or local government.

Section 1.49 "[**] Trial" means the clinical trial identified as [**].

Section 1.50 "**IDH**" means isocitrate dehydrogenase.

Section 1.51 "**IND**" means an Investigational New Drug application for submission to the FDA or any equivalent counterpart application in any country other than the United States (including a clinical trial application in Mainland China), including all supplements and amendments thereto.

Section 1.52 "**Initial Development Outline**" means the initial outline of the Development strategy for Licensed Products in the Territory attached hereto as Exhibit B.

Section 1.53 "**Initial Indication**" means any of (a) first line treatment for acute myelogenous leukemia ("**AML**") for patients who are ineligible for intensive Chemotherapy, (b) first line treatment for AML for patients who are eligible for intensive Chemotherapy, (c) relapse/refractory AML, (d) first line treatment for cholangiocarcinoma ("**CCA**"), (e) second line treatment for CCA and (f) any Brain Cancer indication if Agios determines, in its sole discretion, to Develop Licensed Products in any Brain Cancer indication.

Section 1.54 "**In-License Agreement**" means any agreement between Agios or any of its Affiliates, on the one hand, and one or more Third Parties, on the other hand, entered into after the Effective Date pursuant to which Agios acquires Control of any Know-How related to, or Patent Right that Covers, the Development or Commercialization of any Licensed Product in the Field in the Territory, or the Manufacture of the Licensed Compound, Ivosidenib Materials or Licensed Products, that Licensee has accepted as an In-License Agreement under **Section 2.06**.

Section 1.55 "**Ivosidenib Materials**" means Bulk Drug Product, Brightstock or API Bulk Drug Substance, as applicable.

Section 1.56 "**Joint Combination Therapy Invention**" means any invention (whether patentable or not) conceived or reduced to practice by a Party or any of its Affiliates under this

Agreement during the Term, solely or jointly, that (a) is based on [**], (b) [**] is (A) [**] and (B) [**].

Section 1.57 "**Joint Combination Therapy Know-How**" means any Know-How conceived, identified, discovered, authored, developed or reduced to practice by a Party or any of its Affiliates under this Agreement [**] that comprises, or is necessary for the Development, Manufacture or Commercialization of, any Joint Combination Therapy Invention.

Section 1.58 "**Joint Combination Therapy Patent Rights**" means Patent Rights Covering Joint Combination Therapy Inventions.

Section 1.59 "**Joint Combination Therapy Technology**" means Joint Combination Therapy Inventions, Joint Combination Therapy Know-How and Joint Combination Therapy Patent Rights.

Section 1.60 "**Joint Global Study**" means a Global Study where a Licensee Entity is the Local Registration Agent in the Territory and for which Licensee is responsible for paying a portion of costs as set forth in **Section 8.03(b)**.

Section 1.61 "**Jurisdiction**" means each of the following: (i) Mainland China, (ii) Taiwan, (iii) Hong Kong and (iv) Macau.

Section 1.62 "**Know-How**" means inventions (whether patentable or not), discoveries, trade secrets, technology, information, Regulatory Documents, formulae, practices, methods, knowledge, know-how, processes, procedures, experience, results and test data (including physical, chemical, biological, toxicological, pharmacological, clinical, veterinary, analytical and quality control data), dosage regimens, control assays, product specifications, and marketing, pricing, distribution cost and sales data and descriptions; but excluding Patent Rights.

Section 1.63 "**Launch Plan**" means the strategic plan for the Licensed Products in the Field in the Territory that details the activities to be conducted prior to launch, plans for launch and activities to be conducted during the calendar year in which the launch occurs, which plan Licensee shall ensure is at all times consistent with (a) the terms and conditions of this Agreement and (b) the Global Brand Strategy.

Section 1.64 "**Law**" means any law, statute, rule, regulation, order, judgment, standard or ordinance of any Governmental Authority.

Section 1.65 "**Licensed Compound**" means the compound identified on Schedule 1.65.

Section 1.66 "**Licensed Product**" means any pharmaceutical product that (a) has the Licensed Compound as its sole API and (b) is in a form (i) which is the subject of any clinical trial being conducted by any Agios Entity as of the Effective Date or during the Term or (ii) for which any Agios Entity has received Regulatory Approval to market in the United States or anywhere else outside the Territory after the Effective Date.

Section 1.67 "**Licensee Entity**" means, as applicable, (a) Licensee, (b) any of Licensee's Affiliates or (c) any [**] with respect to any Licensed Product.

Section 1.68 "**Licensee In-License Agreement**" means any agreement other than this Agreement pursuant to which any Licensee Entity has in-licensed or otherwise acquired the right to practice, or in-licenses or otherwise acquires the right to practice, any Know-How related to, or Patent Rights that Cover, any of the Licensed Products in the Field in the Territory.

Section 1.69 "**Licensee Know-How**" means all Know-How that is both (a) Controlled [**] by Licensee and (b) [**] for the Development, Manufacture or Commercialization of the Licensed Compound or any Licensed Product; but excluding [**] and Know-How assigned or licensed by Licensee to Agios pursuant to **Section 9.01(d)**.

Section 1.70 "**Licensee Patent Rights**" means all Patent Rights that both (a) are Controlled [**] by Licensee and (b) [**] the Licensed Compound or any Licensed Product or their respective Development, Manufacture or Commercialization; but excluding [**] and Patent Rights assigned or licensed by Licensee to Agios pursuant to **Section 9.01(d)**.

Section 1.71 "**Licensee Regulatory Documents**" means Regulatory Documents Controlled by Licensee at any time during the Term that relate to the Licensed Compound or a Licensed Product in the Territory, *provided that*, for the avoidance of doubt, Regulatory Documents relating to Global Studies of the Licensed Compound or any Licensed Product in the Territory shall be owned as set forth in **Article V**.

Section 1.72 "**Licensee Technology**" means Licensee Know-How and Licensee Patent Rights.

Section 1.73 "**Local Registration Agent**" means a local entity authorized by the license holder of an imported drug to manage the work associated with obtaining any Regulatory Approval or product registration in the Territory.

Section 1.74 "**Local Study**" means any clinical trial for any Licensed Product that is conducted by a Licensee Entity in the Territory; but excluding all Global Studies.

Section 1.75 "**Mainland China**" means China excluding Taiwan, Hong Kong and Macau.

Section 1.76 "**Manufacture**" or "**Manufacturing**" means, as applicable, all activities associated with the production, manufacture, process of formulating, processing, filling, finishing, packaging, labeling, shipping, importing or storage of pharmaceutical compounds or materials, including process development, process validation, stability testing, manufacturing scale-up, pre-clinical, clinical and commercial manufacture and analytical development, product characterization, quality assurance and quality control development, testing and release.

Section 1.77 "**Manufacturing Technology Transfer**" means the transfer, to Licensee or a CMO approved by the JMC, of Agios Know-How relating to the Manufacturing of Bulk Drug Product from API Bulk Drug Substance supplied by or on behalf of any Agios Entity.

Section 1.78 "**Medical Affairs**" means matters relating to information services; publication, scientific and medical affairs; advisory and collaborative activities with opinion leaders and professional societies including medical education, symposia and other medical programs and communications; but excluding investigator sponsored trials and registry studies and other Development activities.

Section 1.79 "**Net Sales**" means the gross invoice price of a particular Licensed Product sold or otherwise transferred to a Third Party (other than a Licensee Entity) by any Licensee Entity for consideration, reduced by the following amounts to the extent such items are customary under industry practices in the Territory and to the extent such amounts are included in the gross invoiced sales price, all as calculated in accordance with Accounting Standards, consistently applied:

(a) discounts (including trade, quantity and cash discounts) actually allowed, cash and non-cash coupons, retroactive price reductions, and charge-back payments and rebates granted to any Third Party (including to governmental authorities, purchasers, reimbursers, customers, distributors, wholesalers, and group purchasing and managed care organizations or entities (and other similar entities and institutions));

(b) credits or allowances, if any, on account of price adjustments, recalls, claims, damaged goods, rejections or returns of items previously sold (including Licensed Product returned in connection with recalls or withdrawals) and amounts written off by reason of uncollectible debt; *provided* that, if the debt is thereafter paid, the corresponding amount shall be added to the Net Sales of the period during which it is paid;

(c) rebates (or their equivalent), administrative fees, chargebacks and retroactive price adjustments and any other similar allowances granted by a Licensee Entity (including to governmental authorities, purchasers, reimbursers, customers, distributors, wholesalers, and group purchasing and managed care organizations or entities (and other equivalent entities and institutions)) which effectively reduce the selling price or gross sales of the Licensed Product, normal and customary inventory management fees and other bona fide services paid to distributors and wholesalers;

(d) insurance, customs charges, freight, postage, shipping, handling, and other transportation costs incurred by a Licensee Entity in shipping Licensed Product to a Third Party; and

(e) import taxes, export taxes, excise taxes, sales tax, value-added taxes, consumption taxes, duties or other taxes levied on, absorbed, determined or imposed with respect to such sales (excluding income or net profit taxes or franchise taxes of any kind).

If non-monetary consideration is received by a Licensee Entity for any Licensed Product in the relevant Jurisdiction, Net Sales will be calculated based on the average price charged for such Licensed Product, as applicable, during the preceding royalty period, or in the absence of such sales, the fair market value of the Licensed Product, as applicable, as determined by the Parties in good faith. Notwithstanding the foregoing, Net Sales shall not be imputed to transfers of Licensed Products, as applicable, for use in clinical trials, non-clinical Development activities or other Development activities with respect to Licensed Products by or on behalf of the Parties, for *bona fide* charitable purposes or for compassionate use or for Licensed Product samples, if no monetary consideration is received for such transfers.

Section 1.80 "**Ongoing Trials**" means the Global Studies of Licensed Products identified as [**]; provided that, to the extent any such Global Study has multiple study arms, then "Ongoing Trials" includes only those study arms applicable to the Licensed Product.

Section 1.81 "Out-of-Pocket Costs" means amounts paid by a Party or any of its Affiliates to a Third Party for goods or services but shall not include such Party's, or any of its Affiliates', internal or general overhead costs or expenses.

Section 1.82 "**Patent Rights**" means (a) all patents and patent applications (including provisional applications) in any country or jurisdiction, and (b) any substitutions, divisions, continuations, continuations-in-part, reissues, renewals, registrations, confirmations, re-examinations, extensions, supplementary protection certificates and the like.

Section 1.83 "Phase 1 Clinical Trial" means a clinical trial in any country or jurisdiction that would satisfy the requirements of 21 C.F.R. § 312.21(a) or any foreign equivalent thereof.

Section 1.84 "Pivotal Trial" means a clinical trial of a product that satisfies both of the following ((a) and (b)):

(a) such trial includes a sufficient number of subjects and is designed to establish that such product has an acceptable safety and efficacy profile for its intended use, and 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 Regulatory Approval of such product, or a similar clinical study prescribed by an applicable Regulatory Authority; and

(b) such trial is a registration trial designed to be sufficient to support the filing of an application for a Regulatory Approval for such product in an applicable country or jurisdiction or some or all of an extra-national territory, as evidenced by (i) an agreement with or statement from an applicable Regulatory Authority, or (ii) other guidance or minutes issued by an applicable Regulatory Authority, for such registration trial.

Section 1.85 "POC Trial" means a clinical trial that is not a Pivotal Trial, but that is designed such that, if its primary endpoint(s) is(are) met, such clinical trial would support commencement of a Pivotal Trial.

Section 1.86 "Pre-Clinical Research" means preclinical and non-clinical research activities.

Section 1.87 "**Regulatory Approval**" means, with respect to a particular regulatory jurisdiction, an approval, license, registration or authorization of any Governmental Authority (other than any Reimbursement Approval) that provides marketing approval for the commercial sale of a pharmaceutical product in one or more specified indications in such regulatory jurisdiction.

Section 1.88 "**Regulatory Authority**" means, in a particular country or jurisdiction, any applicable Governmental Authority involved in granting Regulatory Approval in such country or jurisdiction, including (a) in the United States, the FDA and any other applicable Governmental Authority in the United States having jurisdiction over pharmaceutical products, (b) in Europe Union, the European Medicines Agency ("**EMA**"), (c) in Mainland China, the SDA and (d) any other applicable Governmental Authority in the Territory having jurisdiction over pharmaceutical products.

Section 1.89 "**Regulatory Documents**" means all (a) applications (including all INDs and Drug Approval Applications), registrations, licenses, authorizations, approvals (including Regulatory Approvals) and marketing or regulatory exclusivities; (b) correspondence and reports submitted to or received from Regulatory Authorities (including minutes and official contact reports relating to any communications with any Regulatory Authority) and all supporting documents with respect thereto, including all regulatory drug lists, advertising and promotion documents, adverse event files and complaint files; and (c) preclinical, clinical and other data, results, analyses, publications, and reports contained or referred to in any of the foregoing. For the avoidance of doubt, Regulatory Documents include Regulatory Approvals and Regulatory Filings.

Section 1.90 "**Regulatory Filings**" means all applications, filings, dossiers and the like submitted to a Regulatory Authority for the purpose of Developing, Manufacturing or Commercializing a product, including obtaining Regulatory Approval from that Regulatory Authority. Regulatory Filings include all INDs, Drug Approval Applications and other Regulatory Approval and Reimbursement Approval applications.

Section 1.91 "**Reimbursement Approval**" means an approval, agreement, determination, or other decision by any applicable Regulatory Authority or other Governmental Authority that establishes prices at which a pharmaceutical product may be priced, or will be reimbursed by the Regulatory Authorities or other applicable Governmental Authorities, in a particular country or jurisdiction.

Section 1.92 "**Safety Data Exchange Agreement**" means that agreement between the Parties regarding receipt, investigation and reporting of product complaints, adverse events, product recalls, and any other information related to the safety of the Licensed Products as set forth in **Section 10.03** (**Adverse Drug Events**).

Section 1.93 "**SDA**" means China's State Drug Administration, including its divisions and the Center for Drug Evaluation, and local counterparts thereto, and any successor agency or authority thereto having substantially the same function.

Section 1.94 "**Serialization**" means a combination of systems and procedures that records the history of the chain of custody of the Finished Drug Product from any applicable Licensee Entity to the point the Finished Drug Product is dispensed.

Section 1.95 "**Supply Price**" means [**] percent ([**]%) of COGS.

Section 1.96 "**Tax**" means any present or future taxes, levies, imposts, duties, tariffs, charges, assessments or fees of any nature imposed by a Governmental Authority in the exercise of its taxing power (including interest, penalties and additions thereto), including value-added tax ("**VAT**") and withholding tax.

Section 1.97 "**Territory**" means any Jurisdiction, or, collectively, all Jurisdictions, as the context requires.

Section 1.98 "**Third Party**" means any person or entity other than the Parties and their Affiliates.

Section 1.99 "**Trade Control Laws**" shall refer to U.S. Laws which prohibit or limit export, distribution or sales of goods from the United States and their re-export from other countries into certain countries, referred to as Sanctioned Countries. More specifically and for purpose of performing this Agreement, Trade Control Laws shall refer to the U.S. Export Administration Regulations and the economic sanctions, rules and regulations implemented under statutory authority or President's Executive Orders and administered by the U.S. Treasury Department's OFAC.

Section 1.100 "**Trademark**" means any trademark, trade name, service mark, service name, brand, domain name, trade dress, logo, slogan or other indicia of origin or ownership, including the goodwill and activities associated with each of the foregoing.

Section 1.101 "**U.S.**" or "**United States**" means the United States of America, including its districts, territories and possessions.

Section 1.102 "**Valid Claim**" means (a) any claim of any Patent Right that has issued, is unexpired and has not been rejected, revoked or held unenforceable or invalid by a final, non-appealable (or unappealed within the time allowable for appeal) decision of a court or other Governmental Authority of competent jurisdiction or (b) any claim of any patent application that has (i) been pending for [**] or less from the date of issuance of the first substantive patent office action considering the patentability of such claim by the applicable patent office in the applicable country or jurisdiction and (ii) not been cancelled, withdrawn, abandoned or finally rejected by an administrative agency action from which no appeal can be taken.

Additional Defined Terms	**Section**
Acquired Party	Section 16.02
Acquirer	Section 16.02
Additional Indication	Section 4.01(a)
Agios	Preamble
Agios Indemnitees	Section 13.02
Agios Product Data	Section 2.04(b)
Agios Trademarks	Exhibit C, Section 2.01(a)
Agios Web Presence	Exhibit C, Section 2.01(b)
Agios Works	Exhibit C, Section 2.02(c)
Agreement	Preamble
Alliance Manager	Section 3.13
AML	Section 1.53
Arbitration Request	Section 15.01(a)
Bankrupt Party	Section 14.06(a)
Breaching Party	Section 14.05
Breach Notice	Section 14.05
CCA	Section 1.53
Clinical Supply Agreement	Section 7.01
CMC	Section 2.05(a)
CMO	Section 3.05(a)(iv)
Commercial Supply Agreement	Section 7.02
Committee	Section 3.01(a)
Confidentiality Agreement	Section 1.27
Effective Date	Preamble

EMA	Section 1.88
Event of Bankruptcy	Section 14.06(a)
Exception	Section 8.03(c)
Executive Officer	Section 3.09
FCPA	Section 11.05(b)(i)
First Defending Party	Section 9.03(d)
Government Official	Section 11.05(a)(A)
ICC	Section 15.01(c)
ICH	Section 10.02
Indemnified Party	Section 13.03
Indemnifying Party	Section 13.03
Infringement Activity	Section 9.03(a)
JCC	Section 3.01(a)
JDC	Section 3.01(a)
JMC	Section 3.01(a)
JSC	Section 3.01(a)
Licensee	Preamble
Licensee Indemnitees	Section 13.01
Licensee Product Data	Section 2.05(a)
Losses	Section 13.01
Materials	Exhibit C, Section 1.03
Non-Breaching Party	Section 14.05
Other Covered Party	Section 11.05(a)(B)
Other Party	Section 14.06(a)
Party or Parties	Preamble

Public Statement	Section 12.04
Recipient	Section 12.02
Rejected Local Study	Section 14.02
Representatives	Section 12.01
Restricted Indication	Section 2.07(b)
Restricted Product	Section 2.07(b)
Royalty Term	Section 8.06(b)
Rules	Section 15.01
Severed Clause	Section 17.03
Subcommittee	Section 3.01(b)
Supply Agreement	Section 7.02
Term	Section 14.01
Terminable Date	Section 14.02
VAT	Section 1.96

Section 1.103 Interpretation. (a) Whenever any provision of this Agreement uses the word "including," "include," "includes," or "*e.g.*," such word shall be deemed to mean "including without limitation" and "including but not limited to"; (b) "herein," "hereby," "hereunder," "hereof" and other equivalent words shall refer to this Agreement in its entirety and not solely to the particular portion of this Agreement in which any such word is used; (c) a capitalized term not defined herein but reflecting a different part of speech from that of a capitalized term which is defined herein shall be interpreted in a correlative manner; (d) wherever used herein, any pronoun or pronouns shall be deemed to include both the singular and plural and to cover all genders; (e) the recitals set forth at the start of this Agreement, along with the schedules and the exhibits to this Agreement, and the terms and conditions incorporated in such recitals and schedules and exhibits, shall be deemed integral parts of this Agreement and all references in this Agreement to this Agreement shall encompass such recitals and schedules and exhibits and the terms and conditions incorporated in such recitals and schedules and exhibits; *provided* that, in the event of any conflict between the terms and conditions of the body of this Agreement and any terms and conditions set forth in the recitals, schedules or exhibits, the terms of the body of this Agreement shall control; (f) in the event of any conflict between the terms and conditions of this Agreement and any terms and conditions that may be set forth on any order, invoice, verbal agreement or otherwise, the terms and conditions of this Agreement shall govern; (g) this Agreement shall be construed as if both Parties drafted it jointly, and shall not be

construed against either Party as principal drafter; (h) unless otherwise provided, all references to Sections, Articles and Schedules in this Agreement are to Sections, Articles, Exhibits and Schedules of and to this Agreement; (i) any reference to any Law shall mean such Law as in effect as of the relevant time, including all rules and regulations thereunder and any successor Law in effect as of the relevant time, and including the then-current amendments thereto; (j) wherever used, the word "shall" and the word "will" are each understood to be imperative or mandatory in nature and are interchangeable with one another; (k) references to a particular person or entity include such person's or entity's successors and assigns to the extent not prohibited by this Agreement; (l) references to a Party's knowledge shall be taken to refer to the actual knowledge of such Party's senior management team as of the Effective Date; (m) the captions and table of contents used herein are inserted for convenience of reference only and shall not be construed to create obligations, benefits or limitations; and (n) the word "year" means any consecutive twelve (12) month period, unless otherwise specified.

ARTICLE II.

LICENSES; EXCLUSIVITY

Section 2.01 Grants of Licenses.

(a) Subject to the terms and conditions of this Agreement (including **Section 8.03(c)**), Agios hereby grants to Licensee (i) an exclusive (including as to Agios and its Affiliates), royalty-bearing, non-sublicensable (except in accordance with **Section 2.02 (Rights to Sublicense or Subcontract)**), non-transferable (except in accordance with **Section 16.01 (Assignment)**) license under the Agios Technology and Agios' interest in the Joint Combination Therapy Technology to Commercialize Licensed Products in the Field in the Territory in accordance with this Agreement, with, for clarity, Agios retaining all rights in the Territory under Agios Technology and Agios' interest in the Joint Combination Therapy Technology to Commercialize Agios' other products to be used in combination with Licensed Products; (ii) a co-exclusive, non-sublicensable (except in accordance with **Section 2.02 (Rights to Sublicense or Subcontract)**), non-transferable (except in accordance with **Section 16.01 (Assignment)**) license under the Agios Technology and Agios' interest in the Joint Combination Therapy Technology to Develop Licensed Products in the Territory in accordance with this Agreement solely for the purpose of Commercializing Licensed Products in the Field in the Territory in accordance with this Agreement; (iii) a non-exclusive, royalty-bearing, non-sublicensable (except in accordance with **Section 2.02 (Rights to Sublicense or Subcontract)**), non-transferable (except in accordance with **Section 16.01 (Assignment)**) license under the Agios Technology and Agios' interest in the Joint Combination Therapy Technology (A) to Manufacture Finished Drug Product from Bulk Drug Product supplied by an Agios Entity and (B) solely from and after the date (if any) on which a Manufacturing Technology Transfer has been completed, to Manufacture Bulk Drug Product from API Bulk Drug Substance supplied by an Agios Entity, in each case ((A) and (B)) in the Territory and solely for the purpose of Developing and Commercializing Licensed Products in the Field in the Territory in accordance with this Agreement; and (iv) a non-exclusive, royalty-free, fully-paid-up, sublicensable, non-transferable (except in accordance with **Section 16.01 (Assignment)**), perpetual, irrevocable license under

the Agios Combination Therapy Technology and Agios' interest in the Joint Combination Therapy Technology to Develop and Commercialize any of [**] (for clarity nothing in this clause (iv) grants to Licensee any rights under any Patent Rights or Know-How owned or otherwise Controlled by Agios to Develop, Manufacture or Commercialize any Licensed Product). For the purposes of clause (ii), a co-exclusive license means that Agios and Agios' Affiliates may, and Agios may grant sublicenses to Third Parties to, Develop Licensed Products in the Territory in support of global Development of the Licensed Products and Commercialization of the Licensed Products outside the Territory.

(b) Subject to the terms and conditions of this Agreement, Licensee hereby grants to Agios, (i) an exclusive (including as to Licensee and its Affiliates), royalty-free, fully-paid-up, transferable, sublicensable, perpetual, irrevocable license under Licensee Technology and Licensee's interest in the Joint Combination Therapy Technology to Develop, Manufacture and Commercialize the Licensed Compound, Ivosidenib Materials and Licensed Products outside the Territory, with, for clarity, Licensee retaining all rights outside the Territory under Licensee Technology and Licensee's interest in the Joint Combination Therapy Technology to Commercialize Licensee's other products to be used in combination with Licensed Products; (ii) a co-exclusive, royalty-free, fully-paid, transferable, sublicensable, perpetual, irrevocable license under the Licensee Technology and Licensee's interest in the Joint Combination Therapy Technology to Develop and Manufacture the Licensed Compound, Ivosidenib Materials and Licensed Products in the Territory; (iii) from and after any early termination of this Agreement, an exclusive (including with regard to Licensee and its Affiliates), royalty-free, fully-paid, transferable, sublicensable, perpetual, irrevocable license under the Licensee Technology and Licensee's interest in the Joint Combination Therapy Technology to Develop, Manufacture and Commercialize the Licensed Compound, Ivosidenib Materials and Licensed Products in the Territory, other than in any Jurisdiction in which Licensee retains a perpetual license in accordance with **Section 8.06(b)**; *provided* that in such Jurisdiction(s) as to which Licensee retains a perpetual license, Agios shall retain its co-exclusive license set forth in clause (ii); and (iv) a non-exclusive, royalty-free, fully-paid-up, sublicensable, non-transferable (except in accordance with **Section 16.01 (Assignment)**), perpetual, irrevocable license under Licensee's interest in the Joint Combination Therapy Technology to Develop and Commercialize any of [**]. For the purposes of clause (ii), a co-exclusive license means that Licensee agrees not to grant a license to a Third Party to Develop or Manufacture the Licensed Compound, Ivosidenib Materials or Licensed Products in the Territory except to support Development and Commercialization in the Territory in accordance with this Agreement.

Section 2.02 Rights to Sublicense or Subcontract. Licensee may not sublicense, except to Affiliates of Licensee, any of the rights granted to Licensee by Agios under **Section 2.01(a)** except with Agios' prior written consent, which consent shall not be unreasonably withheld. Licensee may not subcontract any of Licensee's obligations hereunder except (subject to **Section 8.11 (Methods of Payment)**) to Affiliates of Licensee or as set forth on Exhibit D or with Agios' prior written consent, which consent shall not be unreasonably withheld. Licensee shall ensure that all Licensee Entities comply with all applicable provisions of this Agreement and shall remain responsible for the acts or omissions of all Licensee Entities with respect to this Agreement.

Section 2.03 No Other Rights and Retained Rights. Nothing in this Agreement shall be interpreted to grant either Party any rights under any Patent Rights or Know-How Controlled by the other Party that are not expressly granted herein, whether by implication, estoppel or otherwise, and, notwithstanding the foregoing provisions of **Section 2.01 (Grants of Licenses)**, neither Party grants any right or license in this Agreement to the other Party under Patent Rights or Know-How Controlled by such Party with respect to APIs or drug products other than the Licensed Compound and Licensed Products. Any rights not expressly granted to a Party by the other Party under this Agreement are hereby retained by such other Party.

Section 2.04 Knowledge Transfer.

(a) Within [**] following the Effective Date, Agios shall provide to Licensee all data relating to Licensed Products as included in Regulatory Filings made by any Agios Entity as of the Effective Date, or, upon Licensee's request, that are reasonably necessary for Licensee to file an IND in the Territory. Licensee shall reimburse Agios for any reasonable Out-of-Pocket Costs incurred by Agios or any of its Affiliates in fulfilling its obligations under this **Section 2.04(a)**.

(b) Subject to **Section 8.03(c)**, throughout the Term, upon Licensee's request, Agios shall make available to Licensee copies of Agios Regulatory Documents, clinical and preclinical data, and efficacy, safety and pharmacovigilance data, in each case that are Controlled by Agios (collectively, the "**Agios Product Data**"), to the extent such Agios Product Data are reasonably necessary for any Licensee Entity to Develop, Commercialize or (following the completion of any Manufacturing Technology Transfer) Manufacture any Licensed Product in the Field in the Territory in accordance with this Agreement.

Section 2.05 Product Data and Regulatory Documents.

(a) Throughout the Term, Licensee shall make available to Agios copies of Licensee Regulatory Documents, clinical and preclinical data, efficacy, safety and pharmacovigilance data, and chemistry, manufacturing and controls ("**CMC**") data (collectively, the "**Licensee Product Data**") to the extent such Licensee Product Data is reasonably necessary for any Agios Entity to Develop, Manufacture or Commercialize the Licensed Compound or any Licensed Product in accordance with this Agreement. Notwithstanding anything to the contrary in **Section 15.03**, Licensee shall make available to Agios copies of all Licensee Product Data in Chinese, along with, at no charge to Agios, the table of contents in English and an executive summary in English of each module of each Regulatory Filing, with each such summary to be sufficient for Agios to either comment on the document or determine that it wishes to obtain, at its own expense, an English translation of all or part of such document. Upon Agios' request, Licensee shall make available to Agios copies of Licensee Product Data available in English as well, and, if Licensee uses such English translations solely for purposes of responding to Agios' request (and not for any other purpose), Agios shall bear any reasonable Out-of-Pocket costs incurred by Licensee in translating such Licensee Product Data from Chinese to English. Agios shall reimburse Licensee for any reasonable Out-of-Pocket Costs incurred by Licensee in fulfilling its obligations under this **Section 2.05(a)**, excluding the costs of preparing English tables of contents and executive summaries of Regulatory Filings as described above.

(b) Subject to **Section 8.03(c)**, the Licensee Entities shall be entitled at no cost to access, use, and reference the Agios Regulatory Documents that are necessary for a Licensee Entity to prepare a Regulatory Filing with respect to the Licensed Products in the Field in the Territory, and Agios Product Data for the Development, Manufacture and Commercialization of the Licensed Products in the Field in the Territory in accordance with this Agreement.

(c) The Agios Entities shall be entitled at no cost to access, use and reference the Licensee Regulatory Documents and Licensee Product Data for the Development, Manufacture or Commercialization of the Licensed Compound or Licensed Products in accordance with this Agreement.

Section 2.06 In-License Agreements.

(a) Subject to **Section 16.02 (Acquisitions)**:

In the event that Agios or any of its Affiliates enters into an agreement with a Third Party after the Effective Date that Agios determines is necessary or reasonably useful for the Development or Commercialization of any Licensed Product in the Field in the Territory, or the Manufacture of the Licensed Compound, Ivosidenib Materials or Licensed Products, then Agios will promptly provide Licensee with notice and a copy of the applicable Third Party agreement. Within [**] following receipt of such notice, Licensee will decide, in its sole discretion, whether to accept the applicable Third Party agreement as an In-License Agreement, and provide notice of such decision to Agios. In such event, subject to **Section 8.06(d)**, Licensee shall pay royalties for sales in the Territory in accordance with such In-License Agreement and the *pro rata* share of any other costs associated with such In-License Agreement to the extent that such costs apply to any Licensee Entity's activities under this Agreement. In the event that Licensee declines to accept such Third Party agreement as an In-License Agreement, then (i) such Third Party agreement shall not be deemed to be an "In-License Agreement" hereunder and (ii) any rights granted to Agios under such Third Party agreement will not be deemed to be "Controlled" by Agios or licensed to Licensee under this Agreement. In the event that Licensee accepts such Third Party agreement as an In-License Agreement, such Third Party agreement will thereafter be included within the definition of "In-License Agreement," and any rights granted to Agios under such In-License Agreement will be deemed to be "Controlled" by Agios and sublicensed to Licensee pursuant to the terms of this Agreement.

(b) Licensee acknowledges and agrees that certain of the rights, licenses and sublicenses granted by Agios to Licensee in this Agreement (including any sublicense rights) are subject to the terms of the In-License Agreements and the rights granted to the Third Party counterparties thereunder, the scope of the licenses granted to Agios or any applicable Affiliate thereunder and the rights retained by such Third Party counterparties and any other Third Parties (including Governmental Authorities) set forth therein. Licensee shall, and shall ensure that each Licensee Entity shall, perform and take such actions to allow Agios and its Affiliates to comply with their obligations under each In-License Agreement, to the extent applicable to Licensee's rights or obligations under this Agreement. Without limiting the foregoing, each Licensee Entity shall prepare and deliver to Agios, or assist Agios in preparing, any additional reports required under any In-License Agreement, in each case reasonably sufficiently in advance to enable Agios

and its Affiliates to comply with their obligations thereunder. Each Licensee Entity shall comply with all provisions of each In-License Agreement that are applicable to such Licensee Entity's exercise of rights or performance of obligations under this Agreement. To the extent there is a conflict between the terms of any In-License Agreement and any rights granted to, or obligations imposed upon, Licensee hereunder, the terms of the applicable In-License Agreement(s) shall control. Any breach by any Licensee Entity of any provision of any In-License Agreement applicable to any of them pursuant to this **Section 2.06 (In-License Agreements)** shall be deemed a material breach of this Agreement.

Section 2.07 Exclusivity.

(a) During the Term, Licensee shall not, and Licensee shall ensure that each of its Affiliates and sublicensees shall not, itself or with or through any Third Party, without the prior written consent of Agios, engage in Development, Manufacture or Commercialization of any Competing Product, except Development, Manufacture or Commercialization of Licensed Products in the Field anywhere in the world in accordance with this Agreement.

(b) During the period beginning on the Effective Date and ending on [**], Licensee shall not, and Licensee shall ensure that each of its Affiliates and sublicensees shall not, itself or with or through any Third Party, without the prior written consent of Agios, engage in Development, Manufacture or Commercialization of any compound or product that is not a Competing Product but that directly or indirectly targets patients that have an IDH-1 mutation ("**Restricted Product**") to treat or prevent AML, CCA or, if included by Agios into the Field in accordance with **Section 1.39**, glioma (for clarity, not including glioblastoma multiforme) ("**Restricted Indication**"), except that Licensee and its Affiliates shall be permitted to [**].

(c) During the Term, neither Agios nor any of its Affiliates shall, itself or with or through any Third Party, without the prior written consent of Licensee, (i) Develop or Commercialize any Competing Product in the Territory in the Field or (ii) engage in Commercialization of Licensed Products for use in any Brain Cancer indication in the Territory except, in each case ((i) and (ii)), pursuant to this Agreement.

(d) Each Licensee Entity will use Commercially Reasonable Efforts to monitor and prevent exports or resale of Licensed Products from or outside the Territory for Development or Commercialization outside of the Territory using methods commonly used in the industry for such purpose, and shall promptly inform Agios of any such actual or suspected exports from the Territory, and the actions taken to prevent such exports. Licensee shall take, and shall ensure that each Licensee Entity takes, reasonable actions requested in writing by Agios that are consistent with Law to prevent such exports. If Licensee or any of its Affiliates or, to Licensee's or any of its Affiliates' knowledge, any other Licensee Entity receives a request or order to Develop, Manufacture or Commercialize any Licensed Compound or Licensed Product outside of the Territory, Licensee shall immediately notify Agios thereof, shall not accept such request or order, and shall direct the relevant individual or entity to Agios.

(e) Each Party acknowledges and agrees that the exclusivity obligations set forth in this **Section 2.07 (Exclusivity)**, including the duration and scope thereof, are intended, in part, to protect the Parties' trade secrets and other Confidential Information. In the event that any

arbitrator or court determines that the duration or scope of any provision of this **Section 2.07 (Exclusivity)** is unreasonable and that any such provision is to that extent unenforceable, each Party agrees that such provision shall remain in full force and effect for the greatest time period and to the greatest scope that would not render it unenforceable. The Parties intend that the provisions of this **Section 2.07 (Exclusivity)** shall be deemed to be a series of separate covenants, one for each and every product, indication and jurisdiction where such provision is intended to be effective.

ARTICLE III.

GOVERNANCE

Section 3.01 General.

(a) The Parties shall establish (i) a Joint Steering Committee ("**JSC**") to oversee and coordinate the overall conduct of the Development and Commercialization of Licensed Products and supply and Manufacturing of the Ivosidenib Materials in the Field in the Territory, (ii) a Joint Development Committee ("**JDC**") to oversee and coordinate the Development of the Licensed Products in the Field in the Territory, (iii) a Joint Commercialization Committee ("**JCC**") to oversee and coordinate the Commercialization of the Licensed Products in the Field in the Territory and (iv) a Joint Manufacturing Committee ("**JMC**") to oversee and coordinate the Manufacturing and supply of the Ivosidenib Materials for the Development and Commercialization of the Licensed Products in the Field in the Territory. The JSC, the JDC, the JCC and the JMC shall each be referred to as a "**Committee**". Each Committee shall have decision-making authority with respect to the matters within its purview to the extent expressly provided herein.

(b) From time to time, each Committee may establish one or more subcommittees or working groups to oversee particular projects or activities, as it deems necessary or advisable (each, a "**Subcommittee**"). Each Subcommittee shall consist of such number of members as the applicable Committee determines is appropriate from time to time. Such members shall be individuals with expertise and responsibilities in the relevant areas. Each Subcommittee shall discuss matters within the scope of such Subcommittee's oversight and shall report the outcome of the discussions of such Subcommittee to the Committee that formed such Subcommittee promptly after each meeting. Following the receipt of the report from such Subcommittee, the Committee that formed such Subcommittee shall make any required decisions regarding matters set forth in such report.

Section 3.02 Joint Steering Committee.

(a) Within [**] following the Effective Date, the Parties shall establish the JSC. The JSC shall:

(i) discuss and manage the strategic direction of the Development and Commercialization of the Licensed Products in the Field in the Territory;

(ii) monitor and discuss the progress of the Development and Commercialization of the Licensed Products in the Field in the Territory and serve as a forum for exchanging information regarding the conduct of the Development and Commercialization of the Licensed Products in the Field in the Territory;

(iii) oversee and coordinate all of the matters within the responsibilities of the Committees hereunder;

(iv) determine whether to create any additional Committee;

(v) serve as a forum for dispute resolution in accordance with **Section 3.08 (Committee Decision Making)** with respect to matters that are not resolved at the JDC, JCC or JMC; and

(vi) perform such other duties as are specifically assigned to the JSC under this Agreement.

Section 3.03 Joint Development Committee.

(a) Within [**] following the Effective Date, the Parties shall establish the JDC. The JDC shall:

(i) discuss and approve the Development Plan and any proposed updates or amendments to the Development Plan (including the addition of indications not set forth in the then-current Development Plan), and propose revisions to the Development Plan in accordance with **Section 4.01 (Development in the Field in the Territory)**;

(ii) secure alignment of the Licensee Entities' Development of Licensed Products in the Territory with Agios' Development of the Licensed Products outside of the Territory;

(iii) discuss and determine, with respect to each Global Study and on an indication-by-indication basis, whether to include clinical sites in the Territory in such Global Study and whether such Global Study shall be a Joint Global Study;

(iv) discuss and determine the clinical sites in the Territory to be included in each Local Study;

(v) discuss and approve the protocols for each Local Study and Joint Global Study;

(vi) discuss and determine the clinical sites in the Territory to be included in each Joint Global Study;

(vii) for each Joint Global Study, coordinate the operations of the Agios Entities and Licensee Entities with respect to such Joint Global Study;

(viii) discuss and determine the contract research organizations in the Territory to be used for each Joint Global Study;

(ix) discuss and approve the Licensee Entities' regulatory strategy for the Licensed Products in the Territory based on the then-current Development Plan;

(x) discuss and approve Pre-Clinical Research activities with respect to the Licensed Products that any Licensee Entity wishes to conduct in the Territory;

(xi) provide a forum for the Parties to share information with respect to the Development of the Licensed Products in the Field, including reasonably detailed updates on progress and status of Local Studies and Joint Global Studies in the Territory and commenting on Development activities outside of the Territory and updates regarding interactions with Regulatory Authorities;

(xii) discuss and approve publications and publication plans as to the Development and Commercialization of Licensed Products in the Territory;

(xiii) discuss, coordinate and provide strategic guidance on the Development of the Licensed Products in the Field in the Territory;

(xiv) discuss and approve the content of any IND or Drug Approval Application for any Licensed Product in the Territory; and

(xv) perform such other duties as are specifically assigned to the JDC under this Agreement.

Section 3.04 Joint Commercialization Committee.

(a) Within [**] following the Effective Date, the Parties shall establish the JCC. The JCC shall:

(i) discuss and approve the Launch Plan and discuss the implementation of such Launch Plan;

(ii) discuss and approve the Commercialization Plan each year and discuss implementation of such Commercialization Plan;

(iii) discuss and align Licensee Entities' commercial activities in the Territory with the Global Brand Strategy;

(iv) discuss and determine whether a Manufacturing Technology Transfer to Licensee would allow for rapid inclusion of the Licensed Products in national reimbursement lists in the Territory, and provide the outcome of such discussion to the JMC;

(v) discuss that the Licensee Entities' Medical Affairs strategy for the Licensed Products in the Territory and ensure it is in line with Agios' Global Medical Affairs Strategy;

(vi) discuss and coordinate attendance at national and international conferences and congresses and interactions with key opinion leaders by Licensee Entities in the Territory and by Agios Entities outside the Territory;

(vii) discuss the Licensee Entities' market access activities in the Territory, including the pricing strategy for the Licensed Products in the Territory;

(viii) discuss Licensee Entities' sales achieved during the then-preceding [**] period and the forecasted sales numbers for the next [**]; and

(ix) perform such other duties as are specifically assigned to the JCC under this Agreement.

Section 3.05 Joint Manufacturing Committee.

(a) Within [**] following the Effective Date, the Parties shall establish the JMC. The JMC shall:

(i) oversee and coordinate the clinical supply of Ivosidenib Materials to Licensee for Licensee's Development activities in the Territory;

(ii) oversee and coordinate the commercial supply of Ivosidenib Materials to Licensee for the Commercialization of Licensed Products in the Territory;

(iii) discuss and determine whether to conduct a Manufacturing Technology Transfer to Licensee (after consideration of the outcome of the discussion by the JCC in accordance with **Section 3.04(a)(iv)**) and, if so (A) determine the activities required for the Manufacturing Technology Transfer and timing thereof; and (B) oversee implementation of the Manufacturing Technology Transfer;

(iv) select and approve the Third Party contract manufacturers of Ivosidenib Materials in the Territory, if other than Licensee (each, a "**CMO**"), for the Manufacture of Ivosidenib Materials on behalf of Licensee in the Territory; and

(v) perform such other duties as are specifically assigned to the JMC under this Agreement or under the Clinical Supply Agreement or Commercial Supply Agreement.

Section 3.06 Membership. Each Committee shall be composed of [**] representatives from each of Agios and Licensee, 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 activities within the scope of the authority and responsibility of such Committee. Any representative from either Party can represent such Party on more than one Committee. Each Party may replace any of its representatives on any Committee at any time with written notice to the other Party; *provided* that such replacement meets the standard described in the preceding sentence. Each Party's representatives and any replacement of a representative shall be bound by obligations of confidentiality and non-use applicable to the other Party's Confidential Information that are at least as stringent as those set forth in **Article XII** (**Confidentiality**). Each Party may invite a

reasonable number of its or its Affiliates' employees as required or useful to discuss the applicable agenda items. Each Committee shall appoint a chairperson from among its members, with the first chairperson of the JSC and the JDC being a representative of [**] and the first chairperson of each other Committee being a representative of [**]. Each chairperson (whether initially appointed or any successor therefor) shall serve a term of one (1) year, at which time, the applicable Committee shall select a successor chairperson who is a representative of the Party other than the Party represented by the outgoing chairperson (*e.g.*, the second chairperson of each of the JSC and the JDC shall be a representative of [**], the third chairperson of each of the JSC and the JDC shall be a representative of [**], etc.). Within [**] following each Committee meeting, the chairperson of the applicable Committee shall circulate to all Committee members a draft of the minutes of such meeting. The Committee shall then approve, by mutual agreement, such minutes within [**] following circulation. No chairperson of any Committee shall have any greater authority than any other representative of such Committee.

Section 3.07 Meetings.

(a) Each Committee shall hold an initial meeting within [**] after its formation or as otherwise agreed by the Parties. Thereafter, unless the Parties otherwise agree, (i) the JSC shall meet in person or by video teleconference at least [**] and (ii) the JDC, JCC, JMC and any other Committee (other than the JSC) will meet in person or by video teleconference at least [**]. In the event that a Committee (other than the JSC) is formed in [**], such Committee shall have [**] in such calendar year, but in any other case, each Committee (other than the JSC) shall have [**] meetings each calendar year, including in the year of its formation. Unless otherwise agreed in writing by the Parties, all in-person meetings for each Committee shall be held on an alternating basis between Agios' headquarters in Cambridge, Massachusetts and Licensee's Affiliate's office in Shanghai, China, and each Committee shall meet in person at least [**]. Each Party shall be responsible for all of its own personnel and travel costs and expenses relating to participation in Committee meetings.

(b) Agios may upon reasonable notice include relevant representatives of Agios licensees of any Licensed Product outside the Territory to attend any Committee meeting as non-voting guests; *provided* that such additional representatives shall be bound by obligations of confidentiality and non-use applicable to the other Party's Confidential Information that are at least as stringent as those set forth in **Article XII** (**Confidentiality)**. Agios will use good faith efforts to obtain the right, in future license agreements outside of the Territory concerning Licensed Products, to invite representatives of Licensee to attend committee meetings as non-voting guests.

Section 3.08 Committee Decision Making. 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. If the JDC, JCC, JMC or any other Committee (other than the JSC) is unable to reach agreement on any matter within [**] after the matter is referred to it or first considered by it, such matter shall be referred to the JSC for resolution. If the JSC is unable to reach agreement on any matter within [**] after the matter is referred to it or first considered by it, such matter shall be referred to the Executive Officers for resolution in accordance with **Section 3.09 (Executive Officers; Disputes)**.

Section 3.09 Executive Officers; Disputes. Each Party shall ensure that an executive officer is designated for such Party at all times during the Term for dispute resolution purposes (each such individual, such Party's "**Executive Officer**"), and shall promptly notify the other Party of its initial, or any change in its, Executive Officer. Unless otherwise set forth in this Agreement, in the event of a dispute arising under this Agreement between the Parties, the Parties shall refer such dispute to the Executive Officers, who shall attempt in good faith to resolve such dispute.

Section 3.10 Final Decision-Making Authority. If the Parties are unable to resolve a given dispute within the purview of a Committee within [**] after referring such dispute to the Executive Officers pursuant to **Section 3.09 (Executive Officers; Disputes)**, then, subject to **Section 3.11 (Limitations on Decision-Making)**:

(a) Agios shall have the deciding vote on (i) activities relating to Global Studies worldwide, including selection of sites for Global Studies (in and outside of the Territory), [**] (iv) any matter that could reasonably be expected to have any material adverse effect on Manufacturing, Development or Commercialization for any Licensed Product outside the Territory, which may include adverse effects on the scope, validity or enforceability of any Agios Technology.

(b) Licensee shall have the deciding vote on (i) [**]; *provided* that such matter [**] does not fall under Agios' final decision-making authority pursuant to **Section 3.10(a).**

Any decision made by an Executive Officer in accordance with this **Section 3.10 (Final Decision-Making Authority)** shall be deemed to be a decision of the relevant Committee.

Section 3.11 Limitations on Decision-Making.

(a) Neither Party shall have the deciding vote on, and no Committee shall have decision-making authority regarding, any of the following matters:

(i) the imposition of any requirements on the other Party to undertake obligations beyond those for which it is responsible, or to forgo any of its rights, under this Agreement;

(ii) the imposition of any requirements that the other Party takes or declines to take any action that would result in a violation of any Law or any agreement with any Third Party or the infringement of intellectual property rights of any Third Party;

(iii) the resolution of any dispute involving the breach or alleged breach of this Agreement;

(iv) the determination of whether a Licensee Entity exerts Commercially Reasonable Efforts under this Agreement;

(v) any decision that is expressly stated to require the mutual agreement (or similar language) of a Committee or the Parties or the approval of the other Party (but not "approval" of a Committee);

(vi) any matters that would excuse such Party from any of its obligations under this Agreement; or

(vii) modifying the terms of this Agreement or taking any action to expand or narrow the responsibilities of any Committee.

(b) The decision-making Party shall make its decision in good faith, subject to the terms and conditions of this Agreement.

(c) In no event may the decision-making Party unilaterally determine that it has fulfilled any obligations hereunder or that the non-deciding Party has breached any obligations hereunder.

(d) In no event may Licensee unilaterally determine that the events required for the payment of milestone payments have not occurred.

(e) In no event may Agios unilaterally determine that the events required for the payment of milestone payments have occurred.

(f) For clarity, approval by a Committee shall not be understood to mean approval by a Party.

Section 3.12 Scope of Governance. Notwithstanding the creation of each of the Committees or anything to the contrary in this **Article III**, 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. For clarity, no Committee shall have any rights, powers or discretion to make any decision regarding the Development, Manufacturing or Commercialization of the Licensed Products outside of the Field or outside of the Territory, and, with respect to such matters relating to Licensed Products that are so excluded from the Committees' scope of authority, Agios retains all such rights, powers and discretion.

Section 3.13 Alliance Managers. Each of the Parties shall appoint a single individual to manage Development, Manufacturing and Commercialization obligations between the Parties under this Agreement (each, an "**Alliance Manager**"). The role of the Alliance Manager is to act as a single point of contact between the Parties to ensure a successful relationship under this Agreement. The Alliance Managers may attend any Committee and Subcommittee meetings. Each Alliance Manager shall be a non-voting participant in such Committee and Subcommittee meetings, unless s/he is also appointed a member of such Committee; *provided*, *however*, that an Alliance Manager may bring any matter to the attention of a Committee if such Alliance Manager reasonably believes that such matter warrants such attention. Each Party may change its designated Alliance Manager at any time upon written notice to the other Party. Any Alliance Manager may designate a substitute to temporarily perform the functions of that Alliance Manager by written notice to the other Party. Each Party's Alliance Manager and any substitute for an Alliance Manager shall be bound by obligations of confidentiality and non-use applicable

to the other Party's Confidential Information that are at least as stringent as those set forth in **Article XII** (**Confidentiality**). Each Alliance Manager will also: (a) plan and coordinate cooperative efforts and internal and external communications; and (b) facilitate the governance activities hereunder and the fulfillment of action items resulting from Committee meetings.

ARTICLE IV.

DEVELOPMENT

Section 4.01 Development in the Field in the Territory.

(a) Within [**] after the Effective Date, Licensee shall present the Development Plan, which shall be prepared based on and in accordance with the Initial Development Outline, to the JDC for approval. The Development of Licensed Products in the Field in the Territory shall be governed by the Development Plan, and no Licensee Entity may Develop any Licensed Product in the Field in the Territory other than in accordance with the Development Plan, or as otherwise approved by Agios in advance in writing. Each Development Plan shall provide for each Local Study, Joint Global Study, investigator sponsored trial and registry study to be conducted in the Territory and shall at least contain the Development activities set forth in the Initial Development Outline, unless otherwise approved by Agios in advance in writing. Each Development Plan shall reflect Licensee's participation in the Joint Global Studies. The JDC shall periodically review the Development Plan and update the Development Plan. Each Party may submit to the JDC from time to time proposed amendments to the Development Plan. The JDC shall review and may approve such proposed amendments or any other proposed amendments that the JDC may consider from time to time in its discretion and, upon any such approval by the JDC, the Development Plan shall be amended accordingly. The Development Plan shall, at all times, only permit the Licensee Entities to Develop Licensed Products in the Initial Indications and any additional indication as approved by both Licensee and Agios in advance in writing (each such additional indication, an "**Additional Indication**").

(b) Each Local Study or Joint Global Study conducted in the Territory shall be conducted in accordance with the Development Plan and the study protocol approved by the JDC. Licensee shall be responsible for Local Studies in the Territory and the Parties will be responsible for implementation activities in the Territory as to each Joint Global Study as determined by the JDC. Licensee shall be responsible for paying a portion of the costs of activities with respect to each Joint Global Study in the Territory in accordance with **Section 8.03(b)** and shall bear all costs of activities with respect to each Local Study.

(c) Licensee agrees that the [**] Trial shall be a Joint Global Study. Promptly after the Effective Date, the Parties shall collaborate to transfer certain responsibilities for the [**] Trial in the Territory to Licensee.

(d) If Licensee does not agree to participate in any Global Study, then (i) Agios may, itself or with or through any other Agios Entity, perform such Global Study in the Territory and (ii) **Section 8.03(c)** shall apply with respect to such Global Study.

(e) Licensee shall use Commercially Reasonable Efforts to execute and to perform, or cause to be performed, the activities assigned to it in the Development Plan, in each case in accordance with **Section 4.04 (Standards of Conduct)**. Licensee shall use Commercially Reasonable Efforts to participate in each Global Study requested by Agios.

(f) Licensee shall use Commercially Reasonable Efforts to obtain, or cause to be obtained, Regulatory Approval and, if applicable, Reimbursement Approval, for a Licensed Product in each Initial Indication and Additional Indication in each of (i) Mainland China, (ii) Taiwan and (iii) Hong Kong and Macau (with it being agreed that, if Regulatory Approval is obtained in Hong Kong, Licensee shall not also be required to separately obtain Regulatory Approval in Macau), including by providing all necessary resourcing required to seek and maintain Regulatory Approval and, if applicable, Reimbursement Approval for a Licensed Product.

(g) To the extent permissible under applicable Law, Agios or its designee shall own all biological samples obtained in connection with any Global Study, and, at Agios' request, Licensee shall transfer to Agios or its designee any such biological samples in Licensee's possession or control. If applicable Law prohibits such ownership or transfer, the Parties will work together to provide Agios or its designee with rights and access to such biological samples as close to those described in the preceding sentence as is permitted by applicable Law.

Section 4.02 Development Reports. At least [**] in advance of the first meeting of the JDC in each calendar year, Licensee shall provide Agios with a written report that summarizes the Development and Commercialization of the Licensed Products in the Field in the Territory performed by the Licensee Entities in the year prior to such meeting of the JDC, and at least [**] in advance of each other meeting of the JDC in such calendar year, Licensee shall provide Agios with a written report that updates the previous annual report or update provided to Agios. Any report described in this **Section 4.02 (Development Reports)** shall include the status of each pending and proposed Regulatory Filing for Licensed Products in the Field in the Territory. In addition, Licensee shall provide a simple written notice to Agios within [**] of any significant Development events with respect to Licensed Products in the Field in the Territory (*e.g.*, any clinical trial initiation or completion, clinical holds, Regulatory Filings, Regulatory Approvals, Licensee Product Data). In addition to the reports to be submitted under this **Section 4.02 (Development Reports)**, at Agios' request and to the extent permitted by applicable Law, Licensee shall provide to Agios any information that, at the time of such request, has been generated and is in any Licensee Entity's possession and that is necessary or reasonably useful for the Development or Commercialization of the Licensed Products by Agios Entities outside of the Territory.

Section 4.03 Pre-Clinical Research. Licensee, itself or through Licensee Entities, shall conduct any Pre-Clinical Research in the Territory in relation to Licensed Products solely to support clinical Development of Licensed Products, in accordance with the Development Plan and as determined by the JDC. Licensee shall promptly provide to Agios all data obtained from any Pre-Clinical Research to the extent permitted by applicable Law. Licensee shall bear all costs related to such Pre-Clinical Research activities.

Section 4.04 Standards of Conduct. The Licensee Entities shall perform all Development activities under the Development Plan (a) in a good scientific manner, (b) in

accordance with all applicable GLP, GVP and GCP promulgated or endorsed by any applicable Regulatory Authority in the Territory, or as otherwise specified in the Development Plan, (c) in compliance in all material respects with applicable Laws and (d) in a manner that could not reasonably be expected to have a material adverse effect on the Development, Manufacture or Commercialization of the Licensed Compound or any Ivosidenib Materials or Licensed Product outside of the Territory.

Section 4.05 Records. The Licensee Entities shall maintain written or electronic records in sufficient detail, in a good scientific manner (in accordance with all applicable GLP, GVP and GCP promulgated or endorsed by any applicable Regulatory Authority in the Territory, or as otherwise specified in the Development Plan) and appropriate for regulatory and patent purposes, which are complete and accurate in all material respects and reflect all Development work performed under the Development Plan and results achieved. Agios shall have the right, upon reasonable advance notice, and no more than [**], to inspect and copy all such records (for clarity, including all applicable clinical, regulatory and quality records).

Section 4.06 Companion Diagnostics. Licensee shall use Commercially Reasonable Efforts to Develop or have Developed and make commercially available or have made commercially available, at Licensee's sole cost, a companion diagnostic for each Licensed Product in the Territory, to the extent required in order to obtain Regulatory Approval, or under the Regulatory Approval, for such Licensed Product and not otherwise available in the Territory.

Section 4.07 Brain Cancer. Agios shall notify Licensee in writing after deciding to pursue, not to pursue, or to cease pursuing, Development of Licensed Products in Brain Cancer indications. For clarity, once Brain Cancer indications have been included in the Field, they cannot be removed from the Field except upon mutual written agreement of the Parties.

ARTICLE V.

REGULATORY

Section 5.01 Regulatory Filings.

(a) Under the oversight of the JDC and subject to **Section 4.01(a)** and **(b)**, Licensee shall have the responsibility to prepare, obtain, and maintain all Regulatory Filings and Regulatory Approvals, and to conduct communications with the Regulatory Authorities in the Territory, for the Development or Commercialization of Licensed Products in the Field in the Territory undertaken by any Licensee Entity. All Regulatory Filings and communications with Regulatory Authorities in the Territory shall accurately reflect the datasets used by Agios in its Regulatory Filings outside of the Territory. Licensee shall provide Agios with an opportunity to review and comment on all Regulatory Filings in the Territory and consider Agios' comments in good faith. Licensee shall provide access to interim drafts of all Regulatory Filings to Agios via access methods (such as secure databases) as agreed by the Parties, and Agios shall provide its comments on the final drafts of all Regulatory Filings or of proposed material actions within [**], or such other longer period of time mutually agreed to by the Parties. In the event that a Regulatory Authority establishes a response deadline for any Regulatory Filing or material action shorter than such [**] period, the Parties shall work cooperatively to ensure that Agios has a reasonable opportunity for review and comment within such deadlines.

(b) All IND or Drug Approval Applications for any Licensed Product in the Territory shall be filed only after approval by the JDC; *provided, however,* that (i) Agios may, without approval of the JDC, file an IND in the Territory for (A) the [**] Trial prior to the Effective Date or (B) any Global Study that is not a Joint Global Study but that includes clinical sites in the Territory, and (ii) [**].

(c) All Regulatory Filings for Local Studies of Licensed Products in the Field in the Territory and corresponding applicable applications for marketing or regulatory exclusivity shall be owned by Licensee and shall be filed by Licensee or its designated Licensee Entity in the name of an Agios Entity or a Licensee Entity, as appropriate under applicable Law. All Regulatory Filings for Global Studies of Licensed Products in the Field in the Territory and corresponding applicable applications for marketing or regulatory exclusivity shall be filed in the name of and shall be owned by Agios. Except as set forth above, all Licensee Regulatory Documents (including all Regulatory Approvals therein) shall be owned by, and shall be the sole property of, Licensee or its designated Licensee Entity. All Regulatory Filings and Regulatory Approvals in the Field in the Territory shall be at Licensee's sole expense. Any Confidential Information of Agios or any of its Affiliates that is incorporated into any Regulatory Documents filed in the name of or owned by any Licensee Entity shall remain Confidential Information of Agios or its applicable Affiliate(s) and shall remain subject to the terms of **Article XII (Confidentiality)**.

(d) Subject to **Section 8.03(c)**, Agios shall, in support of Licensee's preparation and filing of any IND or Drug Approval Application with respect to any Licensed Product in the Field in the Territory, to the extent required and upon Licensee's written request, provide Licensee access to a complete electronic copy of Agios Regulatory Documents to the extent permitted by applicable Law. Licensee shall, in support of each Agios Entity's preparation and filing of any IND or Drug Approval Application with respect to any Licensed Product outside of the Territory, to the extent required and upon Agios' written request, provide Agios access to a complete electronic copy of Licensee Regulatory Documents to the extent permitted by applicable Law.

(e) Licensee, itself or with or through any other Licensee Entity, shall be the Local Registration Agent of (a) each Local Study, and each Global Study that includes clinical sites in the Territory, for which an Agios Entity owns the applicable IND(s) and (b) if requested by Agios, the [**] Trial.

ARTICLE VI.

COMMERCIALIZATION

Section 6.01 General, Launch Plan and Commercialization Plan. Under the direction of the JCC and in accordance with the Launch Plan and Commercialization Plan, Licensee (itself or through any of the Licensee Entities) shall have the sole right to Commercialize (including booking sales, establishing pricing and related interactions with Governmental Authorities to be listed on the central or provincial reimbursement list, warehousing, commercial distribution, order processing, invoicing and collection) the Licensed

Products in the Field in the Territory at its sole expense. At least [**] prior to anticipated approval of the first Drug Approval Application for a Licensed Product in the Field in the Territory, Licensee shall present the draft Launch Plan to the JCC for review and discussions. Notwithstanding the foregoing, if the first approval of the first Drug Approval Application for a Licensed Product in the Field in the Territory may be obtained soon enough that is not possible for Licensee to present a draft Launch Plan [**] in advance, Licensee shall present such draft Launch Plan as soon as possible. Within [**] prior to the anticipated approval of the first Drug Approval Application for a Licensed Product in the Field in the Territory, Licensee shall submit to the JCC the final Launch Plan for review and discussions and approval. Each year after the approval of the first Drug Approval Application for a Licensed Product in the Field in the Territory, Licensee shall submit to the JCC the Commercialization Plan for review and discussions and approval.

Section 6.02 Promotional Materials; Conferences and Opinion Leaders. Licensee shall ensure that all promotional materials for the Licensed Products in the Territory are consistent with the Global Brand Strategy and the approved labeling for such Licensed Products in the Territory and that such promotional materials comply in all respects with Law. Licensee shall share the promotional materials used in the Territory by any Licensee Entity in connection with the Licensed Products in the Territory with the JCC on a regular basis, and the JCC shall have the right to review and comment on, which comments shall be considered in good faith by the Licensee Entities, any of the Licensee Entities' promotional materials prior to their use in the Territory. As commercially reasonable, Licensee shall attend international and Territory-specific conferences and congresses in the Territory relating to Licensed Products and shall establish relationships with key opinion leaders with respect to Licensed Products in the Territory. Licensee shall provide Agios with summary reports of conferences that Licensee attended and of key opinion leaders met. Agios may attend conferences or congresses in the Territory, at its option; *provided, however*, that Licensee shall be responsible for leading the presence of the Parties at any Territory-specific conference or congress and Agios shall be responsible for leading the presence of the Parties at any international conference or congress in the Territory. Licensee may attend international conferences or congresses outside of the Territory, at its option; *provided, however*, that Agios shall be responsible for leading the presence of the Parties at any such conference or congress. Licensee may, after consultation with Agios, invite key global opinion leaders to the Territory for educational advisory board purposes.

Section 6.03 Commercialization Reports. At least [**] in advance of each meeting of the JCC, for any meeting of the JCC following the First Commercial Sale of any Licensed Product in the Field in the Territory, Licensee shall provide the JCC with (a) a written report that summarizes Commercialization and Medical Affairs activities performed during the prior [**] period with respect to each Licensed Product in each Jurisdiction in the Territory, (b) detailed sales reports for each month of the prior [**] period of each Licensed Product in each Jurisdiction in the Territory, and (c) [**] sales forecasts for each Licensed Product in each Jurisdiction in the Territory for the next [**]. Licensee shall provide an update of such report at each JCC meeting.

Section 6.04 Commercialization Efforts. Licensee shall use Commercially Reasonable Efforts to Commercialize Licensed Products in each of (i) Mainland China, (ii) Taiwan and (iii) Hong Kong and Macau (it being understood that, if Licensee Commercializes

Licensed Products in Hong Kong, it may be Commercially Reasonable to not separately also Commercialize Licensed Products in Macau given the small number of patients in Macau).

Section 6.05 Standards of Conduct. The Licensee Entities shall perform all Commercialization activities with respect to Licensed Products in the Field in the Territory (a) in a manner consistent with the Global Brand Strategy, (b) in a professional and ethical business manner, (c) in compliance in all material respects with applicable Laws and (d) in a manner that could not reasonably be expected to have a material adverse effect on the Development, Manufacture or Commercialization of the Licensed Compound or any Ivosidenib Materials or Licensed Product outside of the Territory. Licensee shall ensure that the Medical Affairs strategy that each applicable Licensee Entity pursues for the Licensed Products in the Territory is in line with the Global Medical Affairs Strategy and that all Licensed Products Commercialized by Licensee Entities conform to the specifications and quality standards therefor provided by Agios.

Section 6.06 Trademarks. The Parties shall cooperate to choose a Trademark in Chinese for use in the Territory, which may vary by Jurisdiction if agreed to by the Parties, and any such Trademark shall be owned by Agios and subject to the terms of the trademark license set forth in Exhibit C. Except as expressly provided herein, or except as otherwise required by applicable Law or agreed by the Parties in advance in writing, neither Party shall have any right to use the other Party's or the other Party's Affiliates', and Licensee shall not have any right to use any Agios Entity's, corporate names or logos in connection with any Development or Commercialization of any Licensed Product. At Agios' option, and if permitted by local Laws in each Jurisdiction, each Licensed Product in the Territory shall be co-branded with the Agios name and Agios-designated corporate trademark, in a manner to be reasonably agreed by the Parties and subject to the terms of the trademark license set forth in Exhibit C, consistent with the Global Brand Strategy.

ARTICLE VII.

MANUFACTURE AND SUPPLY

Section 7.01 Clinical Supply. The Parties will negotiate in good faith and enter into a supply agreement for clinical supply of Ivosidenib Materials and a related quality agreement (collectively, the "**Clinical Supply Agreement**") within [**] after the Effective Date, or at such later date as may be mutually agreed in writing. The Clinical Supply Agreement will be consistent with the terms set forth in this **Section 7.01 (Clinical Supply)**. From and after the execution of the Clinical Supply Agreement, and subject to the terms of such Clinical Supply Agreement, Agios will use Commercially Reasonable Efforts, either itself or through Third Parties, to supply to Licensee Ivosidenib Materials in quantities that are reasonably sufficient for the conduct of Development of Licensed Products in the Field in the Territory by the Licensee Entities in accordance with the Development Plan. For any Ivosidenib Materials supplied by Agios to Licensee pursuant to this **Section 7.01 (Clinical Supply)** for purposes of Development of Licensed Products in the Field in the Territory, Licensee shall pay to Agios the Supply Price for such Ivosidenib Materials, payable within [**] after receipt of an invoice therefor. Licensee shall be responsible for the labeling and packaging of Bulk Drug Product or Brightstock supplied by Agios for clinical use in the Territory at its sole expense. After the Manufacturing Technology Transfer, Licensee shall be responsible for (subject to **Section 3.10 (Final Decision-Making**

Authority)) the Manufacturing of API Bulk Drug Substance into Finished Drug Product for Local Studies at its sole expense; *provided*, *however*, that Licensee shall only be permitted to Manufacture API Bulk Drug Substance into Finished Drug Product (a) through a CMO approved by the JMC or (b) solely if Licensee is able to conduct such Manufacturing in compliance with cGMP and all specifications provided by Agios from time to time, in-house. All Licensed Products for Global Studies with clinical sites in the Territory shall be supplied by Agios.

Section 7.02 Commercial Supply. The Parties will negotiate in good faith and enter into a supply agreement for commercial supply of Ivosidenib Materials and a related quality agreement (collectively, the "**Commercial Supply Agreement**"; the Commercial Supply Agreement and the Clinical Supply Agreement each a "**Supply Agreement**") at least [**] prior to the anticipated date of receipt of the first Regulatory Approval for the first Licensed Product in the Territory, or at such later date as may be mutually agreed in writing. The Commercial Supply Agreement will be consistent with the terms set forth in this **Section 7.02 (Commercial Supply)** and may include means of addressing disruptions in Manufacturing consistent with **Section 7.07 (Supply Disruption)**, whether such disruptions in Manufacturing are of Licensee, Licensee's CMO or a manufacturer of Agios. From and after the execution of the Commercial Supply Agreement, and subject to the terms of such Commercial Supply Agreement, Agios will use Commercially Reasonable Efforts, either itself or through Third Parties, to Manufacture and supply to Licensee Ivosidenib Materials in quantities that are reasonably sufficient for the conduct of Commercialization of Licensed Products in the Field in the Territory by the Licensee Entities in accordance with the Launch Plan and the Commercial Plan. For any Ivosidenib Materials supplied by Agios to Licensee pursuant to this **Section 7.02 (Commercial Supply)** for purposes of Commercialization of Licensed Products in the Field in the Territory, Licensee shall pay to Agios the Supply Price for such Ivosidenib Materials, payable within [**] after receipt of an invoice therefor. Prior to the Manufacturing Technology Transfer, Licensee shall be responsible for the Manufacturing of Bulk Drug Product into Finished Drug Product for Commercialization in the Territory at its sole expense. After the Manufacturing Technology Transfer, Licensee shall be responsible for the Manufacturing of API Bulk Drug Substance into Finished Drug Product for Commercialization in the Territory at its sole expense; *provided*, *however*, that Licensee shall only be permitted to Manufacture API Bulk Drug Substance into Finished Drug Product (a) through a CMO approved by the JMC or (b) solely if Licensee is able to conduct such Manufacturing in compliance with cGMP and all specifications provided by Agios from time to time, in-house.

Section 7.03 Manufacturing Technology Transfer. The Parties agree that discussions on a potential Manufacturing Technology Transfer shall not be commenced prior to [**]. At any time thereafter (or such earlier date as Agios may agree to in writing), the Parties will discuss at either Party's request, through the JCC and the JMC, a Manufacturing Technology Transfer; *provided*, *however*, that, subject to **Section 3.10**, the final decision regarding whether such a transfer shall be made shall be made by [**]. Licensee shall pay to Agios an amount equal to [**] percent ([**]%) of Agios' and its Affiliates' reasonable, documented Out-of-Pocket Costs related to the Manufacturing Technology Transfer within [**] after receipt of any invoice therefor. Agios shall have the right, at any time upon reasonable advance notice, to inspect Licensee's or the applicable CMO's facilities in which Licensed Products are Manufactured.

Section 7.04 Specifications. Licensee shall ensure that any Manufacturing of Licensed Products conducted by or on behalf of any Licensee Entity is to specifications provided by Agios

from time to time, as may be further described in the Supply Agreements, and is consistent with the license granted to Licensee in **Section 2.01(a)(iii)**.

Section 7.05 Serialization. Licensee shall ensure that any Manufacturing or distribution of Licensed Products by or on behalf of any Licensee Entity complies with any Serialization requirements required by applicable Law.

Section 7.06 Agios Supply Chain Security Requirements. Licensee commits to refrain, and to cause each Licensee Entity to refrain, from selling Licensed Product to unauthorized Third Parties or end users under Trade Control Laws such as any military and law enforcement parties of Sanctioned Countries, including but not limited to military hospitals. Licensee shall perform this Agreement in the Territory in compliance with Trade Control Laws as defined herein and within the limits set forth by any applicable OFAC Authorization. Licensee acknowledges and will ensure that any Licensee Entity shall comply in connection herewith with Trade Control Laws and the scope of any applicable OFAC Authorization. Licensee shall ensure that this duty to comply with such Trade Control Laws and the prohibitions or restrictions it involves will be reflected in the agreement to be entered into by Licensee and each Licensee Entity. Such OFAC Authorization or Trade Control Laws may restrict the selling of Licensed Products to specific Third Parties as mentioned therein. Licensee shall, and shall ensure that each Licensee Entity shall, comply with such restrictions imposed by the OFAC Authorization to the extent they apply to Third Parties to which it sells Licensed Products pursuant to this Agreement. While storing, handling or distributing the Licensed Products, Licensee Entities shall make all reasonable efforts to comply with Agios supply chain security requirements set forth in Exhibit E attached hereto, as may be amended by Agios from time to time, in order in particular to verify the security and integrity of the Licensed Products through all points of the supply chain. Licensee shall also ensure that any subcontractors used by Licensee in the distribution of the Licensed Products are duly informed of such requirements and make reasonable efforts to comply with these requirements. Licensee expressly agrees it will not do anything under this Agreement which could cause Agios to be in breach of Trade Control Laws. In the event that Licensee violates any Trade Control Law or the terms or conditions set by the OFAC Authorization to any Sanctioned Countries (or in the case of a Licensee Entity, the Licensee Entity commits such violation and Licensee fails to terminate its agreement with the Licensee Entity upon becoming aware of such violation), or breaches any provision in this **Section 7.06 (Agios Supply Chain Security Requirements)**, Agios shall have the right to unilaterally terminate this Agreement pursuant to **Section 14.05 (Termination for Breach)**, except that the cure period set forth therein shall not apply.

Section 7.07 Supply Disruptions. If for any reason Agios is in good faith unable to supply any or all of the quantities of the Ivosidenib Materials required to be supplied under a Supply Agreement, it shall provide Licensee with reasonable prior written notice thereof, which shall include a reasonable explanation for such failure and, as soon as practicable, use Commercially Reasonable Efforts to appoint a Third Party designee for the supply of the Ivosidenib Materials to Licensee within the same terms and conditions thereof. In the event of a shortfall in Agios' ability to supply the Ivosidenib Materials, it shall use Commercially Reasonable Efforts to provide Licensee with as much quantity of the Ivosidenib Materials as possible, considering Agios' (and the other Agios Entities') other requirements for the Ivosidenib Materials outside of the Territory. Agios shall use reasonable efforts to equitably allocate supply in the event of a shortfall. Reduction in Licensee's sales of the Licensed Product due to Agios'

inability to supply in good faith any or all of the quantities of the Ivosidenib Materials required shall be taken into consideration when assessing Licensee's obligations relating to Development and Commercialization. Subject to the Supply Agreements, in the event that, following a Manufacturing Technology Transfer, Licensee experiences difficulty in obtaining a sufficient quantity of Bulk Drug Product, Licensee shall promptly notify Agios and Agios may then supply Licensee with API Bulk Drug Substance, Bulk Drug Product or Brightstock, notwithstanding the foregoing in this **Article VII**.

ARTICLE VIII.

PAYMENTS

Section 8.01 Upfront Payment. Within [**] following receipt of an invoice therefor, Licensee shall pay Agios a one-time, non-refundable, non-creditable upfront payment of Twelve Million Dollars ($12,000,000), by wire transfer.

Section 8.02 Technology Transfer Costs. Licensee shall pay to Agios the amounts described in **Section 7.03 (Manufacturing Technology Transfer)** in accordance with the procedures set forth in such Section.

Section 8.03 Development Costs.

(a) Except as expressly provided in this Agreement or the Development Plan, each Party shall bear its own costs incurred in the performance of its obligations under **Article IV (Development)**.

(b) Notwithstanding anything to the contrary in **Section 8.03(a)**, for any Joint Global Study, Licensee shall (i) bear all costs incurred by Licensee Entities and all Out-of-Pocket Costs incurred by Agios and its Affiliates in the performance of such Joint Global Study in the Territory; and in addition (ii) pay to Agios [**] percent ([**]%) of the Out-of-Pocket Costs incurred by Agios and its Affiliates set forth in clause (i) of this **Section 8.03(b)**, as remuneration for Agios' overhead costs directly and solely related to such Joint Global Study.

(c) Notwithstanding Licensee's rights pursuant to Section 2.01(a) or Licensee's access rights pursuant to Section 2.04 (Knowledge Transfer), Section 2.05(b) or Section 5.01(d), for any Global Study (A) for which Agios (and, with respect to the [**] Trial, the Third Party(ies) conducting the [**] Trial) requests any Licensee Entity to be the Local Registration Agent, (B) for which such Licensee Entity(ies) decided not to be the Local Registration Agent, and (C) which, therefore, is not a Joint Global Study (excluding the [**] Trial and the Global Studies included in the Ongoing Trials), except in instances of an Exception, Licensee shall not have access to any Agios Product Data or Agios Regulatory Documents arising out of such Global Study, unless and until Licensee pays to Agios [**] percent ([**]%) of Agios' and its Affiliates' Out-of-Pocket Costs incurred with regards to such Global Study on a worldwide basis. For purposes of this Section, "Exception" shall mean, (i) with respect to a given Global Study, that SDA will not accept such Global Study (with or without any bridging study(ies)) as sufficient to support an application for Regulatory Approval for the applicable Licensed Product in Mainland China and, instead, requires Licensee to conduct one or more alternative studies (other than any bridging study(ies)) to support the filing of an application for Regulatory Approval for such

Licensed Product in Mainland China or (ii) solely with respect to Hong Kong, Macau and Taiwan, that Agios will provide to Licensee the U.S. NDA dossier at no cost for use in Licensee's applications for Regulatory Approval in Hong Kong, Macau and Taiwan. In the instance of an Exception falling under (i), above, Licensee shall not have access to any Agios Product Data or Agios Regulatory Documents arising out of such Global Study, unless and until Licensee pays to Agios [**] percent ([**]%) of Agios' and its Affiliates' Out-of-Pocket Costs incurred with regards to such Global Study on a worldwide basis. For clarity, at all times, safety data from both within and outside the Territory shall be shared between the Parties at no cost to the recipient Party in order to fulfill regulatory requirements, pursuant to a separate pharmacovigilance agreement to be agreed between the Parties as soon as reasonably practicable following the Effective Date. For the avoidance of doubt, if no Licensee Entity is requested to be the Local Registration Agent for the [**] Trial, then this Section 8.03(c) shall not apply to the [**] Trial and Agios shall transmit [**] to Licensee all data arising from the [**] Trial that Agios is required to provide to Licensee pursuant to **Section 2.04(b)**.

(d) Within [**] following the end of each calendar quarter in which a Joint Global Study is being conducted, Agios shall invoice Licensee for the amounts set forth in **Section 8.03(b)** or **Section 8.03(c)**. Licensee shall pay all amounts payable under such invoice within [**] after the end of each calendar quarter.

Section 8.04 Development Milestone Payment.

(a) Licensee shall make the non-refundable, non-creditable milestone payments to Agios set forth in the table below no later than [**] after the earliest date on which the corresponding milestone event has been achieved by any Licensee Entity with respect to any Licensed Product to achieve such milestone event, regardless of whether such milestone event was achieved for such Licensed Product in monotherapy or as part of a combination therapy. The references to achieving milestones in Mainland China set forth in this **Section 8.04(a)** are subject to **Section 8.04(d).**

Milestone Event	Milestone Payment
(i) Dosing of the first patient in a Local Study in any hematological indication in Mainland China	$5,000,000
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]
[**]	[**]

(b) The milestone payments set forth in rows (i) through (viii) above shall be payable only once, upon the first achievement of such milestone event. The milestone set forth in row (ix) above shall be payable for each distinct indication for which any Licensee Entity receives Regulatory Approval in the Territory.

(c) If Licensee has not paid to Agios a milestone payment set forth in row (iii) above, and a milestone event set forth in row (iv) or (v) above occurs, then, upon the occurrence of such milestone event set forth in row (iv) or (v), Licensee shall pay to Agios [**] percent ([**]%) of the milestone payment set forth in row (iii), with the remaining [**] percent ([**]%) to be due upon achievement of [**]. If Licensee has not paid to Agios a milestone payment set forth in row (vi) above, and a milestone event set forth in row (vii) above occurs, then, upon the occurrence of such milestone event set forth in row (vii), Licensee shall pay to Agios [**] percent ([**]%) of the milestone payment set forth in row (vi), with the remaining [**] percent ([**]%) to be due upon achievement of [**].

(d) In the event that Licensee achieves a milestone set forth in rows (iii) through (ix) in a Jurisdiction other than [**], Licensee shall pay to Agios [**] percent ([**]%) multiplied by the applicable milestone payment upon such achievement, with the remaining [**] percent ([**]%) due upon achievement of the applicable milestone in [**].

(e) The partial milestone payment provisions set forth in both of the foregoing **Sections 8.04(c)** and **8.04(d)** may apply to a given milestone payment in accordance with the terms of such Sections. In such event, the unpaid remainders of such milestone payments shall become payable in accordance with the principles set forth in such Sections; *provided* that, for the avoidance of doubt, such principles are intended to apply such that, once the applicable condition for payment of a milestone remainder is satisfied, the remainder amount to be paid,

when aggregated with the prior partial payment under the applicable provision, shall cumulatively add to the milestone payment amount for such milestone that would have been payable had the applicable partial payment provision never applied (*i.e.*, the application of such partial payment provisions shall not result in milestone payments that are larger or smaller following the payment of such remainder amounts than the full milestone payment amounts that would have been payable had the milestone payments been earned in full, assuming the applicable payment conditions are satisfied), as demonstrated in the illustrative examples attached hereto as Schedule 8.04(e).

(f) Upon achievement by any Licensee Entity of any of the milestone events listed above, Licensee shall promptly (but in no event more than [**] after such achievement) notify Agios of such achievement.

Section 8.05 Sales Milestone Payments. Licensee shall pay to Agios the following non-refundable and non-creditable amounts after the first achievement of aggregate Net Sales of all Licensed Products in the Territory in a calendar year that meet or exceed the minimum annual Net Sales thresholds set forth below, which payment shall be made no later than [**] after the end of the calendar quarter in which the applicable threshold(s) is(are) met or exceeded:

Annual Net Sales Threshold	Payment Amount
Equal to or greater than $[**]	[**]
Equal to or greater than $[**]	[**]
Equal to or greater than $[**]	[**]
Equal to or greater than $[**]	[**]
Equal to or greater than $[**]	[**]
Equal to or greater than $[**]	[**]

Each milestone payment in this **Section 8.05 (Sales Milestone Payments)** shall be payable only once upon the first achievement of such milestone in a given calendar year and no amounts shall be due for subsequent or repeated achievements of such milestone in subsequent calendar years. For clarity, the Net Sales of all Licensed Products in a calendar year shall be aggregated for purposes of determining whether any milestone in the table above has been met. If more than one of the milestones set forth in the table above are first achieved in a single calendar year, then Licensee shall pay to Agios in such calendar year all of the payments corresponding to all of the milestones achieved in such calendar year under this **Section 8.05 (Sales Milestone Payments)**.

Section 8.06 Royalties.

(a) Subject to the remainder of this **Section 8.06 (Royalties)**, Licensee shall pay Agios the following royalties on aggregate Net Sales of all Licensed Products, at an incremental royalty rate determined by aggregate annual Net Sales of all Licensed Products in each calendar year during the Term in the Territory:

Portion of Annual Net Sales of all Licensed Products	**Royalty**
Less than or equal to $[**]	15%
Greater than $[**] and less than or equal to $[**]	[**]%
Greater than $[**]	19%

By way of example and not limitation, if Net Sales of all Licensed Products in a calendar year are [**] Dollars ($[**]), then the royalty shall be [**].

(b) Running royalties paid by Licensee under this **Section 8.06** (**Royalties**) shall be paid on a Licensed Product-by-Licensed Product and Jurisdiction-by-Jurisdiction basis until the latest of (i) the expiration of the last-to-expire Valid Claim in the Agios Patent Rights or Joint Combination Therapy Patent Rights that Covers such Licensed Product in the Field in such Jurisdiction, (ii) expiration of marketing or regulatory exclusivity with respect to such Licensed Product in such Jurisdiction, or (iii) ten (10) years from the First Commercial Sale of such Licensed Product in the Field in such Jurisdiction (each, a "**Royalty Term**"). Following the expiration of the Royalty Term with respect to a particular Licensed Product in the Field in a Jurisdiction (but not following an earlier termination of this Agreement), the licenses granted by Agios to Licensee pursuant to **Section 2.01(a)** with respect to such Licensed Product in the Field in such Jurisdiction shall be perpetual, irrevocable, fully-paid and royalty-free, and Net Sales of such Licensed Product shall no longer be included in the aggregate Net Sales calculation in **Section 8.06(a)** but shall be included in calculations of Net Sales for the purposes of **Section 8.05 (Sales Milestones Payments)**.

(c) Notwithstanding the provisions of **Section 8.06(a)**, on a Jurisdiction-by-Jurisdiction basis, during any period in such Jurisdiction in which (i) the sale of a given Licensed Product would not infringe a Valid Claim of the Agios Patent Rights or a Valid Claim of the Joint Combination Therapy Patent Rights and (ii) there is no marketing or regulatory exclusivity with respect to such Licensed Product in such Jurisdiction, Licensee shall pay royalty rates for sales of such Licensed Product in such Jurisdiction that shall be set at [**] percent ([**]%) of the applicable royalty rate determined in accordance with **Section 8.06(a)**.

(d) In the event that Licensee or Agios obtains, after the Effective Date, a license under, or other rights to, Patent Rights or Know-How from any Third Party(ies) that are necessary in order to Commercialize a given Licensed Product in the Field in a given

Jurisdiction, [**] percent ([**]%) of any and all royalty payments actually paid directly, or indirectly in accordance with **Section 2.06(a)**, as applicable, under such Third Party licenses by Licensee or its Affiliates for sales of such Licensed Product in the Field in such Jurisdiction in a given calendar quarter shall be creditable against the royalty payments due to Agios by Licensee for sales of such Licensed Product in such Jurisdiction in such calendar quarter.

(e) Notwithstanding the provisions of **Section 8.06(a)**, on a Jurisdiction-by-Jurisdiction basis, during any period in such Jurisdiction in which (i) the sale of a given Licensed Product would infringe a Valid Claim of the Joint Combination Therapy Patent Rights but not a Valid Claim of the Agios Patent Rights and (ii) there is no marketing or regulatory exclusivity with respect to such Licensed Product in such Jurisdiction, Licensee shall pay royalty rates for sales of such Licensed Product in such Jurisdiction that shall be set at [**] percent ([**]%) of the applicable royalty rate determined in accordance with **Section 8.06(a)**.

(f) Notwithstanding the provisions of the above subparts (c), (d) and (e) of this Section, in no event shall the total royalty rate reduction(s) allowable under such subparts with respect to a given Licensed Product in a given Jurisdiction in a given calendar quarter, alone or together, lead to a reduction of more than [**] percent ([**]%) of the applicable royalty rate determined in accordance with **Section 8.06(a)**.

Section 8.07 Royalty Payments and Reports.

(a) On a Licensed Product-by-Licensed Product and Jurisdiction-by-Jurisdiction basis, until the expiration of the Royalty Term with respect to such Licensed Product in such Jurisdiction, Licensee agrees to (i) send an email to Agios within [**] after the end of each calendar quarter with a good faith estimate of the amount of the royalties owed with respect to such Licensed Product in such Jurisdiction in such calendar quarter and (ii) provide quarterly written reports to Agios within [**] after the end of each calendar quarter, covering all Net Sales of such Licensed Product in such Jurisdiction by any Licensee Entity, each such written report stating for the period in question the amount of gross sales and Net Sales of each Licensed Product in each Jurisdiction in the Territory during the applicable calendar quarter (including such amounts expressed in local currency and as converted to Dollars) and a calculation of the amount of royalty payment due on such Net Sales for such calendar quarter.

(b) Licensee shall make the royalty payments due hereunder within [**] after the end of each calendar quarter.

Section 8.08 Financial Responsibility for Licensee In-License Agreements. Licensee shall be solely responsible for payment of any and all amounts due to any Third Party under or in connection with any Licensee In-License Agreement.

Section 8.09 Recordkeeping.

(a) Each Licensee Entity shall keep full, clear and accurate records of Licensed Products that are made, used or sold under this Agreement and of any costs borne by such Licensee Entity for any Joint Global Study, in accordance with the Accounting Standards consistently applied, for a period of at least [**] after the end of the calendar year to which the records relate, setting forth the sales of Licensed Products in sufficient detail to enable royalties and other amounts payable to Agios hereunder to be determined. Each Licensee Entity further

agrees to permit its books and records to be examined by an independent accounting firm selected by Agios and reasonably acceptable to Licensee no more than [**], to verify any reports and payments delivered under this Agreement during the [**] most recently-ended calendar years, upon reasonable notice (which shall be no less than [**] prior notice) and during regular business hours and subject to a reasonable confidentiality agreement. The Parties shall reconcile any underpayment or overpayment within [**] after the accounting firm delivers the results of any audit. Such examination is to be made at the expense of Agios, except in the event that the results of the audit reveal an underpayment by Licensee of [**] percent ([**]%) or more during the period being audited, in which case reasonable audit fees for such examination shall be paid by Licensee.

(b) Agios shall keep full, clear and accurate records of costs of performance of the Out-of-Pocket Costs for each Global Study and Out-of-Pocket Costs incurred in accordance with **Section 2.04(a)** and **Section 7.03 (Manufacturing Technology Transfer)**, in accordance with the Accounting Standards consistently applied, for a period of at least [**] after the end of the calendar year to which the records relate, in sufficient detail to enable Licensee's payment obligations under **Section 8.03(b)**, **Section 8.03(c)**, **Section 2.04(a)** and **Section 7.03 (Manufacturing Technology Transfer)** to be determined. Agios further agrees to permit its books and records to be examined by an independent accounting firm selected by Licensee and reasonably acceptable to Agios no more than [**], to verify any invoices delivered under **Section 8.03(d)**, **Section 2.04(a)** or **Section 7.03 (Manufacturing Technology Transfer)** during the [**] most recently-ended calendar years, upon reasonable notice (which shall be no less than [**] prior notice) and during regular business hours and subject to a reasonable confidentiality agreement. The Parties shall reconcile any underpayment or overpayment within [**] after the accounting firm delivers the results of any audit. Such examination is to be made at the expense of Licensee, except in the event that the results of the audit reveal an overcharging by Agios of [**] percent ([**]%) or more during the period being audited, in which case reasonable audit fees for such examination shall be paid by Agios.

Section 8.10 Currency Conversion. Wherever it is necessary to convert currencies for Net Sales invoiced in a currency other than the Dollar, such conversion shall be made into Dollars at the conversion rate existing in the United States (as reported in the *Wall Street Journal*) on the last Business Day of the applicable calendar quarter or, if such rate is unavailable, a substitute therefor reasonably selected by Agios. All payments due to Agios under this Agreement shall be made without deduction of exchange, collection or other charges. Once the amount of Net Sales paid to Agios in respect of a particular calendar quarter has been converted into Dollars, such amount of Dollars shall be used for the purpose of calculating the total amount of Net Sales during the calendar year that includes such calendar quarter.

Section 8.11 Methods of Payment. All payments due to Agios under this Agreement shall be made by Licensee (and not any Affiliate of Licensee) in Dollars by wire transfer to a bank account of Agios (and not any Affiliate of Agios). In the event of any action by, or change in the circumstances of, a Party (including a Change in Control of such Party) that results in an increased or additional tax payable by the other Party, such first Party shall reimburse such other Party for such increase.

Section 8.12 Taxes. Without prejudice to the provisions of **Section 8.11**, Agios shall be liable for all United States taxes imposed upon, or measured by, net income (including interest

thereon) derived from its receipt of any payments made by Licensee to Agios under this Agreement. Licensee shall indemnify and hold Agios harmless from and against all other taxes imposed upon, or measured by, such payments, and shall make all such payments without deduction or withholding of any taxes except to the extent required by applicable Laws. If applicable Laws require the deduction or withholding of such taxes, Licensee shall deduct, withhold and timely pay over such taxes as required by applicable Laws, and shall submit to Agios appropriate proof of payment of the withheld taxes as well as the official receipts within a reasonable period of time. In the event of any such deduction or withholding of taxes imposed by or under color of any Laws in force in Mainland China on account of payments from Licensee to Agios hereunder, such payments shall be increased so that, after all required deductions or withholding of tax (including on such increased amounts) have been made, Agios receives the same amount as would have been payable hereunder if no such deduction or withholding had been required or made. In the case of any such deduction or withholding of taxes by any other Governmental Authority, no increased payment described in the preceding sentence shall be required.

Section 8.13 Late Payments. Interest shall be payable by Licensee on any amounts payable to Agios under this Agreement which are not paid by the due date for payment. All interest shall accrue and be calculated on a daily basis (both before and after any judgment) at a rate per month equal to the lesser of (a) [**] percentage points above the then-current "prime rate" in effect published in *The Wall Street Journal* or (b) the maximum rate permissible under applicable Law, for the period from the due date for payment until the date of actual payment. The payment of such interest shall not limit Agios from exercising any other rights it may have as a consequence of the lateness of any payment.

Section 8.14 Invoices. Agios acknowledges that Licensee requires invoices for all payments due under this Agreement, which invoices may be delivered by email to [**] (which email address may be changed by Licensee from time to time upon written notice to Agios), with a hard copy confirmed by mailing to:

CStone Pharmaceuticals
P.O. Box 31119
Grand Pavilion
Hibiscus Way
802 West Bay Road
Grand Cayman, KY1-1205, Cayman Islands

with copies to:

CStone Pharmaceuticals (Shanghai) Co., Ltd.
1000 Zhangheng Road, Building 25
Pudong New District, Shanghai
China 201203
Attention: Chief Executive Officer

and

CStone Pharmaceuticals (Shanghai) Co., Ltd.
1000 Zhangheng Road, Building 25
Pudong New District, Shanghai
China 201203
Attention: Head of Global Corporate Development
Email: [**]

(which addresses may be changed by Licensee from time to time upon written notice to Agios).

ARTICLE IX.

INTELLECTUAL PROPERTY

Section 9.01 Ownership.

(a) Ownership of the Agios Technology and Agios Combination Therapy Technology shall remain vested at all times in Agios.

(b) Ownership of the Licensee Technology shall remain vested at all times in Licensee.

(c) Ownership of Joint Combination Therapy Technology shall be vested jointly in Agios and Licensee. Each Party shall promptly disclose to the other Party any Joint Combination Therapy Technology upon becoming aware thereof, but in any event no later than [**] after the identification, conception, discovery, authorship, development or reduction to practice thereof and hereby assigns to the other Party, subject to **Section 2.01(a)** and **Section 2.01(b)**, a one-half undivided interest in such Joint Combination Therapy Technology. Each Party shall, without cost to the other Party, obtain all necessary assignment documents for the other Party to give effect to the one-half undivided ownership described above, render all signatures that shall be necessary for the relevant patent filings and assist the other Party in all other reasonable ways that are necessary for the filing, prosecution, issuance and maintenance of the Joint Combination Therapy Patent Rights by the other Party as set forth in **Section 9.02(c)**.

(d) Ownership of Know-How, including inventions (whether or not patentable), and Patent Rights arising during the Term that relate to Licensed Products, other than Joint Combination Therapy Technology, shall (to the extent allowable under Chinese Law, if Chinese Law applies) be vested solely in Agios. Licensee shall promptly disclose to Agios any such Know-How, including inventions (whether or not patentable), and Patent Rights upon becoming aware thereof, but in any event no later than [**] after the identification, conception, discovery, authorship, development or reduction to practice thereof and (to the extent allowable under Chinese Law, if Chinese Law applies) hereby assigns to Agios all right, title and interest in such Know-How, including inventions (whether or not patentable), and Patent Rights. In the case of such assignment, Licensee shall, without cost to Agios, obtain all necessary assignment documents for Agios, render all signatures that shall be necessary for the relevant patent filings and assist Agios in all other reasonable ways that are necessary for the filing, prosecution, issuance and maintenance of the Agios Patent Rights assigned to Agios pursuant to this **Section**

9.01(d). In the event that Chinese Law applies with respect to any Know-How, including inventions (whether or not patentable), or Patent Rights arising during the Term that relate to Licensed Products (other than Joint Combination Therapy Technology), then, to the extent that Chinese Law prohibits the assignment of such Know-How, including inventions, or Patent Rights to Agios, in lieu of the assignment of such Know-How, including inventions, or Patent Rights to Agios, Licensee hereby grants to Agios as broad, exclusive and unrestricted a license to, with the broadest enforcement rights with respect to, such Know-How, including inventions, or Patent Rights as may be allowable under Chinese Law. In such case, such Know-How, including inventions, shall be deemed Agios Know-How, and such Patent Rights shall be deemed Agios Patent Rights, hereunder, and Licensee shall provide to Agios any necessary or reasonably requested documentation reflecting such license and shall assist Agios in all other reasonable ways that are necessary for Agios to enjoy and exploit or enforce any such Agios Know-How and Agios Patent Rights.

(e) For purposes of determination of ownership hereunder, inventorship shall be determined according to United States patent Laws.

(f) Each Party shall be solely responsible for payments due under applicable inventor remuneration Laws in any Jurisdiction to each inventor as to any Patent Right described in the foregoing **Sections 9.01(a)-(d)** to which such Party is assigned an ownership interest by such inventor.

Section 9.02 Prosecution of Patent Rights.

(a) Subject to the terms of each In-License Agreement:

(i) Agios shall have the first right, but not the obligation, to file, prosecute and maintain all Agios Patent Rights. Licensee shall reimburse Agios for all Out-of-Pocket Costs incurred by Agios or any of its Affiliates after the Effective Date in filing, prosecuting and maintaining Agios Patent Rights (for the avoidance of doubt, including amounts paid by Agios after the Effective Date to any Third Party counterparty under any In-License Agreement with respect to such Third Party counterparty's filing, prosecution and maintenance of applicable Agios Patent Rights), within [**] after receiving an invoice therefor. If Agios elects not to, or is unable to, file, prosecute or maintain any Agios Patent Right in any Jurisdiction, Agios shall give Licensee prompt notice thereof, and, in such cases, shall permit Licensee and its Affiliates at Licensee's own expense to take such actions itself. In such case, (A) Licensee shall consult with Agios in order to allow its actions to be consistent with Agios' global patent strategy for Licensed Products, and (B) Agios shall execute such documents and perform such acts as may be reasonably necessary for Licensee to perform such actions.

(ii) The Party prosecuting an Agios Patent Right in accordance with **Section 9.02(a)(i)** shall consult with the other Party on the preparation, filing, prosecution and maintenance of such Agios Patent Right, and shall take into consideration the commercial strategy of (A) if such prosecuting Party is Agios, Licensee in the Territory, and (B) if such prosecuting Party is License, Agios outside the Territory. The prosecuting Party shall furnish the other Party with copies of each document relevant to such preparation, filing, prosecution and maintenance at least [**] prior (or such shorter period prior if it is not reasonably practicable to

provide such copies [**] prior) to filing such document or making any payment due thereunder to allow for review and comment by such other Party and shall consider in good faith timely comments from such other Party thereon. The prosecuting Party shall also furnish the other Party with copies of all final filings and responses made to any patent authority with respect to the Agios Patent Rights being prosecuted by such Party in a timely manner following submission thereof.

(iii) In preparing, filing, prosecuting and maintaining any Agios Patent Right, in no event shall Licensee take any position that is contrary to or detrimental to the scope or enforceability of any other Agios Patent Right or any Patent Rights owned or otherwise controlled by Agios outside of the Territory that are counterparts to any Agios Patent Rights.

(b) Subject to the terms of each Licensee In-License Agreement:

(i) Licensee shall have the first right, but not the obligation, to file, prosecute and maintain all Licensee Patent Rights at its sole expense. If Licensee elects not to, or is unable to, file, prosecute or maintain any Licensee Patent Right in any Jurisdiction, Licensee shall give Agios prompt notice thereof, and, in such cases, shall permit Agios at Agios' own expense to take such actions itself. In such case, (A) Agios shall consult with Licensee in order to allow its actions to be consistent with Licensee's overall patent strategy for Licensed Products in the Territory, and (B) Licensee shall execute such documents and perform such acts as may be reasonably necessary for Agios to perform such actions.

(ii) The Party prosecuting a Licensee Patent Right in accordance with **Section 9.02(b)(i)** shall consult with the other Party on the preparation, filing, prosecution and maintenance of such Licensee Patent Right, and shall take into consideration the commercial strategy of (A) if such prosecuting Party is Agios, Licensee in the Territory, and (B) if such prosecuting Party is License, Agios outside the Territory. The prosecuting Party shall furnish the other Party with copies of each document relevant to such preparation, filing, prosecution and maintenance at least [**] prior (or such shorter period prior if it is not reasonably practicable to provide such copies [**] prior) to filing such document or making any payment due thereunder to allow for review and comment by such other Party and shall consider in good faith timely comments from such other Party thereon. The prosecuting Party shall also furnish the other Party with copies of all final filings and responses made to any patent authority with respect to the Licensee Patent Rights being prosecuted by such Party in a timely manner following submission thereof.

(iii) In preparing, filing, prosecuting and maintaining Licensee Patent Rights, in no event shall Licensee take any position that is contrary to or detrimental to the scope or enforceability of any Agios Patent Rights or any Patent Rights owned or otherwise controlled by Agios outside of the Territory that are counterparts to any Agios Patent Rights.

(c) Subject to the terms of each In-License Agreement and Licensee In-License Agreement:

(i) Licensee shall have the first right, but not the obligation, to file, prosecute and maintain all Joint Combination Therapy Patent Rights in the Territory and Agios shall have the first right, but not the obligation, to file, prosecute and maintain all Joint Combination Therapy Patent Rights outside the Territory. If the Party with such first right elects not to, or is unable to, file, prosecute or maintain any Joint Combination Therapy Patent Rights in any country or jurisdiction, such Party shall give the other Party prompt notice and, in such case, shall permit the other Party at such other Party's own expense to take such actions itself. In such case, (A) such other Party shall consult with such first Party in order to allow its actions to be consistent with such first Party's overall patent strategy, and (B) such first Party shall execute such documents and perform such acts as may be reasonably necessary for such other Party to perform such actions. The Parties shall each bear [**] percent ([**]%) of all Out-of-Pocket Costs incurred by either Party or any of its Affiliates after the Effective Date in filing, prosecuting and maintaining such Joint Combination Therapy Patent Rights inside and outside the Territory in accordance with the first sentence of this clause (i). The reimbursing Party shall reimburse such costs within [**] after receiving an invoice from the other Party therefor.

(ii) Each Party shall consult with the other Party on the preparation, filing, prosecution and maintenance of all Joint Combination Therapy Patent Rights, shall furnish the other Party with copies of each document relevant to such preparation, filing, prosecution and maintenance at least [**] prior (or such shorter period prior if it is not reasonably practicable to provide such copies [**] prior) to filing such document or making any payment due thereunder to allow for review and comment by the other Party and shall consider in good faith timely comments from the other Party thereon. Each Party shall also furnish the other Party with copies of all final filings and responses made to any patent authority with respect to the Joint Combination Therapy Patent Rights in a timely manner following submission thereof.

(iii) In preparing, filing, prosecuting and maintaining Joint Combination Therapy Patent Rights, in no event shall Licensee take any position that is contrary to or detrimental to the scope or enforceability of any Agios Patent Rights or any Patent Rights owned or otherwise controlled by Agios outside of the Territory that are counterparts to any Agios Patent Rights.

Section 9.03 Enforcement and Defense. Subject to the terms of each In-License Agreement:

(a) If either Party becomes aware of any Third Party activity, including any Development activity (whether or not an exemption from infringement liability for such Development activity is available under applicable Law), that infringes (or that is directed to the Development of a product that would infringe) an Agios Patent Right or a Joint Combination Therapy Patent Right, or that misappropriates any Agios Know-How, Joint Combination Therapy Know-How or Joint Combination Therapy Invention, then the Party becoming aware of such activity shall give prompt written notice to the other Party regarding such alleged infringement or misappropriation (collectively, "**Infringement Activity**").

(b) Agios shall have the first right, but not the obligation, to attempt to resolve any Infringement Activity anywhere in the world by commercially appropriate steps at its own

expense, including the filing of an infringement or misappropriation suit using counsel of its own choice. If Agios fails to resolve such Infringement Activity in the Territory or, solely with respect to Joint Combination Therapy Patent Rights, outside the Territory, but solely where the allegedly infringing product is or would be competitive with [**], or to initiate a suit with respect thereto by the date that is [**] before any deadline for taking action to avoid any loss of material enforcement rights or remedies, then, with Agios' written consent (which shall not be unreasonably withheld, conditioned or delayed), Licensee shall have the right, but not the obligation, to attempt to resolve such Infringement Activity by commercially appropriate steps at its own expense, including the filing of an infringement or misappropriation suit using counsel of its own choice.

(c) Any amounts recovered by a Party as a result of an action pursuant to **Section 9.03(b)**, whether by settlement or judgment, shall be allocated first to pay to [**] with respect to such enforcement action, and any remaining amount shall be retained by [**].

(d) If a Third Party in the context of an enforcement action under this **Section 9.03** asserts that a Joint Combination Therapy Patent Right is invalid or unenforceable, then the Party responsible for such enforcement action will be responsible for defending against such assertion. If a Third Party asserts that an Agios Patent Right is invalid or unenforceable, then Agios shall have the first right to defend against such assertion. If a Third Party outside of an enforcement action under this **Section 9.03** asserts that a Joint Combination Therapy Patent Right is invalid or unenforceable, then Agios shall have the sole right, but not the obligation, outside the Territory, and Licensee shall have the first right, but not the obligation, within the Territory, to defend against such assertion (such Party with a sole or first right to defend being known as the "**First Defending Party**") and, at the First Defending Party's request and expense, the other Party shall provide reasonable assistance in defending against such Third Party assertion. The First Defending Party shall (i) keep the other Party reasonably informed regarding such assertion and such defense (including by providing such other Party with drafts of each filing a reasonable period before the deadline for such filing and promptly providing such other Party with copies of all final filings and correspondence), (ii) consult with the other Party on such defense, and (iii) consider in good faith all comments from the other Party regarding such defense. The non-defending Party shall have the right to join as a party to such defense and participate with its own counsel at its sole expense; *provided*, *however*, that the First Defending Party shall retain control of such defense. Should Agios (with respect to Agios Patent Rights or Joint Combination Therapy Patent Rights within the Territory, including in the context of an applicable enforcement action) or Licensee (with respect to Joint Combination Therapy Patent Rights within the Territory or in the context of an applicable enforcement action) decide that it is not, or is no longer, interested in controlling such defense with respect to a Joint Combination Therapy Patent Right, it shall promptly (and in any event by the date that is [**] before any deadline for taking action to avoid any loss of material rights) provide the other Party written notice of this decision. The other Party may, upon written notice to such first Party, assume such defense at such other Party's sole expense.

(e) In any event, at the request and expense of the Party bringing an infringement or misappropriation action under **Section 9.03(b)** or defending an action under **Section 9.03(d)**, the

other Party shall provide reasonable assistance in any such action (including entering into a common interest agreement if reasonably deemed necessary by any Party) and be joined as a party to the suit if necessary for the initiating or defending Party to bring or continue such suit. Neither Party may settle any action or proceeding brought under **Section 9.03(b)** or **Section 9.03(d)**, or knowingly take any other action in the course thereof, in a manner that materially adversely affects the other Party's interest in any Agios Patent Rights or Joint Combination Therapy Patent Rights or counterpart Patent Rights outside of the Territory without the written consent of such other Party. Each Party shall always have the right to be represented by counsel of its own selection and its own expense in any suit or other action instituted by the other Party pursuant to **Section 9.03(b)** or **Section 9.03(d)**.

Section 9.04 Defense of Third Party Infringement and Misappropriation Claims. Subject to the terms of each In-License Agreement:

(a) If a Third Party asserts that a Patent Right or other right Controlled by it in the Territory is infringed or misappropriated by a Party's activities under this Agreement or a Party becomes aware of a Patent Right or other right that might form the basis for such a claim, the Party first obtaining knowledge of such a claim or such potential claim shall immediately provide the other Party with notice thereof and the related facts in reasonable detail. The Parties shall discuss what commercially appropriate steps, if any, to take to avoid infringement or misappropriation of said Third Party Patent Right or other right controlled by such Third Party in the Territory.

(b) If a Third Party asserts that a Patent Right or other right Controlled by it in the Territory is infringed or misappropriated by a Party's activities under this Agreement, then such Party shall have the first right, but not the obligation, to defend against such assertion and, at such Party's request and expense, the other Party will provide reasonable assistance in defending against such Third Party assertion. Such Party shall keep the other Party reasonably informed regarding such assertion and such defense.

Section 9.05 Patent Term Extensions. Subject to the terms of each In-License Agreement, Agios shall have the first right to select the appropriate Agios Patent Rights and Licensee shall have the first right to select the appropriate Joint Combination Therapy Patent Rights for filing to obtain patent term extensions, including supplementary protection certificates and any other extensions that are now available or become available in the future, based on Regulatory Approvals for Licensed Products in the Field in the Territory, and the selecting Party shall consult with the other Party with respect to such decisions and shall consider the comments and concerns of the other Party in good faith. Each Party shall cooperate with the other Party in gaining any such patent term extensions, including by signing all necessary papers. If Licensee elects not to, or is unable to, file to obtain any patent term extension described in this **Section 9.05 (Patent Term Extensions)**, it shall give Agios prompt notice thereof, and, in such cases, shall permit Agios at Agios' own expense to take such actions itself. If Agios elects not, or is unable to, to file to obtain any patent term extension described in this **Section 9.05 (Patent Term Extensions)**, it shall give Licensee prompt notice thereof, and, in such cases, Licensee may, with Agios' prior written consent (which may not be unreasonably withheld), take such actions itself at its own expense. In such case, such first Party shall execute such documents and perform such acts as may be reasonably necessary for such other Party to perform such actions. In seeking or

obtaining patent term extensions (including supplementary protection certificates and any other extensions that are now available or become available in the future) with respect to Agios Patent Rights, in no event shall Licensee take any position that is contrary to or detrimental to the scope or enforceability of any other Agios Patent Right.

ARTICLE X.

DATA SECURITY AND ADVERSE DRUG EVENTS AND REPORTS

Section 10.01 Data Security. During the Term, each Licensee Entity will maintain safety and facility procedures, data security procedures and other safeguards against the disclosure, destruction, loss, or alteration of Agios' information in its possession, at least as robust as those required by Agios' data security procedures in effect at the time of the Effective Date.

Section 10.02 Complaints. Each Party shall maintain a record of all non-medical and medical product-related complaints it receives with respect to the Licensed Compound or any Licensed Product. Each Party shall notify the other Party of any such complaint received by it in sufficient detail and in accordance with the timeframes and procedures for reporting established by the Parties, and in any event in sufficient time to allow each Agios Entity and each Licensee Entity to comply with any and all regulatory requirements imposed upon it, including in accordance with International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use ("**ICH**") guidelines. The Party that holds the applicable Regulatory Filing(s) in a particular country or jurisdiction shall investigate and respond to all such complaints in such country or jurisdiction with respect to the Licensed Compound or any Licensed Product as soon as reasonably practicable. All such responses shall be made in accordance with the procedures established pursuant to ICH, FDA, EMA, SDA and other applicable guidelines. The Party responsible for responding to such complaint shall promptly provide the other Party a copy of any such response.

Section 10.03 Adverse Drug Events. Within [**] after the Effective Date, the Parties shall enter into the Safety Data Exchange Agreement. Such Safety Data Exchange Agreement shall provide for the exchange by the Parties of any information of which a Party becomes aware concerning any adverse event experienced by a subject or patient being administered any Licensed Product, whether or not such adverse event is determined to be attributable to any Licensed Product, including any such information received by either Party from any Third Party (subject to receipt of any required consents from such Third Party). It is understood that each Party and, in the case of Agios, the Agios Entities, and, in the case of Licensee, the Licensee Entities, shall have the right to disclose such information if such disclosure is reasonably necessary to comply with applicable Laws or requirements of any applicable Regulatory Authority. Licensee shall be responsible for handling all returns, recalls, suspensions and withdrawals of each Licensed Product in the Territory at its sole expense. The Safety Data Exchange Agreement will detail Licensee's responsibilities relating to such returns, recalls, suspensions and withdrawals.

Section 10.04 No Admissions by Licensee in Response to Product Complaints that May Be Adverse to Agios. If Licensee (including any Licensee Entity) receives any complaint relating to the quality or condition of any Licensed Product or its packaging, or any Agios

Trademark, from any Third Party, Licensee shall forthwith acknowledge receipt of such complaint but shall use good faith efforts not to make any admissions in respect thereof which could reasonably be expected to result in liability to Agios (or any other Agios Entity), through indemnification or otherwise. Licensee shall notify Agios in writing as soon as practicable (and, to the extent permitted by Law, prior to notifying any Regulatory Authority), and in any event in sufficient time to permit all applicable Agios Entities to comply with all applicable Laws for any matter relating to the safety of the Licensed Product, of receipt of such complaint. Licensee shall offer reasonable cooperation to Agios (and other Agios Entities designated by Agios) in investigating any complaint and the circumstances surrounding it and shall comply with any operating procedures that the Parties may agree upon in their Supply Agreements or pharmacovigilance agreement.

ARTICLE XI.

REPRESENTATIONS, WARRANTIES, AND COVENANTS

Section 11.01 Mutual Representations and Warranties. Each of Licensee and Agios hereby represents and warrants to the other Party as of the Effective Date that:

(a) it is a corporation or entity duly organized and validly existing under the Laws of the state, municipality, province, administrative division or other jurisdiction of its incorporation or formation;

(b) the execution, delivery and performance of this Agreement by it has been duly authorized by all requisite corporate action;

(c) it has the power and authority to execute and deliver this Agreement and to perform its obligations hereunder, and such performance does not conflict with or constitute a breach of any of its agreements with any Third Party;

(d) it has the right to grant the rights and licenses described in this Agreement;

(e) it has not made any commitment to any Third Party in conflict with the rights granted by it hereunder;

(f) to its knowledge, no consent, approval or agreement of any person or Governmental Authority is required to be obtained in connection with the execution and delivery of this Agreement; and

(g) it has not been debarred by the FDA, is not the subject of a conviction described in Section 306 of the FD&C Act, and is not subject to any similar sanction of any other Governmental Authority outside of the U.S., and neither it nor any of its Affiliates has used, in any capacity, any person or entity who either has been debarred by the FDA, is the subject of a conviction described in Section 306 of the FD&C Act or is subject to any such similar sanction inside or outside of the U.S.

Section 11.02 Mutual Covenants. Each of Licensee and Agios hereby covenants to the other Party that:

(a) it will not engage, in any capacity in connection with this Agreement or any ancillary agreement, any person or entity who either has been debarred by the FDA, is the subject of a conviction described in Section 306 of the FD&C Act or is subject to any similar sanction inside or outside of the U.S., and such Party shall inform the other Party in writing promptly if such Party or any person or entity engaged by such Party who is performing services under this Agreement, or any ancillary agreement, is debarred or is the subject of a conviction described in Section 306 of the FD&C Act or any similar sanction inside or outside of the U.S., or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to such Party's knowledge, is threatened, relating to any such debarment or conviction of a Party, any of its Affiliates or any such person or entity performing services hereunder or thereunder;

(b) during the Term, it will not make any commitment to any Third Party in conflict with the rights granted by it hereunder; and

(c) it will comply with all applicable Laws in performing its activities hereunder.

Section 11.03 Additional Agios Warranties. Agios hereby represents and warrants to Licensee as of the Effective Date that:

(a) to Agios' knowledge, Exhibit A contains a list of all Patent Rights that are Controlled by Agios as of the Effective Date and Cover (i) Development or Commercialization of the Licensed Products as they exist on the Effective Date in the Field in the Territory or (ii) the Manufacture in the Territory of the Ivosidenib Materials as they exist on the Effective Date, in each case ((i) and (ii)) in accordance with this Agreement;

(b) all of the issued Patent Rights on Exhibit A are in full force and effect, and, to the best of Agios' knowledge, are not invalid or unenforceable, in whole or in part;

(c) to Agios' knowledge, Agios is unaware of any challenge in the Territory to the validity or enforceability of any of the Agios Patent Rights listed in Exhibit A;

(d) to Agios' knowledge, no Third Party is infringing or misappropriating any Agios Technology in the Field in the Territory in derogation of the rights granted to Licensee in this Agreement;

(e) Agios and its Affiliates have not, prior to the Effective Date, assigned, transferred, conveyed or otherwise encumbered their right, title and interest in any Agios Technology within the Territory;

(f) neither Agios nor any of its Affiliates has received any written notification from a Third Party that the research, development, manufacture, use, sale or import of Licensed Products in the Territory would infringe or misappropriate the Patent Rights or Know-How owned or controlled by such Third Party;

(g) Agios has not formed a belief that any Third Party has a valid basis upon which to claim that the research, development, manufacture, use, sale or import of Licensed Products in the Field and in the Territory, in each case as contemplated by this Agreement, would infringe or misappropriate such Third Party's Patent Rights or Know-How; and

(h) to Agios' knowledge, Agios has not received written notice of any investigations, inquiries, actions or other proceedings pending before or threatened by any Regulatory Authority or other Governmental Authority in the Territory with respect to the Licensed Products in the Territory arising from any action or default by Agios or any of its Affiliates or a Third Party acting on behalf Agios in the discovery or Development of the Licensed Products.

Section 11.04 Additional Licensee Warranties and Covenants. Licensee hereby represents, warrants and covenants to Agios that:

(a) Licensee has the capability to Develop, obtain Regulatory Approval and, if applicable, Reimbursement Approval for, and Commercialize Licensed Products as contemplated in this Agreement;

(b) each Licensee Entity (other than Licensee) and each Licensee Entity's employees and permitted agents and contractors have executed agreements or have existing obligations under applicable Laws, or, upon their engagement by Licensee or any of its Affiliates, will execute such agreements, requiring automatic assignment to Licensee of all inventions (whether patentable or not) or other Know-How identified, discovered, authored, developed, conceived or reduced to practice during the course of and as the result of their association with Licensee or its Affiliates, and all intellectual property rights therein, and obligating the relevant individual or entity to maintain as confidential Licensee's confidential information related to any Licensed Product or Ivosidenib Materials as well as confidential information of other parties (including Agios and any Agios Entity) which such individual or entity may receive, to the extent required to support Licensee's obligations under this Agreement;

(c) there is no pending or threatened litigation, arbitration or investigation before any regulatory or administrative body of any country or jurisdiction (including any Governmental Authority), or pending or threatened civil, economic, administrative or criminal litigation in any country or jurisdiction (including letters asserting claims, complaints, answers, briefs, motion papers, etc.), that would affect the ownership of assets or business regulation of Licensee or any of its Affiliates, or would negatively impact Licensee's or any of its Affiliates' business or operations, including litigation against such entity's management, group leaders, directors or scientists, pertaining to performance of such entity's obligations under this Agreement, or pertaining to the conduct of clinical research, including without limitation Licensee's or any of its Affiliates' intellectual property rights;

(d) neither Licensee nor any of its Affiliates is (i) state-owned, (ii) subject to any state-owned assets administrations or other authorities with respect to the registration of state-owned assets or ownership of scientific data or (iii) under collective ownership;

(e) Licensee and each of its Affiliates has (i) passed all annual inspections by Governmental Authorities and (ii) paid all Taxes imposed upon such party by any Governmental Authority as such Taxes have become due, in each case ((i) and (ii)) since its inception;

(f) neither Licensee nor any of its Affiliates is, and, during the Term, neither Licensee nor any of its Affiliates will become, a relevant scientific research institution or higher-level educational school under the Notice of the General Office of the State Council on Issuing the Measures for the Management of Scientific Data, Guo Ban Fa (2018) No. 17, as such Law exists as of the Effective Date; and

(g) the Development to be undertaken under this Agreement will not be funded by the government of Mainland China.

Section 11.05 Anti-Corruption.

(a) Anti-Corruption Provisions. Each Party represents and warrants to the other Party that such Party has not, directly or indirectly, offered, promised, paid, authorized or given, and each Party agrees that such Party will not, in the future, offer, promise, pay, authorize or give, money or anything of value, directly or indirectly, to any Government Official (as defined below) or Other Covered Party (as defined below) for the purpose, pertaining to this Agreement, of: (i) influencing any act or decision of such Government Official or Other Covered Party; (ii) inducing such Government Official or Other Covered Party to do or omit to do an act in violation of a lawful duty; (iii) securing any improper advantage; or (iv) inducing such Government Official or Other Covered Party to influence the act or decision of a Governmental Authority, in order to obtain or retain business, or direct business to, any person or entity, in any way related to this Agreement.

For purposes of this Agreement: (A) "**Government Official**" means any official, officer, employee or representative of: (1) any Governmental Authority; (2) any public international organization or any department or agency thereof; or (3) any company or other entity owned or controlled by any Governmental Authority; and (B) "**Other Covered Party**" means any political party or party official, or any candidate for political office.

(b) Anti-Corruption Compliance.

(i) In performing under this Agreement, each Party, on behalf of itself, its respective Affiliates and (in the case of Agios) other Agios Entities and (in the case of Licensee) other Licensee Entities, agrees to comply with all applicable anti-corruption Laws, including the Foreign Corrupt Practices Act of 1977, as amended from time to time ("**FCPA**") and all anti-corruption Laws of the Territory.

(ii) Each Party represents and warrants to the other Party that such Party is not aware of any Government Official or Other Covered Party having any financial interest in the subject matter of this Agreement or in any way personally benefiting, directly or indirectly, from this Agreement.

(iii) No Party, nor any Affiliate of any Party (and (in the case of Agios) no other Agios Entity and (in the case of Licensee) no other Licensee Entity), shall give, offer, promise or pay any political contribution or charitable donation at the request of any Government Official or Other Covered Party that is in any way related to this Agreement or any related activity.

(iv) Licensee Entities shall in all cases, refrain from engaging in any activities or conduct which would cause any Agios Entity to be in violation of the FCPA and any applicable anti-bribery Laws. To the extent allowed by Law, if any Licensee Entity proposes to provide any information, data or documentation to any governmental or regulatory authority in respect of the Licensed Product that relates to or may result in a violation of the FCPA or any applicable anti-bribery Law, it shall first obtain the prior written approval of Agios, which will not be unreasonably withheld, or shall provide such information, data or documentation in accordance with Agios' written instructions.

(v) Licensee agrees that it will, and will cause each of its directors, officers, employees, agents or other representatives who have any direct involvement with any of the management or operations of the business of Licensee under this Agreement to, at the request of Agios, and at least annually, provide Agios with a certification in the form hereto attached and incorporated by reference as Exhibit F.

(vi) Licensee agrees that should it learn or have reason to know of: (i) any payment, offer, or agreement to make a payment to a foreign official or political party for the purpose of obtaining or retaining business or securing any improper advantage for Agios under this Agreement or otherwise, or (ii) any other development during the Term that in any way makes inaccurate or incomplete the representations, warranties and certifications of Licensee hereunder given or made as of the date hereof or at any time during the Term, relating to the FCPA, Licensee will immediately advise Agios in writing of such knowledge or suspicion and the entire basis known to Licensee therefor.

(vii) Notwithstanding any other provisions contained in this Agreement, Licensee agrees that full disclosure of information relating to a possible violation of the FCPA or the existence and terms of this Agreement, including the compensation provisions hereof, may be made at any time and for any reason to the U.S. government and its agencies, and to whomsoever Agios determines has a legitimate need to know.

(viii) In the event that a Party violates the FCPA, any anti-corruption Law of the Territory or any other applicable anti-corruption Law, or breaches any provision in this **Section 11.05 (Anti-Corruption)**, the other Party shall have the right to unilaterally terminate this Agreement pursuant to **Section 14.05** (**Termination for Breach**), except that the cure period set forth therein shall not apply.

Section 11.06 Exportation of Data or Biological Samples. Licensee shall ensure that the export of all Licensee Product Data and biological samples that Licensee is required to provide to Agios under this Agreement complies with all applicable Laws in the Territory and shall use Commercially Reasonable Efforts to obtain any approval of any Governmental Authority required, and to take all other steps required under applicable Laws, for such export.

To the extent that export of any Licensee Product Data or biological samples is prohibited by applicable Laws, the Parties will work together in good faith to endeavor to provide Agios or its designee with rights and access to such Licensee Product Data or biological samples as close to those described in the preceding sentence as is permitted by applicable Law.

Section 11.07 Disclaimer. EXCEPT AS EXPRESSLY SET FORTH HEREIN, THE INTELLECTUAL PROPERTY RIGHTS PROVIDED BY AGIOS TO LICENSEE HEREIN ARE PROVIDED "AS IS" AND WITHOUT WARRANTY. EXCEPT AS EXPRESSLY SET FORTH HEREIN, EACH OF THE PARTIES EXPRESSLY DISCLAIMS ANY AND ALL WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING THE WARRANTIES OF DESIGN, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, VALIDITY OR ENFORCEABILITY OF THEIR RESPECTIVE INTELLECTUAL PROPERTY RIGHTS, AND NONINFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES.

Section 11.08 Limitation of Liability. NEITHER PARTY SHALL BE ENTITLED TO RECOVER FROM THE OTHER PARTY ANY SPECIAL, INCIDENTAL, EXEMPLARY, INDIRECT, CONSEQUENTIAL OR PUNITIVE DAMAGES OR DAMAGES FOR LOSS OF PROFIT OR LOST OPPORTUNITY IN CONNECTION WITH THIS AGREEMENT, ITS PERFORMANCE OR LACK OF PERFORMANCE HEREUNDER, OR ANY LICENSE GRANTED HEREUNDER. THE FOREGOING SHALL NOT LIMIT (a) ANY INDEMNIFICATION OBLIGATIONS HEREUNDER OR (b) REMEDIES AVAILABLE TO EITHER PARTY WITH RESPECT TO A BREACH OF **Article XII** (**CONFIDENTIALITY)** OR **SECTION 2.07 (EXCLUSIVITY)** OR FRAUD COMMITTED BY THE OTHER PARTY.

ARTICLE XII.

CONFIDENTIALITY

Section 12.01 Generally. During the Term and for a period of [**] thereafter, each Party (a) shall maintain in confidence all Confidential Information of the other Party or any of such Party's Affiliates; (b) shall not use such Confidential Information for any purpose except to fulfill its obligations or exercise its rights (for the avoidance of doubt, including, with respect to Agios, the right to Commercialize the Licensed Compound and Licensed Products outside of the Field or Territory (and inside of the Field and Territory after any termination of this Agreement) and to Develop and Manufacture the Licensed Compound and Licensed Products in accordance with this Agreement) under this Agreement; and (c) shall not disclose such Confidential Information to anyone other than those of its Affiliates, directors, investors, prospective investors, lenders, prospective lenders, acquirers, prospective acquirers, licensees, prospective licensees, sublicensees, prospective sublicensees, employees, consultants, financial or legal advisors, or other agents or contractors (collectively, "**Representatives**") who are bound by written obligations of nondisclosure and non-use no less stringent than those set forth in this **Article XII (Confidentiality)** and to whom such disclosure, under this Agreement, is necessary in connection with the fulfillment of such Party's obligations or exercise of such Party's rights under this Agreement or in connection with *bona fide* financing or acquisition activities. Each Party shall (i) ensure that such Party's Representatives who receive any of the other Party's (or any of such Party's Affiliates') Confidential Information comply with the obligations set forth in

this **Article XII (Confidentiality)** and (ii) be responsible for any breach of these obligations by any of its Representatives who receive any of the other Party's (or any of such Party's Affiliates') Confidential Information. Each Party shall notify the other Party promptly on discovery of any unauthorized use or disclosure of the other's (or any of its Affiliates') Confidential Information. Notwithstanding anything to the contrary in this **Article XII** (**Confidentiality**), Agios may disclose Licensee's (or any of Licensee's Affiliates') Confidential Information to each Third Party counterparty under any In-License Agreement as reasonably required to fulfill Agios' obligations under such In-License Agreement, and Licensee acknowledges and agrees that, with respect to any such Confidential Information, such Third Party counterparty(ies) shall only be bound by the confidentiality obligations set forth in the applicable In-License Agreement(s).

Section 12.02 Exceptions. The obligations of confidentiality, non-disclosure, and non-use set forth in **Section 12.01 (Generally)** shall not apply to, and "Confidential Information" shall exclude, any information to the extent the receiving Party (the "**Recipient**") can demonstrate that such information: (a) was in the public domain or publicly available at the time of disclosure to the Recipient or any of its Affiliates by the disclosing Party or any of its Affiliates pursuant to this Agreement or the Confidentiality Agreement, or thereafter entered the public domain or became publicly available, in each case other than as a result of any action of the Recipient, or any of its Representatives, in breach of this Agreement or the Confidentiality Agreement; (b) was rightfully known by the Recipient or any of its Affiliates (as shown by its written records) prior to the date of disclosure to the Recipient or any of its Affiliates by the disclosing Party or any of its Affiliates pursuant to this Agreement or the Confidentiality Agreement; (c) was received by the Recipient or any of its Affiliates on an unrestricted basis from a Third Party rightfully in possession of such information and not under a duty of confidentiality to the disclosing Party or any of its Affiliates; or (d) was independently developed by or for the Recipient or any of its Affiliates without reference to or reliance on the Confidential Information of the other Party or any of its Affiliates (as demonstrated by written records).

Section 12.03 Permitted Disclosures. Notwithstanding any other provision of this Agreement, Recipient's (or its Affiliates') disclosure of the other Party's (or any of such Party's Affiliates') Confidential Information shall not be prohibited if such disclosure: (a) is in response to a valid order of a court or other Governmental Authority, including the rules and regulations promulgated by the Securities and Exchange Commission (or similar foreign authority) or any other Governmental Authority; (b) is otherwise required by applicable Law or rules of a nationally or internationally recognized securities exchange or Nasdaq or (c) is 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 the Licensed Products as contemplated by this Agreement; *provided* that such disclosure may be made only to the extent reasonably necessary to seek or obtain such Patent Rights or Regulatory Approvals, and the Recipient (or its applicable Affiliate(s)) shall use Commercially Reasonable Efforts to obtain confidential treatment of such information. If a Recipient is required to disclose Confidential Information pursuant to **Section 12.03(a)** or **Section 12.03(b)**, prior to any disclosure the Recipient shall, to the extent legally permitted and practicable, provide the disclosing Party with prior written notice of such disclosure in order to permit the disclosing Party to seek a protective order or other confidential treatment of such disclosing Party's Confidential Information.

Section 12.04 Publicity. The Parties recognize that each Party may from time to time desire to issue press releases and make other public statements or public disclosures (each, a "**Public Statement**") in respect of this Agreement, including the Development or Commercialization of Licensed Products in the Territory. If Licensee desires to make a Public Statement, it shall provide Agios a copy of such Public Statement at least [**] prior to the date it desires to make such public disclosure. Licensee shall not issue a Public Statement without Agios' prior written approval, which advance approval shall not be unreasonably withheld, conditioned or delayed. Agios shall provide to Licensee a preliminary draft of any Public Statement that it intends to make on a global basis with respect to Development of Licensed Products at least [**] in advance of such public disclosure and shall provide a final draft of such Public Statement at least [**] in advance of such public disclosure; *provided* that, if such Public Statement includes data owned by Licensee with respect to a Local Study or Pre-Clinical Research conducted by Licensee in the Territory, Agios shall obtain Licensee's prior written approval to include such data, which approval shall not be unreasonably withheld, conditioned or delayed. Once any public statement or public disclosure has been approved in accordance with this **Section 12.04** (**Publicity**), then the applicable Party may appropriately communicate information contained in such permitted statement or disclosure. Notwithstanding anything to the contrary in this **Section 12.04 (Publicity)**, nothing in this **Section 12.04 (Publicity)** shall be deemed to limit either Party's rights under **Section 12.03 (Permitted Disclosures)** or either Party's ability to issue press releases or make other public statements or public disclosures required by applicable Law or rules of a nationally or internationally recognized securities exchange or Nasdaq.

Section 12.05 Publications. Agios acknowledges Licensee's interest in publishing certain key results of Licensee's Development and Commercialization of Licensed Products in the Field in the Territory. Licensee recognizes the mutual interest in obtaining valid patent protection and Agios' interest in protecting its proprietary information. Consequently, except for disclosures permitted pursuant to **Section 12.02 (Exceptions)**, **Section 12.03 (Permitted Disclosures)** or **Section 12.04 (Publicity)**, if Licensee wishes to make a publication or public presentation with respect to its Development or Commercialization of Licensed Products in the Field in the Territory, Licensee shall deliver to Agios a copy of the proposed written publication or presentation at least [**] prior to submission for publication or presentation. Agios shall have the right (a) to require modifications to the publication or presentation for patent or any other business reasons, and Licensee will remove all of Agios' Confidential Information if requested by Agios, and (b) to require a reasonable delay in publication or presentation in order to protect patentable information. If Agios requests a delay, then Licensee shall delay submission or presentation for a period of [**] (or such shorter period as may be mutually agreed by the Parties) to enable Agios to file patent applications protecting Agios' rights in such information.

Section 12.06 Injunctive Relief. Each Party acknowledges and agrees that there may be no adequate remedy at law for any breach of its obligations under this **Article XII (Confidentiality)**, that any such breach may result in irreparable harm to the other Party and, therefore, that upon any such breach or any threat thereof, such other Party may seek appropriate equitable relief in addition to whatever remedies it might have at law, without the necessity of showing actual damages.

ARTICLE XIII.

INDEMNIFICATION

Section 13.01 Indemnification by Agios. Agios shall indemnify, hold harmless and defend Licensee and its Affiliates, and their respective directors, officers, consultants, agents, contractors and employees (the "**Licensee Indemnitees**") from and against any and all Third Party suits, claims, actions, demands, liabilities, expenses, costs, damages, deficiencies, obligations or losses (including reasonable attorneys' fees, court costs, witness fees, damages, judgments, fines and amounts paid in settlement) ("**Losses**") to the extent that such Losses arise out of (a) any breach of this Agreement by Agios, (b) the Development, Manufacture or Commercialization of the Licensed Compound or any Licensed Product by or on behalf of any Agios Entity or (c) the gross negligence or willful misconduct of any Agios Indemnitee. Notwithstanding the foregoing, Agios shall not have any obligation to indemnify the Licensee Indemnitees to the extent that the applicable Losses arise out of the negligence or willful misconduct of any Licensee Indemnitee or any breach of this Agreement by Licensee.

Section 13.02 Indemnification by Licensee. Licensee shall indemnify, hold harmless and defend Agios and its Affiliates, and their respective directors, officers, consultants, agents, contractors and employees (the "**Agios Indemnitees**") from and against any and all Losses, to the extent that such Losses arise out of (a) any breach of this Agreement by Licensee, or any act or failure to act by any Licensee Entity that causes a breach of any In-License Agreement, (b) the Development, Manufacture or Commercialization of the Licensed Compound or any Licensed Product by or on behalf of any Licensee Entity or (c) the gross negligence or willful misconduct of any Licensee Indemnitee. Notwithstanding the foregoing, Licensee shall not have any obligation to indemnify the Agios Indemnitees to the extent that the applicable Losses arise out of the negligence or willful misconduct of any Agios Indemnitee or any breach of this Agreement by Agios.

Section 13.03 Procedure. In the event of a claim by a Third Party against an Licensee Indemnitee or Agios Indemnitee entitled to indemnification under this Agreement ("**Indemnified Party**"), the Indemnified Party shall promptly notify the Party obligated to provide such indemnification ("**Indemnifying Party**") in writing of the claim and the Indemnifying Party shall undertake and solely manage and control, at its sole expense, the defense of the claim and its settlement. The Indemnified Party shall cooperate with the Indemnifying Party. The Indemnified Party may, at its option and expense, be represented in any such action or proceeding by counsel of its choice. The Indemnifying Party shall not be liable for any litigation costs or expenses incurred by the Indemnified Party without the Indemnifying Party's written consent. The Indemnifying Party shall not settle any such claim unless such settlement fully and unconditionally releases the Indemnified Party from all liability relating thereto and does not impose any obligations on the Indemnified Party, unless the Indemnified Party otherwise agrees in writing. No Indemnified Party may settle any claim for which it is being indemnified under this Agreement without the Indemnifying Party's prior written consent.

Section 13.04 Insurance. Licensee shall, at its own expense, obtain and maintain insurance with a reputable insurance carrier with respect to the Licensee Entities' Development, Manufacture and Commercialization of Licensed Products in the Field in the Territory under this Agreement in such type and amount and subject to such deductibles and other limitations as biopharmaceutical companies in the Territory customarily maintain with respect to the

Development, Manufacture and Commercialization of similar products, but in any event no less than (a) prior to the First Commercial Sale of the first Licensed Product in the Territory, [**] Dollars ($[**]) per incident and (b) following the First Commercial Sale of the first Licensed Product in the Territory, [**] Dollars ($[**]) per incident and [**] Dollars ($[**]) annual aggregate. Such insurance policy shall provide product liability coverage and broad form contractual liability coverage for Licensee's indemnification obligations under this Agreement and shall name the Agios Indemnitees as additional insureds. Licensee shall provide a copy of such insurance policy to Agios upon reasonable request by Agios. Licensee shall provide Agios with written notice at least [**] prior to any cancellation, non-renewal or material change in such insurance. If Licensee does not obtain replacement insurance providing comparable coverage within such [**] period, Agios shall have the right to terminate this Agreement effective at the end of such [**] period without notice or any additional waiting periods. This **Section 13.04 (Insurance)** shall survive expiration or termination of this Agreement and last until [**] after the last sale of any Licensed Product in the Field in the Territory by any Licensee Entity.

ARTICLE XIV.

TERM AND TERMINATION

Section 14.01 Term. The term of this Agreement shall begin on the Effective Date and, unless earlier terminated in accordance with the terms of this **Article XIV** (**Term and Termination**), will expire upon the expiration of the last-to-expire Royalty Term (the "**Term**").

Section 14.02 Termination at Will by Licensee. At any time after both (a) Licensee has obtained Regulatory Approval for a Licensed Product in Mainland China in relapse/refractory AML (and paid to Agios all applicable milestone payments associated with such Regulatory Approval) and (b) the last patient has been enrolled in the [**] Trial (the "**Terminable Date**"), Licensee may terminate this Agreement for any or no reason upon giving twelve (12) months' notice to Agios (which notice may not be provided until after the Terminable Date has occurred); *provided*, *however*, that Licensee may provide a notice of termination pursuant to this **Section 14.02 (Termination at Will by Licensee)** earlier than the Terminable Date if Licensee has given Agios notice of its intent to terminate this Agreement following an applicable Change in Control pursuant to **Section 16.03(a)(ii)**. Simultaneously with providing Agios a notice of termination under this **Section 14.02 (Termination at Will by Licensee)**, Licensee shall provide to Agios a list of all Local Studies that are ongoing at such time. During the twelve (12) month period after Licensee notifies Agios that Licensee is terminating this Agreement under this **Section 14.02 (Termination at will by Licensee)**, Licensee shall continue to be subject to all obligations, including all payment and diligence obligations, under this Agreement; *provided*, *however*, that, at any time during such twelve (12) month period, Agios may, by providing [**] prior written notice to Licensee, assume, for the remainder of such twelve (12) month period, all Development of Licensed Products in the Field in the Territory, other than any ongoing Local Studies that Agios elects not to pursue (each such Local Study a "**Rejected Local Study**"), in which case Licensee shall (a) promptly wind down all Rejected Local Studies in compliance with all applicable Laws at Licensee's sole expense and (b) within [**] days after receiving any invoice therefor, reimburse Agios for the lesser of (i) [**] percent ([**]%) of all Out-of-Pocket Costs incurred by Agios or any of its Affiliates in Developing Licensed Products in the Field in the

Territory (or Manufacturing Ivosidenib Materials or Licensed Products for such Development) during such remainder of such twelve (12) month period and (ii) the costs budgeted for the activities set forth in the then-current Development Plan for the remainder of such twelve (12) month period. If any Rejected Local Study continues beyond the effective date of termination under this **Section 14.02 (Termination at Will by Licensee)**, then Licensee shall, at Agios' option, either (x) reimburse Agios for all Out-of-Pocket Costs incurred by Agios or any of its Affiliates in winding down such Rejected Local Study within [**] after receipt of any invoice therefor or (y) wind down such Rejected Local Study in compliance with all applicable Laws at Licensee's sole expense. For all Local Studies that are not Rejected Local Studies, all costs after the effective date of termination under this **Section 14.02 (Termination at Will by Licensee)** shall, as between the Parties, be borne by Agios. Licensee shall supply each applicable Agios Entity with all Finished Drug Product required to conduct any Local Study being conducted by such Agios Entity, either before or after the effective date of termination under this **Section 14.02 (Termination at Will by Licensee)**. Such supply shall be at Licensee's sole expense (A) for all Local Studies prior to the effective date of termination under this **Section 14.02 (Termination at Will by Licensee)** and (B) for all Rejected Local Studies after the effective date of termination under this **Section 14.02 (Termination at Will by Licensee)**, and Agios shall pay to Licensee the Supply Price (for clarity, based on Licensee's cost of goods calculated on the same basis as Cost of Goods is calculated) for such Finished Drug Product for all Local Studies that are not Rejected Local Studies that is supplied after the effective date of termination under this **Section 14.02 (Termination at Will by Licensee)**.

Section 14.03 Termination Right in Event of No FDA Approval. In the event that Agios does not obtain Regulatory Approval from the U.S. FDA for any Licensed Product in relapse/refractory AML by December 31, 2018, Licensee may, at its sole discretion, terminate this Agreement upon giving ninety (90) days' notice to Agios.

Section 14.04 Termination for Patent Right Challenge. In the event that any Licensee Entity challenges, or assists any individual or entity in challenging, the validity, patentability or enforceability of any Patent Right that (a) is owned by or licensed to Agios or any of its Affiliates and (b) Covers or otherwise claims the Licensed Compound or any Licensed Product or their respective Development, Manufacture or Commercialization anywhere in the world, or otherwise opposes the validity, patentability or enforceability of any such Patent Right (except, in each case, as required by Law), then, to the extent consistent with applicable Law, Agios may immediately terminate this Agreement by providing written notice thereof to Licensee.

Section 14.05 Termination for Breach. Subject to the terms and conditions of this **Section 14.05** (**Termination for Breach**), a Party (the "**Non-Breaching Party**") shall have the right, in addition to any other rights and remedies available to such Party at law or in equity, to terminate this Agreement in the event the other Party (the "**Breaching Party**") is in material breach of its obligations under this Agreement. The Non-Breaching Party shall first provide written notice to the Breaching Party, which notice shall identify with particularity the alleged breach (the "**Breach Notice**"). With respect to material breaches of any payment provision hereunder, the Breaching Party shall have a period of [**] after such Breach Notice is provided to cure such breach. With respect to all other breaches, the Breaching Party shall have a period of [**] after such Breach Notice is provided to cure such breach. If such breach is not cured within the applicable period set forth above, the Non-Breaching Party may, at its election, terminate this Agreement upon written notice to the Breaching Party. The waiver by either Party

of any breach of any term or condition of this Agreement shall not be deemed a waiver as to any subsequent or similar breach.

Section 14.06 Termination for Bankruptcy and Rights in Bankruptcy.

(a) To the extent permitted under applicable Law, if, at any time during the Term, an Event of Bankruptcy (as defined below) relating to either Party (the "**Bankrupt Party**") occurs, the other Party (the "**Other Party**") shall have, in addition to all other legal and equitable rights and remedies available to such Party, the option to terminate this Agreement upon sixty (60) days written notice to the Bankrupt Party. It is agreed and understood that, if the Other Party does not elect to terminate this Agreement upon the occurrence of an Event of Bankruptcy, except as may otherwise be agreed with the trustee or receiver appointed to manage the affairs of the Bankrupt Party, the Other Party shall continue to make all payments required of it under this Agreement as if the Event of Bankruptcy had not occurred, and the Bankrupt Party shall not have the right to terminate any license granted herein. The term "**Event of Bankruptcy**" means: (a) filing in any court or agency pursuant to any statute or regulation of any state or country, a petition in bankruptcy or insolvency or for reorganization or for an arrangement or for the appointment of a receiver or trustee of the Bankrupt Party or of its assets or (b) being served with an involuntary petition against the Bankrupt Party, filed in any insolvency proceeding, where such petition is not dismissed within sixty (60) days after the filing thereof.

(b) All rights and licenses granted under or pursuant to this Agreement by Licensee and Agios are and shall otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code or any analogous provisions in any other country or jurisdiction, licenses of right to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code. The Parties agree that the Parties, as licensees of such rights under this Agreement, shall retain and may fully exercise all of their rights and elections under the U.S. Bankruptcy Code or any analogous provisions in any other country or jurisdiction. The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against either Party under the U.S. Bankruptcy Code or any analogous provisions in any other country or jurisdiction, the Party hereto that is not a Party to such proceeding shall be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property, which, if not already in the non-subject Party's possession, shall be promptly delivered to it (i) upon any such commencement of a bankruptcy proceeding upon the non-subject Party's written request therefor, unless the Party subject to such proceeding elects to continue to perform all of its obligations under this Agreement or (ii) if not delivered under clause (i) above, following the rejection of this Agreement by or on behalf of the Party subject to such proceeding upon written request therefor by the non-subject Party. The Parties acknowledge and agree that payments made under **Section 8.04 (Development Milestone Payments)** or **Section 8.05 (Sales Milestone Payments)** or pursuant to any Supply Agreements shall not (x) constitute royalties within the meaning of Section 365(n) of the U.S. Bankruptcy Code or any analogous provisions in any other country or jurisdiction or (y) relate to licenses of intellectual property hereunder.

Section 14.07 Effect of Termination.

(a) In the event of any termination (but not expiration) of this Agreement, the following shall apply:

(i) All license grants in this agreement from Agios to Licensee shall immediately terminate with the exception of the license granted under **Section 2.01(a)(iv)**;

(ii) To the extent permitted under applicable Law, and subject to **Section 14.02**, Licensee shall, as requested by Agios on a clinical trial-by-clinical trial basis: (A) promptly wind down any clinical trial then being conducted with respect to any Licensed Product in the Territory or (B) transfer any clinical trial then being conducted with respect to any Licensed Product in the Territory to any Agios Entity or a Third Party as specified by Agios; *provided* that Licensee shall be permitted to take all reasonable steps necessary to minimize liability and harm to patients in this process;

(iii) Licensee shall cease using the Agios Technology and return all inventory of the Ivosidenib Materials to Agios, together with all copies of the Agios Know-How and other Confidential Information of Agios in the possession or control of Licensee or any of its Representatives;

(iv) Licensee shall, at Agios' written request, to the extent feasible under applicable Law, promptly: (A) assign and transfer to Agios all of the Licensee Entities' right, title, and interest in and to all Licensee Regulatory Documents (including Regulatory Approvals), clinical trial agreements (to the extent assignable), confidentiality and other agreements, and materials and Know-How relating to any Licensed Product, and solely to the extent in any Licensee Entity's possession or control, and (B) disclose to Agios all documents embodying the foregoing that are in any Licensee Entity's possession or control or that any Licensee Entity is able to obtain using reasonable efforts;

(v) Upon termination of this Agreement for any reason set forth herein and at Agios' request, Licensee shall promptly take all action that may be reasonably required to transfer to Agios or a Third Party designated by Agios all portions of customers lists, promotional materials and any other information it has generated for selling the Licensed Product in the Territory that are (A) solely related to the Licensed Products and (B) not subject to any confidentiality obligations to any Third Parties, as well as any remaining inventories of Licensed Product. In addition, Licensee shall promptly transfer to Agios or to the legal entity designated by Agios all portions of documents Controlled by Licensee that solely relate to the Licensed Product and are not subject to any confidentiality obligations to any Third Parties, as well as all Licensee Regulatory Documents (including Regulatory Approvals), necessary for a smooth transition of the right to sell Licensed Products back to Agios. In addition, all rights granted by Agios to Licensee (including to any Licensee Entity) under this Agreement shall revert to Agios, and Licensee shall reasonably cooperate with Agios (or its designated Agios Entities) to take all necessary steps, at Agios' option, to cancel or transfer to Agios all registrations made by Licensee, if any, of any Trademark associated with any Licensed Product;

(vi) Upon expiration or any termination of this Agreement, Licensee (including each Licensee Entity) shall cease forthwith the use of all samples, advertising and promotional

literature, technical data, point of sale and other material relating to the Licensed Product and in the possession or under the control of Licensee, or any Licensee Entity or its respective sales representatives, and shall destroy them and certify such destruction to Agios in writing. Licensee shall also cease immediately the use of any Internet website relating to any Licensed Product as well as any Trademark associated with any Licensed Product;

(vii) Licensee hereby grants, and shall cause each Licensee Entity to grant, to Agios an exclusive (even as to Licensee and each Licensee Entity), royalty-free, worldwide, sublicensable, transferable, perpetual, irrevocable, paid-up license under the Licensee Technology and Licensee's interest in the Joint Combination Therapy Technology to Develop, Manufacture and Commercialize the Licensed Compound, Ivosidenib Materials and Licensed Products in the Territory, as set forth in **Section 2.01(b)**;

(viii) The Out-of-Pocket Costs associated with the activities set forth in subsections (a)(ii), (a)(iii) and (a)(iv) of this **Section 14.07 (Effect of Termination)** shall be borne by (A) Licensee, if this Agreement is terminated by Agios pursuant to **Section 13.04 (Insurance)**, **Section 14.04 (Termination for Patent Right Challenge)**, **Section 14.05 (Termination for Breach)**, **Section 14.06 (Termination for Bankruptcy and Rights in Bankruptcy)** or **Section 17.01 (Force Majeure)**, or by Licensee pursuant to **Section 14.02 (Termination by Licensee)**, or (B) Agios, if this Agreement is terminated by Licensee pursuant to **Section 14.05 (Termination for Breach)**, **Section 14.06 (Termination for Bankruptcy and Rights in Bankruptcy)** or **Section 17.01 (Force Majeure)**; and

(ix) Notwithstanding any expiration or termination of this Agreement, the Safety Data Exchange Agreement (with respect to Licensee's obligations thereunder) shall continue in accordance with its terms.

Section 14.08 Survival; Accrued Rights. The following articles and sections of this Agreement shall survive expiration or early termination for any reason: **Article I (Definitions)**, **Section 2.01(a)(iv), Section 2.01(b)**, **Section 2.03 (No Other Rights and Retained Rights)**, **Section 2.05(c)**, **Section 2.06 (In-License Agreements)** (solely to the extent applicable to Licensee's exercise of any rights, or performance of any obligations, retained by Licensee hereunder following the applicable expiration or termination), **Section 4.01(g)**, **Section 6.06 (Trademarks)** (second sentence only), **Section 7.06 (Agios Supply Chain Security Requirements)** (solely with respect to any Licensed Product sold following expiration or early termination of this Agreement), **Article VIII (Payments)** (solely with respect to any payment obligations incurred prior to expiration or termination), **Section 9.01 (Ownership)**, **Section 9.02 (Prosecution of Patent Rights)** (with respect to Joint Combination Therapy Patent Rights), **Section 9.03 (Enforcement and Defense)** (with respect to Joint Combination Therapy Patent Rights), **Section 11.06 (Exportation of Data or Biological Samples)**, **Section 11.07 (Disclaimer)**, **Section 11.08 (Limitation of Liability)**, **Article XII (Confidentiality)**, **Article XIII (Indemnification)**, **Section 14.02 (Termination at Will by Licensee)**, **Section 14.07 (Effect of Termination)**, **Section 14.08 (Survival; Accrued Rights)**, **Article XV (Dispute Resolution; Governing Law)**, **Section 16.01, Section 16.02, Article XVII (Miscellaneous)**, Exhibit C, Section 2.02 (Ownership of Trademark) and Exhibit C, Section 2.03 (Similar Trademarks). In any event, expiration or termination of this Agreement shall not relieve either

Party of any liability which accrued hereunder prior to the effective date of such expiration or 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.

ARTICLE XV.

DISPUTE RESOLUTION; GOVERNING LAW

Section 15.01 Arbitration. Subject to **Section 15.01(e) (Intellectual Property Disputes)** and **Section 15.01(d)**, any disputes, claims or controversies in connection with this Agreement, including any questions regarding its formation, existence, validity, enforceability, performance, interpretation, breach or termination, that are not resolved in accordance with **Article III (Governance)** and are not subject to a Party's final decision-making authority in accordance with **Article III (Governance)** shall be referred to and finally resolved by binding arbitration under the International Chamber of Commerce Rules of Arbitration (the "**Rules**"), which rules are deemed to be incorporated by reference into this **Section 15.01** (**Arbitration**), in the manner described below:

(a) Arbitration Request. If a Party intends to begin an arbitration to resolve a dispute arising under this Agreement, such Party shall provide written notice (the "**Arbitration Request**") to the other Party of such intention and the issues for resolution. Any such dispute that is not to be resolved in accordance with **Section 15.01(d)** or **Section 15.01(e)** shall be resolved in accordance with **Section 15.01(c)**; any such dispute that relates to a dispute, claim or controversy with respect to whether or not Agios has final decision-making authority pursuant to **Section 3.10(a)(iv)** (but not, for the avoidance of doubt, as to the exercise of such final decision-making authority) shall be resolved in accordance with **Section 15.01(d)**; and any such dispute that relates to validity or enforceability of a Patent Right shall be resolved in accordance with **Section 15.01(e)**.

(b) Additional Issues. Within [**] after the receipt of an Arbitration Request, the other Party may, by written notice, add additional issues for resolution.

(c) General Arbitration Procedure for Disputes. The seat of arbitration will be in New York, New York unless another venue is agreed upon by Parties, and it will be conducted in the English language. The arbitrators may not decide based on equity. Unless agreed by the Parties to choose a single common arbitrator, the arbitration will be conducted by three arbitrators, one appointed by each Party, according to the Rules. The two arbitrators appointed by the Parties will by mutual agreement appoint the third arbitrator, who will preside over the arbitration. Any dispute or omission regarding the appointment of the arbitrators by the Parties, as well as the choice of the third arbitrator, will be resolved by the International Chamber of Commerce ("**ICC**"). The arbitral award shall be final, definitive and binding on the Parties and their successors. The Parties reserve the right to apply to a competent judicial court to obtain urgent remedies to protect rights before establishment of the arbitration panel, without such recourse being considered as a waiver of arbitration. Except as otherwise determined by the arbitrators, the Parties shall each bear half of the fees and expenses of the arbitrators and the ICC,

and each Party shall bear the costs and fees of its attorneys. Nothing in this Agreement shall be deemed as preventing either Party from seeking injunctive relief (or any other provisional remedy) from any court having jurisdiction over the Parties and the subject matter of the dispute as necessary to protect either Party's name, Confidential Information, Know-How, intellectual property rights or any other proprietary right or otherwise to avoid irreparable harm. If the issues in dispute involve scientific or technical matters, any arbitrators chosen hereunder shall have educational training or experience sufficient to demonstrate a reasonable level of knowledge in the field of biotechnology and pharmaceuticals. Judgment on the award rendered by the arbitrator may be entered in any court having jurisdiction thereof. The Parties intend that each award rendered by an Arbitrator hereunder shall be entitled to recognition and enforcement under the United Nations Convention on the Recognition and Enforcement of Arbitral Awards (New York, 1958).

(d) Baseball Arbitration Procedure for Certain Disputes. The procedures set forth in **Section 15.01(c)** shall apply to disputes, claims or controversies regarding whether or not Agios has final decision-making authority pursuant to **Section 3.10(a)(iv)** (but not, for the avoidance of doubt, as to the exercise of such final decision-making authority). Within [**] following the selection of the third arbitrator, each Party shall provide the arbitrators and the other Party with a written report setting forth its position with respect to the applicable dispute, and may submit a revised or updated report within [**] of receiving the other Party's report. The arbitrators may request oral submissions by each Party, and each Party shall have the right to be present during oral submissions by the other Party. Within [**] after the last submission of the written reports or any oral submissions, the arbitrators shall select one of the Party's positions as their final decision by majority vote of the arbitrators, and shall not have the authority to modify either Party's position or render any substantive decision other than to so select the position of a Party as set forth in its respective written report.

(e) Intellectual Property Disputes. Unless otherwise agreed by the Parties, a dispute between the Parties relating to the validity or enforceability of any Patent Right shall not be subject to arbitration and shall be submitted to a court or patent office of competent jurisdiction in the relevant country or jurisdiction in which such patent was issued or, if not issued, in which the underlying patent application was filed.

Section 15.02 Choice of Law. This Agreement and all amendments, modifications, alterations, or supplements hereto, and the rights of the Parties hereunder, shall be construed under and governed by the Laws of the State of New York, exclusive of its conflicts of laws principles.

Section 15.03 Language. This Agreement has been prepared in the English language and the English language shall control its interpretation. All consents, notices, reports and other written documents to be delivered or provided by a Party under this Agreement shall be in the English language, and, in the event of any conflict between the provisions of any document and the English language translation thereof, the terms of the English language translation shall control.

ARTICLE XVI.

ASSIGNMENT AND ACQUISITIONS

Section 16.01 Assignment.

(a) Neither this Agreement nor any of the rights, interests or obligations hereunder shall be assigned by either Party (and, for these purposes, a merger, sale of assets, operation of law or other transaction shall be deemed an assignment) without the prior written consent of the other Party. Notwithstanding the foregoing, either Party may, without the other Party's written consent, assign this Agreement and its rights and obligations hereunder in whole or in part to (i) an Affiliate of such Party or (ii) a Third Party that acquires, by or otherwise in connection with, a merger, sale of assets or otherwise, all or substantially all of the business of such Party to which the subject matter of this Agreement relates; *provided* that the assignee agrees in writing to assume all of such Party's obligations under this Agreement. The assigning Party will remain responsible for the performance by its assignee of this Agreement or any obligations hereunder so assigned.

(b) The terms of this Agreement will be binding upon and will inure to the benefit of the successors, heirs, administrators and permitted assigns of the Parties. Any purported assignment in violation of this **Section 16.01 (Assignment)** will be null and void *ab initio*.

Section 16.02 Acquisitions. Each Party agrees that, in the event that a Party or any of its Affiliates (the "**Acquired Party**") is acquired through a Change in Control by one or more persons or entities (collectively, the "**Acquirer**"), the Acquired Party shall be deemed not to "Control" for purposes of this Agreement, and the non-Acquired Party shall not obtain any rights or access under this Agreement to, any Know-How or Patent Rights owned by or licensed to such Acquirer, or any of such Acquirer's Affiliates that were not Affiliates of the Acquired Party immediately prior to the consummation of such Change in Control, that were not already within Agios Technology (if the Acquired Party is Agios or any of its Affiliates) or Licensee Technology (if the Acquired Party is Licensee or any of its Affiliates) or Joint Combination Therapy Technology immediately prior to the consummation of such Change in Control. Each Party shall notify the other Party promptly after any Change in Control of such Party or any of its Affiliates.

Section 16.03 Consequences of Certain Changes in Control of Licensee.

(a) If, during the term of the exclusivity covenant in **Section 2.07(a)** or **(b)**, Licensee or any of its Affiliates acquires or becomes an Affiliate of a Third Party (whether by way of a purchase of assets, merger, consolidation, Change in Control or otherwise) that is, at such time, Developing, Manufacturing or Commercializing a Competing Product or Restricted Product in a manner that, if performed by Licensee or any of its Affiliates, would violate **Section 2.07(a)** or **(b)**, then Licensee or its applicable Affiliate will, no later than [**] following the closing date of the relevant acquisition or other event, unless otherwise agreed by Agios, notify Agios in writing that Licensee or such Affiliate will:

(i) Divest, whether by license, divestiture of assets or otherwise, its interest in such Competing Product or Restricted Product, as applicable, in the Territory to a Third Party, to the extent necessary to be in compliance with **Section 2.07(a)** or **(b)**, as applicable, provided that Licensee or its applicable Affiliate may retain an economic interest through such a license, divestiture of assets or other transaction as long as Licensee does not retain any other material

rights as to such Competing Product or Restricted Product, as applicable, in the Territory beyond a passive economic interest;

(ii) Terminate this Agreement in accordance with Section 14.02 (Termination by Licensee); or

(iii) Terminate the Development, Manufacture and Commercialization of such Competing Product or Restricted Product, as applicable, in the Territory, to the extent necessary to be in compliance with **Section 2.07(a)** or **(b)**, as applicable.

(iv) If Licensee or any of its Affiliates notifies Agios in writing that it or its relevant Affiliate intends to divest such Competing Product or Restricted Product, as applicable, or terminate the Development, Manufacture and Commercialization of the Competing Product or Restricted Product, as applicable, in the Territory as provided in this **Section 16.03 (Consequences of Certain Changes in Control of Licensee)**, then Licensee or its relevant Affiliate will effect such divestiture or termination within [**] after the date of the relevant acquisition or other event, subject to compliance with applicable Law, and will confirm to Agios in writing when such divestiture or termination has been completed. Licensee will keep Agios reasonably informed of its and its Affiliates' efforts and progress in effecting such divestiture or termination until it is completed. Until such divestiture or termination occurs, Licensee shall keep its and its Affiliates' activities with respect to such Competing Product or Restricted Product, as applicable, separate from their activities with respect to the Licensed Products and shall continue to fully perform all of their obligations hereunder with respect to Licensed Products, including their applicable diligence obligations with respect to the Development and Commercialization of Licensed Products hereunder.

(b) Notwithstanding anything to the contrary in the foregoing **Section 16.03(a)**, if, during the term of the exclusivity covenant in **Section 2.07(b)**, Licensee or any of its Affiliates acquires or becomes an Affiliate of a Third Party (whether by way of a purchase of assets, merger, consolidation, Change in Control or otherwise) that is, at such time, Developing, Manufacturing or Commercializing a Restricted Product in a manner that, if performed by Licensee or any of its Affiliates, would violate **Section 2.07(b)**, then, if Licensee so requests within [**] after the closing of the transaction that resulted in Licensee or its applicable Affiliate(s) acquiring or becoming an Affiliate of such Third Party, Agios shall, for a period of [**], discuss with Licensee in good faith whether it would be beneficial to the Development, Manufacture or Commercialization of Licensed Products under this Agreement to waive, in whole or in part, Licensee's compliance with **Section 2.07(b)** and **Section 16.03(a)** with respect to such Development, Manufacture or Commercialization of such Restricted Product. Following such discussions, Agios may elect, in its sole discretion, to waive, in whole or in part, Licensee's compliance with **Section 2.07(b)** and **Section 16.03(a)** with respect to such Development, Manufacture or Commercialization of such Restricted Product.

(c) If, during the Term, Licensee or any of its Affiliates becomes an Acquired Party, then, (i) Agios shall thereafter have the right to assume final decision-making authority over all matters described in **Section 3.10(b)** relating to Development, and, if Agios exercises such right, Licensee shall no longer have such final decision-making authority, (ii) without limiting

Licensee's obligations under **Section 6.04**, following such event Licensee shall, to Agios' reasonable satisfaction, continue to devote at least the level of efforts and resources to Commercializing Licensed Products that Licensee would have devoted to such Commercialization had Licensee not become an Acquired Party and had continued to pursue such Commercialization in accordance with **Section 6.04** and Licensee's then-existing plans for such activities, and (iii) if Licensee does not, to Agios' reasonable satisfaction, continue to devote efforts and resources to Commercializing Licensed Products as described in the foregoing clause (ii), then Agios shall have the right to terminate this Agreement pursuant to **Section 14.04**.

Section 16.04 Consequences of Certain Changes in Control of Agios.

(a) If, during the term of the exclusivity covenant in **Section 2.07(c)**, Agios or any of its Affiliates acquires or becomes an Affiliate of a Third Party (whether by way of a purchase of assets, merger, consolidation, Change in Control or otherwise) that is, at such time, Developing, Manufacturing or Commercializing a Competing Product in a manner that, if performed by Agios or any of its Affiliates, would violate **Section 2.07(c)**, then Agios or its applicable Affiliate will, no later than [**] following the closing date of the relevant acquisition or other event, unless otherwise agreed by Licensee, notify Licensee in writing that Agios or such Affiliate will:

(i) Divest, whether by license, divestiture of assets or otherwise, its interest in such Competing Product in the Territory to a Third Party, to the extent necessary to be in compliance with **Section 2.07(c),** provided that Agios or its applicable Affiliate may retain an economic interest through such a license, divestiture of assets or other transaction as long as Agios does not retain any other material rights as to such Competing Product in the Territory beyond a passive economic interest; or

(ii) Terminate the Development, Manufacture and Commercialization of such Competing Product in the Territory, to the extent necessary to be in compliance with **Section 2.07(c)**.

(iii) If Agios or any of its Affiliates notifies Licensee in writing that it or its relevant Affiliate intends to divest such Competing Product or terminate the Development, Manufacture and Commercialization of the Competing Product in the Territory as provided in this **Section 16.04 (Consequences of Certain Changes in Control of Agios)**, then Agios or its relevant Affiliate will effect such divestiture or termination within [**] after the date of the relevant acquisition or other event, subject to compliance with applicable Law, and will confirm to Licensee in writing when such divestiture or termination has been completed. Agios will keep Licensee reasonably informed of its and its Affiliates' efforts and progress in effecting such divestiture or termination until it is completed. Until such divestiture or termination occurs, Agios shall keep its and its Affiliates' activities with respect to such Competing Product separate from their activities with respect to the Licensed Products and shall continue to fully perform all of their obligations hereunder with respect to Licensed Products.

ARTICLE XVII.

MISCELLANEOUS

Section 17.01 Force Majeure. Subject to the terms of each In-License Agreement, if either Party shall be delayed, interrupted in or prevented from the performance of any obligation hereunder by reason of force majeure, which may include any act of God, fire, flood, earthquake, war (declared or undeclared), public disaster, act of terrorism, government action, strike or labor differences, in each case outside of such Party's reasonable control, such Party shall not be liable to the other therefor, and the time for performance of such obligation shall be extended for a period equal to the duration of the force majeure which occasioned the delay, interruption or prevention. The Party invoking the force majeure rights of this **Section 17.01** (**Force Majeure**) must notify the other Party by courier or overnight dispatch (*e.g.*, Federal Express) within a period of thirty (30) days of both the first and last day of the force majeure unless the force majeure renders such notification impossible, in which case notification will be made as soon as possible. If the delay resulting from the force majeure exceeds one hundred eighty (180) days, the other Party may terminate this Agreement immediately upon written notice to the Party invoking the force majeure rights of this **Section 17.01** (**Force Majeure**).

Section 17.02 Entire Agreement. This Agreement, together with the exhibits and schedules attached hereto, constitutes the entire agreement between Agios or any of its Affiliates, on the one hand, and Licensee or any of its Affiliates, on the other hand, with respect to the subject matter hereof, supersedes all prior understandings and writings between Agios or any of its Affiliates, on the one hand, and Licensee or any of its Affiliates, on the other hand relating to such subject matter, including the Confidentiality Agreement, and, subject to **Section 4.01 (Development in the Field in the Territory)**, shall not be modified, amended or (subject to **Article XIV (Term and Termination)**) terminated, except by another agreement in writing executed by the Parties.

Section 17.03 Severability. If, under applicable Law, any provision of this Agreement is invalid or unenforceable, or otherwise directly or indirectly affects the validity of any other material provision of this Agreement (such invalid or unenforceable provision, a "**Severed Clause**"), it is mutually agreed that this Agreement shall endure except for the Severed Clause. The Parties shall consult one another and use their reasonable efforts to agree upon a valid and enforceable provision that is a reasonable substitute for the Severed Clause in view of the intent of this Agreement.

Section 17.04 Notices. Any notice required or permitted to be given under this Agreement shall be in writing and shall be mailed by internationally recognized express delivery service, or sent by facsimile or email and confirmed by mailing, as follows (or to such other address as the Party to whom notice is to be given may have furnished to the other Party in writing in accordance herewith):

If to Agios:

Agios Pharmaceuticals
88 Sidney Street
Cambridge, MA 02139 USA
Attention: General Counsel
Facsimile: [**]

With a copy to (which shall not constitute notice for purposes of this Agreement):

WilmerHale LLP
60 State Street
Boston, Massachusetts 02109 USA

Attention: Steven D. Barrett, Esq.

Facsimile: (617) 526-5000

If to Licensee:

CStone Pharmaceuticals
P.O. Box 31119
Grand Pavilion
Hibiscus Way
802 West Bay Road
Grand Cayman, KY1-1205, Cayman Islands

with copies to:

CStone Pharmaceuticals (Shanghai) Co., Ltd.
1000 Zhangheng Road, Building 25
Pudong New District, Shanghai
China 201203
Attention: Chief Executive Officer

and

CStone Pharmaceuticals (Shanghai) Co., Ltd.
1000 Zhangheng Road, Building 25
Pudong New District, Shanghai
China 201203
Attention: Head of Global Corporate Development
Email: [**]

Any such notice shall be deemed to have been given (a) when delivered if personally delivered, (b) on receipt if sent by overnight courier or (c) on receipt if sent by mail.

Section 17.05 Agency. Neither Party is, nor will be deemed to be a partner, employee, agent or representative of the other Party for any purpose. Each Party is an independent contractor of the other Party. Neither Party shall have the authority to speak for, represent or obligate the other Party in any way without prior written authority from the other Party.

Section 17.06 No Waiver. Any omission or delay by either Party at any time to enforce any right or remedy reserved to it, or to require performance of any of the terms, covenants or provisions hereof, by the other Party, shall not constitute a waiver of such Party's rights to the enforcement of any of its rights under this Agreement. Any waiver by a Party of a particular breach or default by the other Party shall not operate or be construed as a waiver of any subsequent breach or default by the other Party.

Section 17.07 Cumulative Remedies. Except as may be expressly set forth herein, no remedy referred to in this Agreement is intended to be exclusive, but each shall be cumulative and in addition to any other remedy referred to in this Agreement or otherwise available under law or in equity.

Section 17.08 No Third Party Beneficiary Rights. This Agreement is not intended to and shall not be construed to give any Third Party any interest or rights (including any third party beneficiary rights) with respect to or in connection with any agreement or provision contained herein or contemplated hereby, other than (a) to the extent provided in **Section 13.01 (Indemnification by Agios)**, the Licensee Indemnitees and (b) to the extent provided in **Section 13.02 (Indemnification by Licensee)**, the Agios Indemnitees.

Section 17.09 Performance by Affiliates, Sublicensees or Subcontractors. To the extent that this Agreement imposes any obligation on any Licensee Entity, Licensee shall cause such Licensee Entity to perform such obligation. Subject to **Section 8.11 (Methods of Payment)**, either Party may use one or more of its Affiliates to perform its obligations and duties hereunder; *provided* that such Party so notifies the other Party in writing and *provided*, *further*, that such Party shall remain liable hereunder for the prompt payment and performance of all of its obligations hereunder.

Section 17.10 Counterparts. This Agreement may be executed in counterparts, all of which taken together shall be regarded as one and the same instrument.

[*Signature page follows*]

IN WITNESS WHEREOF, the Parties have executed this Agreement through their duly authorized representatives to be effective as of the Effective Date.

AGIOS PHARMACEUTICALS, INC.

By: /s/ David Schenkein

Name: David Schenkein

Title: CEO

CSTONE PHARMACEUTICALS

By: /s/ Frank Jiang

Name: Frank Jiang

Title: CEO

Exhibit A

List of Agios Patent Rights Existing as of the Effective Date

Agios Docket	Case Type	Status	Application Number	Filing Date	Patent No.	Issue Date	Pub No.	Pub Date	App Title
[**]	[**]	[**]	[**]	[**]	[**]	[**]	[**]	[**]	[**]

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of three pages were omitted. [**]

Exhibit B

Initial Development Outline

The initial clinical development plan described below, in whole or in part, is subject to approval by Regulatory Authority and the JDC.

Confidential Materials omitted and filed separately with the Securities and Exchange Commission. A total of two pages were omitted. [**]

Exhibit C

TRADEMARK LICENSE

ARTICLE I.

LICENSE

Section 1.01 License .

(a) Subject to the terms and conditions specified in the Agreement, Agios hereby grants to Licensee (i) an exclusive (including as to Agios and its Affiliates), non-sublicensable (except in accordance with **Section 2.02 (Rights to Sublicense or Subcontract)**), non-transferable (except in accordance with **Section 16.01 (Assignment)**) license in the Territory to use the Agios Trademarks and Agios Web Presence solely in connection with exercising the Commercialization license granted to Licensee under **Section 2.01(a)(i)** and (ii) a non-exclusive, non-sublicensable (except in accordance with **Section 2.02 (Rights to Sublicense or Subcontract)**), non-transferable (except in accordance with **Section 16.01 (Assignment)**) license in the Territory to use the Agios Trademarks and Agios Web Presence solely in connection with exercising the Manufacturing license granted to Licensee under **Section 2.01(a)(iii)**. Agios retains all right, title and interest throughout the world in and to the Agios Trademarks and Agios Web Presence not expressly granted herein, and all rights shall revert to Agios upon expiration or termination of the Agreement. No other, further or different license is granted or implied and no assignment of any right or interest is made or intended herein. In particular, no license is granted to permit any Third Party to use the Agios Trademarks or Agios Web Presence, and Licensee may only use the Agios Trademarks and Agios Web Presence on or in connection with the Licensed Products subject to the terms of the Agreement.

(b) Licensee shall, and shall ensure that each Licensee Entity shall, use only the Agios Trademarks with the Licensed Products and shall use such Agios Trademarks in a manner consistent with the Commercialization Plan, Global Brand Strategy and the terms of the Agreement, and shall not, and shall ensure that each Licensee Entity shall not, associate any other Trademark with the Licensed Products or otherwise engage in dual branding of the Licensed Products except as provided in **Section 6.06**. In accordance with **Section 6.06**, if Agios elects to co-brand any Licensed Product in the Territory with the Agios name and Agios-designated corporate trademark, then Licensee shall, and shall ensure that each Licensee Entity shall, include such Agios name and Agios-designated corporate trademark on the packaging of such Licensed Product in the manner agreed by the Parties.

Section 1.02 Quality Control .

(a) Agios shall have the right to monitor and, no more than [**], inspect all stages of the Manufacture conducted by any Licensee Entity and Commercialization of all Licensed Products and Materials in the Territory for the purpose of determining Licensee’s compliance

with the terms of the Agreement. No more than [**], Licensee shall permit Agios or Agios' designees to enter Licensee's, or any applicable Licensee Entity's, premises at reasonable times and with reasonable advance notice, to inspect Licensee's Manufacturing and Commercialization facilities and operations, and to inspect and test any and all Licensed Products. If Agios at any time finds that any of such Licensed Products (i) are not being (A) Manufactured by Licensee Entities in compliance with Parties' agreed-upon specifications for same or (B) Commercialized in compliance with the Global Brand Strategy, or (ii) are packaged, advertised or marketed in a misleading or deceptive manner, or are otherwise prepared, packaged, advertised or sold in a manner in violation of Exhibit C, Section 1.03 (Advertising and Packaging), Agios may notify Licensee in writing of such deficiencies, and, if Licensee fails to correct such deficiencies within [**] after receipt of such notice, Agios may terminate the license granted under Exhibit C, Section 1.01.

(b) Upon Agios' request, Licensee shall furnish or make available to Agios a reasonable number of representative samples of the Licensed Products to permit Agios to determine that such Licensed Products meet the quality standards set forth herein. The costs associated with the submission and shipping of such samples shall be borne by Agios.

Section 1.03 Advertising and Packaging .

(a) All packages, labels, designs, descriptive materials and advertising and promotional materials of every type and in every media to be used by any Licensee Entity in connection with publicizing, offering, selling, advertising, marketing, promoting or distributing the Licensed Products or making use of the Agios Web Presence (collectively "**Materials**") shall be consistent with the Global Brand Strategy.

ARTICLE II.

TRADEMARK DEVELOPMENT AND OWNERSHIP

Section 2.01 Trademark Development .

(a) Prior to any Commercialization of any Licensed Product in the Territory, the Parties shall, in accordance with **Section 6.06**, choose a Trademark in Chinese for use in the Territory, which may vary by Jurisdiction if agreed to by the Parties (together with any Agios name or Agios-designated corporate trademark with which Agios elects to co-brand Licensed Products in the Territory in accordance with **Section 6.06**, the "**Agios Trademarks**"), and the domain names and social media account names comprising the Agios Web Presence as defined below. Any disagreements between the Parties regarding the selection of Agios Trademarks or the Agios Web Presence, shall be decided by Agios.

(b) Licensee shall be responsible for registering domain names in the Territory using the Agios Trademarks, in the name or on behalf of Agios, at Licensee's expense. Subject to Exhibit C, Section 1.03 (Advertising and Packaging), Licensee shall be responsible for creating

and operating websites using such domain names, and for creating and operating related social media accounts, including WeChat and Weibo and such other social media platforms as the Parties may agree to from time to time (collectively, domain names and social media accounts, "**Agios Web Presence**").

Section 2.02 Ownership of Trademark .

(a) In accordance with **Section 6.06 (Trademarks)**, Agios expressly reserves the sole and exclusive ownership of each Agios Trademark and Agios Web Presence (including all domain names and social media accounts included within the Agios Web Presence), and all rights relating thereto. Licensee hereby acknowledges that Agios is the sole and exclusive owner of each Agios Trademark and the Agios Web Presence and agrees not to challenge at any time, directly or indirectly, the rights of Agios thereto or the validity or distinctiveness thereof. All goodwill and all use of any Agios Trademark or the Agios Web Presence by Licensee under the Agreement shall inure exclusively to Agios. Licensee hereby assigns and agrees to assign, on behalf of all Licensee Entities, to Agios all of the Licensee Entities' rights, title and interest in and to the Agios Trademarks and Agios Web Presence and all intellectual property rights therein. At all times during and after the Term, the Licensee Entities shall cause their respective employees, agents and contractors to execute and deliver all requested applications, assignments and other documents, and take such other measures as Agios may reasonably request, in order to perfect and enforce Agios' rights in any Agios Trademark or Agios Web Presence (and any intellectual property rights therein) without additional compensation. Each Licensee Entity, on behalf of itself and its employees, agents and contractors, hereby appoints Agios its attorney to execute and deliver any such documents on behalf of such Licensee Entity and its employees, agents and contractors in the event such Licensee Entity or any of its employees, agents or contractors fails to do so.

(b) Licensee agrees to fully cooperate and assist Agios in the protection and defense of any of Agios' rights in the Agios Trademarks, in the filing and prosecution of any Trademark, copyright, industrial model or design application, registration, renewal and the like, in the recording of this Exhibit C or any other relevant agreements, including, without limitation, registered user agreements, and in the doing of any other act with respect to the Agios Trademarks, including the prevention of the use thereof by any unauthorized person, that in the sole discretion and judgment of Agios may be necessary or desirable.

(c) Any copyright which may exist or be created in any materials provided by Agios hereunder, including, without limitation, any sketch, design, drawing, print, packaging, label, tag or the like furnished, designed or authored by Agios, whether in English or the Chinese language translation thereof, (collectively, "**Agios Works**") shall be the exclusive property of Agios. Licensee shall not, at any time, do or suffer to be done any act or thing which may adversely affect any rights of Agios in any such Agios Works, including, without limitation, disclosing such information or filing any application in Licensee's name to register or record any claims to copyrights in any of the Agios Works. Licensee shall do all things reasonably required by Agios to preserve and protect such rights, including, without limitation, placing Agios' copyright notice on all applicable Materials used in or for the Territory.

Section 2.03 Similar Trademarks .

(a) Licensee agrees that it shall not, during the Term or thereafter, register or apply to register any of the Agios Trademarks, any other Trademarks owned by Agios, or any Trademarks similar thereto anywhere in the world. Further, Licensee agrees not to produce, sell, advertise, market or distribute, at any time, whether, directly or indirectly, any other product whose Trademark or other designation is confusingly similar to any Agios Trademark.

Section 2.04 Maintenance of Trademark .

(a) Licensee shall use its best efforts not to do or permit to be done any act likely to prejudice, affect, impair or destroy the reputation, title or interest of Agios in or to any Agios Trademark or the Agios Web Presence. If Licensee knows that any person, firm or corporation is infringing any Agios Trademark, Licensee will promptly notify Agios and cooperate fully with Agios (at the expense of Agios) in the defense and protection of such Agios Trademark.

(b) Agios shall have the sole right, but not the obligation, to determine whether or not any action shall be taken on account of any infringement, passing off, unfair competition or like activities or other enforcement of Agios' rights in the Agios Trademarks. If Agios so desires, it may prosecute any actions, claims, lawsuits or proceedings in its own name or join Licensee as a party thereto. Agios shall be entitled to recover any and all sums of money awarded and materials delivered up as a result of such actions, claims, lawsuits or proceedings. Licensee shall have no recourse against Agios or otherwise should Agios decide not to initiate enforcement or to prosecute any such actions, claims, lawsuits or proceedings.

Section 2.05 Defense of Litigation . Agios agrees to defend, indemnify and hold harmless Licensee for and from any and all actions, claims, proceedings or lawsuits arising from or related in any way to claims that Licensee's use of the Agios Trademarks hereunder infringes the trademark rights of Third Parties in the Territory, *provided*, however, that Agios shall not bear any duty, obligation or liability pursuant to this Exhibit C, Section 2.05 (Defense of Litigation) to the extent and with respect to any use of any of the Agios Trademarks in a manner not authorized by the Agreement, with products other than the Licensed Products, or in connection with other Trademarks that form at least in part a basis for the claim. The obligation of Agios to Licensee for such infringement or claims of infringement, shall be conditioned on Licensee's compliance with the procedures set forth in **Section 13.03 (Procedure)**, *mutatis mutandis*.

Exhibit D

Permitted Subcontractors

[**]

Exhibit E

Supply Chain Security Requirements

Agios considers supply chain security critical to the safety of patients. Therefore, Agios expects Licensee Entities to verify the security of Ivosidenib Materials, Licensed Product, and Finished Drug Product while under the control of Licensee Entities.

Licensee agrees to use Commercially Reasonable Efforts to comply with the supply chain security requirements set forth by Agios from time to time and shall ensure that any Licensee Entity shall also use Commercially Reasonable efforts to comply with such supply chain security requirements below:

Supply Chain Security requirements:

- [**]

Exhibit F

Form of Annual Compliance Certification

I. [name] a duly authorized representative of [LICENSEE] do hereby certify for and on behalf of such company, that neither I nor to my knowledge any other person, including but not limited to every officer, director, stockholder, employee, representative and agent of [LICENSEE] has improperly made, offered to make, or agreed to make any loan, gift, donation or payment, or transfer of any other thing of value directly or indirectly, whether in cash or in kind, to or for the benefit of any entities, persons or class of persons listed below in connection with any business activity of Agios Pharmaceuticals, Inc. or any of its wholly or partially owned affiliates.

For purposes of this certification, these entities, persons and classes of persons include private entities, government and public bodies, political parties, party officials, candidates for political office, local councils, judicial officers, public international organizations and their employees, agents and officials.

I hereby confirm that should I learn of any of the prohibited activities described above, or if there are any changes in the ownership or control of [LICENSEE], I will immediately advise Agios Pharmaceuticals, Inc.

[LICENSEE]

Date: _____

By: _____

Name: _____

Title: _____

Schedule 1.65

Ivosidenib (AG-120)

Schedule 8.04(e)

Milestone Examples

For purposes of this Schedule 8.04(e), the following terms have the following meanings:

[**]" means the milestone event set forth in **Section 8.04(a)(iv)**

[**] means [**]

[**] means the milestone event set forth in **Section 8.04(a)(iii)**

[**] means [**]

[**] means the milestone event set forth in **Section 8.04(a)(v)**

Example 1

[**]

Example 2

[**]

[**]

Exhibit 31.1

CERTIFICATION

I, David P. Schenkein, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Agios Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 2, 2018

/s/ David P. Schenkein

David P. Schenkein
President and Chief Executive Officer
(principal executive officer)

Exhibit 31.2

CERTIFICATION

I, Andrew Hirsch, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Agios Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 2, 2018

/s/ Andrew Hirsch

Andrew Hirsch

Chief Financial Officer and Head of Corporate Development

(principal financial officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Agios Pharmaceuticals, Inc. (the "Company") for the fiscal quarter ended June 30, 2018, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, David P. Schenkein, President and Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 2, 2018

/s/ David P. Schenkein

David P. Schenkein
President and Chief Executive Officer
(principal executive officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Quarterly Report on Form 10-Q of Agios Pharmaceuticals, Inc. (the "Company") for the fiscal quarter ended June 30, 2018, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Andrew Hirsch, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 2, 2018

/s/ Andrew Hirsch

Andrew Hirsch
Chief Financial Officer and Head of Corporate Development
(principal financial officer)