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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, 2020
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)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock, Par Value $0.001 per share	**AGIO**	**Nasdaq Global Select Market**

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 every Interactive Data File required to be submitted 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 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.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	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 24, 2020: 69,110,084

AGIOS PHARMACEUTICALS, INC.

FORM 10-Q

FOR THE THREE AND SIX MONTHS ENDED JUNE 30, 2020

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements (Unaudited)

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Balance Sheets
(Unaudited)

(In thousands, except share and per share data)	June 30, 2020	December 31, 2019
Assets		
Current assets:		
Cash and cash equivalents	$ 295,858	$ 80,931
Marketable securities	494,270	483,946
Accounts receivable, net	12,023	8,952
Collaboration receivable – related party	2,537	1,539
Collaboration receivable – other	1,827	1,928
Royalty receivable – related party	1,650	2,900
Inventory	11,231	7,331
Prepaid expenses and other current assets	26,959	24,177
Total current assets	846,355	611,704
Marketable securities	4,285	152,929
Operating lease assets	89,208	93,643
Property and equipment, net	33,925	31,472
Financing lease assets	793	993
Other assets	1,575	—
Total assets	$ 976,141	$ 890,741
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 15,461	$ 21,896
Accrued expenses	41,911	53,142
Deferred revenue – related party	—	10,933
Operating lease liabilities	6,672	6,642
Financing lease liabilities	309	273
Total current liabilities	64,353	92,886
Deferred revenue, net of current portion – related party	—	50,580
Operating lease liabilities, net of current portion	101,874	106,074
Financing lease liabilities, net of current portion	491	673
Liability related to the sale of future revenue, net of debt issuance costs	250,958	—
Total liabilities	417,676	250,213
Stockholders' equity:		
Preferred stock, $0.001 par value; 25,000,000 shares authorized; no shares issued or outstanding at June 30, 2020 and December 31, 2019	—	—
Common stock, $0.001 par value; 125,000,000 shares authorized; 69,058,696 and 68,401,105 shares issued and outstanding at June 30, 2020 and December 31, 2019, respectively	69	68
Additional paid-in capital	2,203,599	2,156,363
Accumulated other comprehensive income	1,636	202
Accumulated deficit	(1,646,839)	(1,516,105)
Total stockholders' equity	558,465	640,528
Total liabilities and stockholders' equity	$ 976,141	$ 890,741

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Operations
(Unaudited)

(In thousands, except share and per share data)	Three Months Ended June 30, 2020	Three Months Ended June 30, 2019	Six Months Ended June 30, 2020	Six Months Ended June 30, 2019
Revenues:				
Product revenue, net	$ 27,581	$ 13,727	$ 50,255	$ 22,865
Collaboration revenue – related party	5,735	8,979	65,832	26,898
Collaboration revenue – other	692	812	1,685	1,782
Royalty revenue – related party	3,339	2,703	6,673	4,903
Total revenue	37,347	26,221	124,445	56,448
Cost and expenses:				
Cost of sales	675	303	1,208	637
Research and development	90,917	107,389	182,173	202,974
Selling, general and administrative	35,951	32,390	74,452	64,181
Total cost and expenses	127,543	140,082	257,833	267,792
Loss from operations	(90,196)	(113,861)	(133,388)	(211,344)
Interest income, net	1,769	3,990	4,705	8,395
Non-cash interest expense for the sale of future revenue	(2,051)	—	(2,051)	—
Net loss	$ (90,478)	$ (109,871)	$ (130,734)	$ (202,949)
Net loss per share – basic and diluted	$ (1.31)	$ (1.87)	$ (1.90)	$ (3.46)
Weighted-average number of common shares used in computing net loss per share – basic and diluted	68,958,091	58,722,244	68,784,109	58,589,167

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Comprehensive Loss
(Unaudited)

(In thousands)	Three Months Ended June 30, 2020	Three Months Ended June 30, 2019	Six Months Ended June 30, 2020	Six Months Ended June 30, 2019
Net loss	$ (90,478)	$ (109,871)	$ (130,734)	$ (202,949)
Other comprehensive income				
Unrealized gain on available-for-sale securities	1,562	974	1,434	2,661
Comprehensive loss	$ (88,916)	$ (108,897)	$ (129,300)	$ (200,288)

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Stockholders' Equity
(Unaudited)

(in thousands, except share amounts)	Common Stock Shares	Common Stock Amount	Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2019	68,401,105	$ 68	$ 2,156,363	$ 202	$ (1,516,105)	$ 640,528
Common stock issued under stock incentive plan and ESPP	388,820	1	5,464	—	—	5,465
Stock-based compensation expense	—	—	19,690	—	—	19,690
Other comprehensive loss	—	—	—	(128)	—	(128)
Net loss	—	—	—	—	(40,256)	(40,256)
Balance at March 31, 2020	68,789,925	$ 69	$ 2,181,517	$ 74	$ (1,556,361)	$ 625,299
Common stock issued under stock incentive plan and ESPP	268,771	$ —	$ 1,652	$ —	$ —	$ 1,652
Stock-based compensation expense	—	—	20,430	—	—	20,430
Other comprehensive income	—	—	—	1,562	—	1,562
Net loss	—	—	—	—	(90,478)	(90,478)
Balance at June 30, 2020	69,058,696	$ 69	$ 2,203,599	$ 1,636	$ (1,646,839)	$ 558,465

(in thousands, except share amounts)	Common Stock Shares	Common Stock Amount	Additional Paid-In Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2018	58,218,653	$ 58	$ 1,794,283	$ (2,171)	$ (1,104,633)	$ 687,537
Common stock issued under stock incentive plan and ESPP	441,168	1	6,002	—	—	6,003
Stock-based compensation expense	—	—	18,108	—	—	18,108
Other comprehensive income	—	—	—	1,687	—	1,687
Net loss	—	—	—	—	(93,078)	(93,078)
Balance at March 31, 2019	58,659,821	$ 59	$ 1,818,393	$ (484)	$ (1,197,711)	$ 620,257
Common stock issued under stock incentive plan and ESPP	89,365	$ —	$ 2,770	$ —	$ —	$ 2,770
Stock-based compensation expense	—	—	18,547	—	—	18,547
Other comprehensive income	—	—	—	974	—	974
Net loss	—	—	—	—	(109,871)	(109,871)
Balance at June 30, 2019	58,749,186	$ 59	$ 1,839,710	$ 490	$ (1,307,582)	$ 532,677

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Cash Flows
(Unaudited)

(In thousands)	Six Months Ended June 30, 2020	2019
Operating activities		
Net loss	$ (130,734)	$ (202,949)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	4,906	4,042
Stock-based compensation expense	40,120	36,655
Net accretion of premium and discounts on investments	473	(2,019)
Non-cash operating lease expense	4,435	4,208
Non-cash interest expense associated with the sale of future revenue	2,051	—
Non-cash royalty revenue	(1,650)	—
Changes in operating assets and liabilities:		
Accounts receivable, net	(3,071)	(2,071)
Collaboration receivable – related party	(998)	(62)
Collaboration receivable – other	101	(1,552)
Royalty receivable – related party	1,250	(466)
Inventory	(3,900)	(3,790)
Prepaid expenses and other current and non-current assets	(4,357)	(2,517)
Accounts payable	(7,524)	(1,874)
Accrued expenses	(8,595)	7,071
Deferred revenue – related party	(61,513)	(22,449)
Operating lease liabilities	(4,149)	(3,649)
Net cash used in operating activities	(173,155)	(191,422)
Investing activities		
Purchases of marketable securities	(189,601)	(144,231)
Proceeds from maturities and sales of marketable securities	328,883	343,372
Purchases of property and equipment	(8,688)	(3,309)
Net cash provided by investing activities	130,594	195,832
Financing activities		
Payments on financing lease obligations	(166)	—
Net proceeds from stock option exercises and employee stock purchase plan	7,117	8,668
Proceeds from the sale of future revenue, net of issuance costs	250,537	—
Net cash provided by financing activities	257,488	8,668
Net change in cash and cash equivalents	214,927	13,078
Cash and cash equivalents at beginning of the period	80,931	70,502
Cash and cash equivalents at end of the period	$ 295,858	$ 83,580
Supplemental disclosure of non-cash investing and financing transactions		
Additions to property and equipment in accounts payable and accrued expenses	$ 3,621	$ 535
Proceeds from stock option exercises in other current assets	$ —	$ 112
Operating lease liabilities arising from obtaining operating lease assets	$ —	$ 42,856

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 and adjacent areas of biology, with the goal of creating differentiated, small molecule medicines for patients in the areas of hematologic malignancies, solid tumors and rare genetic diseases, or RGDs. To address these focus areas, we take a systems biology approach to deeply understand disease states, drive the discovery and validation of novel therapeutic targets, and define patient selection strategies, thereby increasing the probability that our experimental medicines will have the desired therapeutic effect. We are located in Cambridge, Massachusetts.

Basis of presentation

The condensed consolidated balance sheet as of June 30, 2020, the condensed consolidated statements of operations, comprehensive loss and stockholders' equity for the three and six months ended June 30, 2020 and 2019, and the condensed consolidated statements of cash flows for the six months ended June 30, 2020 and 2019 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, 2020, our results of operations and stockholders' equity for the three and six months ended June 30, 2020 and 2019, and cash flows for the six months ended June 30, 2020 and 2019. 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 periods are also unaudited. The results of operations for the three and six months ended June 30, 2020 are not necessarily indicative of the results to be expected for the year ending December 31, 2020 or for any other future annual or interim period. The condensed consolidated balance sheet data as of December 31, 2019 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. 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, 2019 that was filed with the Securities and Exchange Commission, or the SEC, on February 19, 2020.

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

Use of estimates

The preparation of our condensed consolidated financial statements requires us to make estimates, judgments and assumptions that may affect the reported amounts of assets, liabilities, equity, revenues and expenses and related disclosure of contingent assets and liabilities. On an ongoing basis we evaluate our estimates, judgments and methodologies. We base our estimates on historical experience and on various other assumptions that we believe are reasonable, the results of which form the basis for making judgments about the carrying values of assets, liabilities and equity and the amount of revenues and expenses. The full extent to which the COVID-19 pandemic will directly or indirectly impact our business, results of operations and financial condition, including sales, expenses, reserves and allowances, clinical trials, research and development costs and employee-related amounts, will depend on future developments that are highly uncertain, including as a result of new information that may emerge concerning COVID-19 and the actions taken to contain it or treat COVID-19, as well as the economic impact on local, regional, national and international customers and markets. We have made estimates of the impact of COVID-19 within our financial statements and there may be changes to those estimates in future periods. Actual results may differ from these estimates.

Liquidity

On June 11, 2020, we sold our tiered, sales-based royalty rights on worldwide net sales of IDHIFA® (enasidenib), as well as our rights to receive up to $55.0 million in outstanding regulatory milestone payments from Bristol Myers Squibb, or BMS, to Royalty Pharma, or RPI, for $255.0 million. Under the 2010 Agreement, we remain eligible to receive a $25.0 million potential

milestone payment for the enasidenib program upon achievement of a specified ex-U.S. commercial milestone event, as well as reimbursement for costs incurred for our co-commercialization efforts and development activities.

As of June 30, 2020, we had cash, cash equivalents and marketable securities of $794.4 million, which included the $255.0 million proceeds from RPI received in the second quarter of 2020. 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

Significant accounting policies

In June 2016, the Financial Accounting Standards Board, or FASB issued Accounting Standards Update, or ASU 2016-13, *Financial Instruments - Credit Losses (Topic 326)*, which introduces new guidance for the accounting for credit losses on instruments within its scope. The new guidance introduces an approach based on expected losses to estimate credit losses on certain types of financial instruments. Credit losses relating to available-for-sale debt securities will also be recorded through an allowance for credit losses rather than as a reduction in the amortized cost basis of the securities. The guidance is effective for fiscal years beginning after December 31, 2019, including interim periods within those years.

In the quarter ended March 31, 2020, we adopted ASU 2016-13, which eliminated the concept of other-than-temporary impairments and required credit losses on debt securities to be recorded through an allowance for credit losses instead of as a reduction in the amortized cost basis of the securities. Application of the amendments is through a cumulative-effect adjustment to retained earnings as of the effective date. Based upon our analysis, the adoption of this final rule did not have a material impact on the financial statements.

Liability related to sale of future revenue

We treat the sale of future revenue to RPI as a debt financing, as we have significant continuing involvement in the generation of the cash flows. As result, we recorded the proceeds from this transaction as a liability related to the sale of future revenue to be amortized to interest expense using the effective interest rate method over the life of the arrangement.

The liability related to sale of future revenue and the related interest expense are based on our current estimates of future royalties expected to be paid over the life of the arrangement. We will periodically assess the expected royalty payments using a combination of internal projections and forecasts from external sources. To the extent our future estimates of royalty payments are greater or less than previous estimates or the estimated timing of such payments is materially different than its previous estimates, we will prospectively recognize related non-cash interest expense.

For further discussion of the sale of future revenue, refer to Note 10, *Sale of Future Revenue*.

Amortization of issuance costs

We treated the liability related to sale of future revenue as a debt financing. As such, the long-term liability is initially recorded at its proceeds, net of deferred costs. Issuance costs, fees directly related to the sale of future revenue, are offset against initial carrying value of the long-term liability and are amortized on a straight-line basis over the remaining patent life of the product to an operating expense.

There have been no other material changes to the significant accounting policies previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2019.

Recent accounting pronouncements

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. Accounting Standards Codification, or 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, 2020:

(In thousands)	Level 1	Level 2	Level 3	Total
Cash equivalents	$ 215,368	$ 13,593	$ —	$ 228,961
Total cash equivalents	215,368	13,593	—	228,961
Marketable securities:				
U.S. Treasuries	—	165,283	—	165,283
Government securities	—	83,653	—	83,653
Corporate debt securities	—	249,619	—	249,619
Total marketable securities	—	498,555	—	498,555
Total cash equivalents and marketable securities	$ 215,368	$ 512,148	$ —	$ 727,516

Cash equivalents and marketable securities have been initially valued at the transaction price and subsequently, at the end of each reporting period, valued 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, 2020.

There have been no changes to the valuation methods during the six months ended June 30, 2020. We evaluate transfers between levels at the end of each reporting period. We have no financial assets or liabilities that were classified as Level 3 at any point during the six months ended June 30, 2020.

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. Unrealized gains are included as a component of accumulated other comprehensive income in the condensed consolidated balance sheets and statements of stockholders' equity and a component of total comprehensive loss in the condensed consolidated statements of comprehensive loss, until realized. Unrealized losses are evaluated for impairment under ASC 326, *Financial Instruments - Credit Losses*, to determine if the impairment is credit-related or noncredit-related. Credit-related impairment is recognized as an allowance on the balance sheet with a corresponding adjustment to earnings, and noncredit-related impairment is recognized in other comprehensive income, net of taxes. Realized gains and losses are included in investment income on a specific-identification basis. There were no material realized gains or losses on marketable securities for the three and six months ended June 30, 2020 and 2019.

Marketable securities at June 30, 2020 consisted of the following:

(In thousands)	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
U.S. Treasuries	$ 164,611	$ 679	$ (7)	$ 165,283
Government securities	81,011	166	(23)	81,154
Corporate debt securities	247,003	861	(31)	247,833
Total Current	492,625	1,706	(61)	494,270
Non-current:				
U.S. Treasuries	—	—	—	—
Government securities	2,499	—	—	2,499
Corporate debt securities	1,786	—	—	1,786
Total Non-current	4,285	—	—	4,285
Total marketable securities	$ 496,910	$ 1,706	$ (61)	$ 498,555

Marketable securities at December 31, 2019 consisted of the following:

(In thousands)	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
U.S. Treasuries	$ 178,721	$ 58	$ (38)	$ 178,741
Government securities	80,228	17	(16)	80,229
Corporate debt securities	224,928	139	(91)	224,976
Total Current	483,877	214	(145)	483,946
Non-current:				
U.S. Treasuries	35,296	3	(13)	35,286
Government securities	17,587	14	(10)	17,591
Corporate debt securities	99,913	239	(100)	100,052
Total Non-current	152,796	256	(123)	152,929
Total marketable securities	$ 636,673	$ 470	$ (268)	$ 636,875

As of June 30, 2020 and December 31, 2019, 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 greater than one year, and (ii) we do not intend to liquidate within the next twelve months, although these funds are available for use and, therefore, are classified as available-for-sale.

As of June 30, 2020 and December 31, 2019, we held 28 and 113 debt securities, respectively, that were in an unrealized loss position for less than one year. We did not record an allowance for credit losses as of June 30, 2020 and December 31, 2019 related to these securities. The aggregate fair value of debt securities in an unrealized loss position at June 30, 2020 and December 31, 2019 was $129.7 million and $345.7 million, respectively. There were no individual securities that were in a significant unrealized loss position as of June 30, 2020 and December 31, 2019. Given our intent and ability to hold such securities until recovery, and the lack of significant change in the credit risk of these investments, we do not consider these marketable securities to be impaired as of June 30, 2020 and December 31, 2019.

5. Inventory

Inventory, which consists of commercial supply of TIBSOVO®, consists of the following:

(In thousands)	June 30, 2020	December 31, 2019
Raw materials	$ 1,329	$ 180
Work-in-process	8,679	6,808
Finished goods	1,223	343
Total inventory	$ 11,231	$ 7,331

6. Leases

Our building leases are comprised of office and laboratory space under non-cancelable operating leases. These lease agreements have remaining lease terms of eight years and contain various clauses for renewal at our option. The renewal options were not included in the calculation of the operating lease assets and the operating lease liabilities as the renewal option is not reasonably certain of being exercised. The lease agreements do not contain residual value guarantees. Operating lease costs for the three and six months ended June 30, 2020 were $3.8 million and $7.6 million, respectively, and cash paid for amounts included in the measurement of operating lease liabilities for the three and six months ended June 30, 2020 were $3.5 million and $7.4 million, respectively. Operating lease costs for the three and six months ended June 30, 2019 were $3.8 million and $6.8 million, respectively, and cash paid for amounts included in the measurement of operating lease liabilities for the three and six months ended June 30, 2019 were $3.2 million and $6.3 million, respectively.

We have not entered into any material short-term leases or financing leases as of June 30, 2020.

As of June 30, 2020, undiscounted minimum rental commitments under non-cancelable leases, for each of the next five years and total thereafter were as follows:

(In thousands)		
Remaining 2020	$	5,886
2021		14,380
2022		16,773
2023		18,126
2024		18,660
2025		19,507
Thereafter		44,385
Undiscounted minimum rental commitments	$	137,717
Interest		(29,171)
Operating lease liabilities	$	108,546

In arriving at the operating lease liabilities as of June 30, 2020 and December 31, 2019, we applied the weighted-average incremental borrowing rate of 5.7% for both periods over a weighted-average remaining lease term of 7.7 years and 8.2 years, respectively.

7. Accrued Expenses

Accrued expenses consist of the following:

(In thousands)		June 30, 2020		December 31, 2019
Accrued compensation	$	12,897	$	18,982
Accrued research and development costs		18,697		21,777
Accrued professional fees		4,393		8,335
Accrued other		5,924		4,048
Total accrued expenses	$	41,911	$	53,142

8. Product Revenue

We sell TIBSOVO®, our wholly owned product, to a limited number of specialty distributors and specialty pharmacy providers, or collectively, the Customers. The Customers subsequently resell TIBSOVO® to pharmacies or dispense directly to patients. In addition to distribution agreements with Customers, we enter into arrangements with healthcare providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of TIBSOVO®.

The performance obligation related to the sale of TIBSOVO® is satisfied and revenue is recognized when the Customer obtains control of the product, which occurs at a point in time, typically upon delivery to the Customer.

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2020	2019	2020	2019
Product revenue, net	$ 27,581	$ 13,727	$ 50,255	$ 22,865

Reserves for Variable Consideration

Revenues from product sales are recorded at the net sales price, or transaction price, which includes estimates of variable consideration for which reserves are established and result from contractual adjustments, government rebates, returns and other allowances that are offered within the contracts with our Customers, healthcare providers, payors and other indirect customers relating to the sale of our products.

Contractual Adjustments

We generally provide Customers with discounts, including prompt pay discounts, and allowances that are explicitly stated in the contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized. In addition, we receive sales order management, data and distribution services from certain Customers.

Chargebacks for fees and discounts represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to Customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are estimated using the expected value method, based upon a range of possible outcomes that are probability-weighted for the estimated channel mix and are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue.

Government Rebates

Government rebates consist of Medicare, TriCare, and Medicaid rebates, which we estimate using the expected value method, based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program.

Returns

We estimate the amount of product sales that may be returned by Customers and record this estimate as a reduction of revenue in the period the related product revenue is recognized. We currently estimate product return liabilities using the expected value method, based on available industry data, including our visibility into the inventory remaining in the distribution channel.

The following table summarizes balances and activity in each of the product revenue allowance and reserve categories for the six months ended June 30, 2020:

(In thousands)	Contractual Adjustments	Government Rebates	Returns	Total
Balance at December 31, 2019	$ 874	$ 1,124	$ 1,798	$ 3,796
Current provisions relating to sales in the current year	6,522	4,266	726	11,514
Adjustments relating to prior years	(3)	22	(476)	(457)
Payments/returns relating to sales in the current year	(5,522)	(1,422)	—	(6,944)
Payments/returns relating to sales in the prior years	(653)	(677)	—	(1,330)
Balance at June 30, 2020	$ 1,218	$ 3,313	$ 2,048	$ 6,579

Total revenue-related reserves above, included in our condensed consolidated balance sheets, are summarized as follows:

(In thousands)	June 30, 2020	December 31, 2019
Reduction of accounts receivable	$ 694	$ 540
Component of accrued expenses	5,885	3,256
Total revenue-related reserves	$ 6,579	$ 3,796

The following table presents changes in our contract assets during the six months ended June 30, 2020:

(In thousands)	December 31, 2019	Additions	Deductions	June 30, 2020
Contract assets [1]				
Accounts receivable, net	$ 8,952	$ 61,312	$ (58,241)	$ 12,023

(1) Additions to contract assets relate to amounts billed to Customers for product sales and deductions to contract assets primarily relate to collection of receivables during the reporting period.

9. Collaboration and License Agreements

Accounting analysis and revenue recognition

Our collaboration and license agreements typically involve us granting licenses of our intellectual property and performing research and development services in exchange of upfront fees, milestone payments and royalty payments. Since December 31,

2019, there have been no material changes to the key terms of our collaboration or license agreements. For further information on the terms and conditions of our existing collaboration and license agreements, please see the notes to the consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2019.

Collaboration revenue

We recognize revenue when the customer obtains control of promised goods or services, in an amount that reflects the consideration that we expect to receive in exchange for those goods or services. 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.

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).

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 considered constrained and are excluded from the transaction price until those approvals are received.

Celgene Corporation

We have entered into the following collaboration agreements, or collectively, the Collaboration Agreements, with Celgene, a wholly-owned subsidiary of BMS, which 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, which was amended in October 2011 and July 2014. The discovery phase of the 2010 Agreement expired in April 2016. On August 15, 2016, we terminated the 2010 Agreement as to the program directed to the isocitrate dehydrogenase 1, or IDH1, target, for which ivosidenib was the lead development candidate. Accordingly, the sole program remaining under the 2010 Agreement is IDHIFA® (enasidenib), a co-commercialized licensed program for which Celgene leads and funds global development and commercialization activities. On June 11, 2020, we sold our tiered, sales-based royalty rights on worldwide net sales of IDHIFA® (enasidenib), as well as our rights to receive up to $55.0 million in outstanding regulatory milestone payments from BMS, to RPI for $255.0 million. Under the 2010 Agreement, we remain eligible to receive a $25.0 million potential milestone payment for the enasidenib program upon achievement of a specified ex-U.S. commercial milestone event, as well as reimbursement for costs incurred for our co-commercialization efforts and development activities.
- 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 vorasidenib products. Under the AG-881 Agreements, we and Celgene split all worldwide development costs for vorasidenib, subject to specified exceptions. The AG-881 Agreements were terminated effective September 4, 2018, upon which we received sole global rights to vorasidenib. In connection with the termination of the AG-881 Agreements, Celgene will be eligible to receive royalties from us at a low single-digit percentage rate on worldwide net sales of products containing vorasidenib.
- In May 2016, we entered into a master research and collaboration agreement with Celgene, or 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. The initial four-year research term of the 2016 Agreement ended May 2020. On March 25, 2020 Celgene declined the option to extend the research agreement for up to two, or in specified cases, up to four additional one-year terms which would have required the payment of a $40.0 million extension fee. Further, on April 10, 2020 Celgene notified us that they will be declining to elect any program as a continuation program under the 2016 agreement. Celgene had designated AG-270, our inhibitor of methionine adenosyltransferase 2a, or MAT2A, as a development candidate under the 2016 Agreement. On March 25, 2020, Celgene notified us of their decision to decline their option to enter into a Development & Commercialization Agreement with respect to the MAT2A program under the 2016 Agreement which

would have required the payment of a $30.0 million fee. As a result of the decisions, the research services were fully satisfied as of May 17, 2020, no additional performance obligations remain under the 2016 Agreement and we are no longer eligible for any milestone payments for the 2016 agreement.

Collaboration revenue

During the three and six months ended June 30, 2020 and 2019, we recognized the following collaboration revenue:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2020	2019	2020	2019
Services performed that were considered performance obligations as of the modification dates				
On-going research and development services	$ 4,714	$ 8,155	$ 63,934	$ 25,220
Services performed that were not considered performance obligations as of the modification dates				
Commercialization activities	1,021	824	1,898	1,678
Total collaboration revenue - related party	$ 5,735	$ 8,979	$ 65,832	$ 26,898

The following table presents changes in our contract assets and liabilities during the six months ended June 30, 2020:

(In thousands)	December 31, 2019	Additions	Deductions	June 30, 2020
Contract assets				
Collaboration receivable – related party [1]	$ 1,539	$ 2,876	$ (3,284)	$ 1,131
Unbilled receivable - related party [2]	—	1,406	—	1,406
Royalty receivable – related party [3]	2,900	5,023	(6,273)	1,650
Contract liabilities				
Deferred revenue – related party, current and net of current portions [4]	61,513	2,421	(63,934)	—

(1) Additions to collaboration receivables - related party relate to amounts billed to Celgene for reimbursable costs incurred by us during the reporting period. Deductions to receivables relate to collection of receivables during the reporting period.
(2) Unbilled receivables - related party amounts relate to future reimbursable costs to Celgene.
(3) Additions to royalty receivables - related party relate to amounts billed to Celgene during the reporting period. Deductions to receivables relate to collection of receivables during the reporting period.
(4) Additions to deferred revenue - related party relate to consideration from Celgene during the reporting period. Deductions relate to deferred revenue recognized as revenue during the reporting period.

The change in collaboration revenue from on-going research and development services during the three and six months ended June 30, 2020 is primarily due to our updated estimate of the future costs that would be incurred from on-going research and development services to complete one of our performance obligations under the 2016 collaboration agreement that is recognized over time using an input method, due to Celgene's decision to decline extending the research term in Q1 2020.

During the three and six months ended June 30, 2020 and 2019, we recognized the following as revenue due to changes in the contract liability balances:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2020	2019	2020	2019
Amounts included in the contract liability at the beginning of the period	$ 4,748	$ 8,009	$ 61,513	$ 24,419
Performance obligations satisfied in previous periods	—	—	—	—

As of June 30, 2020, the aggregate amount of the transaction price allocated to performance obligations that are partially unsatisfied was $5.2 million. This amount is expected to be recognized as performance obligations are satisfied through September 2023.

Royalty revenue

As the underlying performance obligation, or delivery of the enasidenib license, 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, 2020 and 2019, we recognized the following as royalty revenue:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2020	2019	2020	2019
Royalty revenue – related party	$ 3,339	$ 2,703	$ 6,673	$ 4,903

On June 11, 2020, we sold our tiered, sales-based royalty rights on worldwide net sales of IDHIFA® (enasidenib), as well as our rights to receive up to $55.0 million in outstanding regulatory milestone payments from BMS, to RPI for $255.0 million. For further discussion of the sale of future revenue, refer to Note 10, *Sale of Future Revenue*.

Milestone revenue

No milestones were achieved during the three and six months ended June 30, 2020 or 2019. The next potential milestone expected to be achieved under the remaining terms of our Collaboration Agreements is the achievement of a specified ex-U.S. commercial milestone event, which would result in a milestone payment of $25.0 million under the 2010 Agreement.

CStone Pharmaceuticals

In June 2018, we and CStone Pharmaceuticals, or CStone, entered into an exclusive license agreement, or the CStone Agreement, to grant CStone specified intellectual property licenses to enable CStone to develop and commercialize certain products containing ivosidenib in mainland China, Hong Kong, Macau and Taiwan, or the CStone Territory. We retain development and commercialization rights for the rest of the world. On March 2, 2020, we amended the CStone Agreement to include Singapore as part of the CStone Territory. Pursuant to the CStone Agreement, CStone will initially be responsible for the development and commercialization of ivosidenib in acute myeloid leukemia, or AML, cholangiocarcinoma, and, at our discretion, brain cancer indications. CStone is responsible for all costs it incurs in developing, obtaining regulatory approval of, and commercializing ivosidenib in the CStone Territory, as well as certain costs incurred by us. Pursuant to 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 $407.0 million in milestone payments upon the achievement of certain development, regulatory and sales milestone events. We will also be entitled to receive tiered royalties, ranging from 15% to 19% percent, on annual net sales, if any, of ivosidenib in the CStone Territory.

Collaboration revenue

During the three and six months ended June 30, 2020 and 2019, we recognized the following collaboration revenue -other:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2020	2019	2020	2019
Services performed that were considered performance obligations as of the inception date				
License and other services	$ —	$ —	$ 192	$ —
Services performed that were not considered performance obligations as of the inception date				
Other services	692	812	1,493	1,782
Total collaboration revenue - other	$ 692	$ 812	$ 1,685	$ 1,782

The following table presents changes in our contract assets during the six months ended June 30, 2020:

(In thousands)	December 31, 2019	Additions	Deductions	June 30, 2020
Contract assets (1)				
Collaboration receivable - other	$ 1,928	$ 1,685	$ (1,786)	$ 1,827

(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, 2020, the aggregate amount of the transaction price allocated to performance obligations that are partially unsatisfied was $0.5 million.

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.

Milestone revenue

No milestones were earned during the three and six months ended June 30, 2020 and 2019. 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 solid tumor indication in mainland China. Achievement of this event will result in a milestone payment of $5.0 million.

10. Sale of Future Revenue

On June 11, 2020, we sold our tiered, sales-based royalty rights on worldwide net sales of IDHIFA® (enasidenib), as well as our rights to receive up to $55.0 million in outstanding regulatory milestone payments from BMS, to RPI for $255.0 million. The gross proceeds of $255.0 million approximate the fair value of the liability related to the sale of future revenue based on a discounted cash flow model. The fair value for the liability related to the sale of future revenue at the time of the transaction was based on our current estimates of future royalties expected to be paid to RPI over the remaining patent life of the product, which are considered level 3 inputs.

Under the terms of the Purchase Agreement, although we sold all of our rights to receive royalties on worldwide net sales of IDHIFA® and future regulatory milestone payments, we continue to co-promote IDHIFA® and are therefore involved in the generation of these royalties. Due to our continuing involvement, we will continue to account for any royalties earned as revenue. We recorded the net proceeds from this transaction as a liability related to sale of future revenue, or Royalty Obligation, that will be amortized using the effective interest method over the remaining patent life.

As royalties are remitted to RPI from BMS, the balance of the Royalty Obligation will be effectively repaid over the life of the BMS License Agreement. In order to determine the amortization of the Royalty Obligation, we are required to estimate the total amount of future royalty payments to RPI over the life of the BMS License Agreement. The $255.0 million recorded will be accreted to the total of these royalty payments as interest expense over the life of the Royalty Obligation. At execution, our estimate of this total interest expense resulted in an effective annual interest rate of approximately 16.4%. This estimate contains significant assumptions that impact both the amount recorded at execution and the interest expense that will be recognized over the royalty period. We will periodically assess the estimated royalty payments to RPI from BMS and to the extent the amount or timing of such payments is materially different than the original estimates, an adjustment will be recorded prospectively to increase or decrease interest expense. There are a number of factors that could materially affect the amount and timing of royalty payments to RPI from BMS, and correspondingly, the amount of interest expense recorded by us, most of which are not within our control. Such factors include, but are not limited to, delays or discontinuation of development of enasidenib, regulatory approval, changing standards of care, the introduction of competing products, manufacturing or other delays, generic competition, intellectual property matters, adverse events that result in governmental health authority imposed restrictions on the use of the drug products, significant changes in foreign exchange rates as the royalties remitted to RPI are made in U.S. dollars (USD) while the underlying sales of enasidenib will be made in currencies other than USD, and other events or circumstances that are not currently foreseen. Changes to any of these factors could result in increases or decreases to both royalty revenues and interest expense.

The following table shows the activity of the Royalty Obligation since the transaction inception through June 30, 2020:

(in thousands)		**June 30, 2020**
Proceeds from the sale of future revenue	$	255,000
Issuance costs		(4,463)
Non-cash royalty revenue		(1,650)
Non-cash interest expense associated with the sale of future revenue		2,051
Amortization of issuance costs		20
Liability related to the sale of future royalties	$	250,958

During the three and six months ended June 30, 2020, $3.3 million and $6.7 million of royalty revenue from net sales of IDHIFA® were recognized, respectively, of which $1.65 million is non-cash royalty revenue.

11. 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 to employees, non-employees and non-employee directors. 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 remain outstanding and effective. As of June 30, 2020, the total number of shares reserved under the 2007 Plan and the 2013 Plan was 10,749,789, and we had 2,688,890 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, 2020:

	Number of Stock Options		Weighted-Average Exercise Price
Outstanding at December 31, 2019	6,201,485	$	58.61
Granted	922,820		50.09
Exercised	(284,814)		18.65
Forfeited/Expired	(241,540)		70.26
Outstanding at June 30, 2020	6,597,951	$	58.72
Exercisable at June 30, 2020	3,927,185	$	61.05
Vested and expected to vest at June 30, 2020	6,597,951	$	58.72

At June 30, 2020, there was approximately $94.2 million of total unrecognized compensation expense related to unvested stock option awards, which we expect to recognize over a weighted-average period of approximately 2.5 years.

Restricted stock units

The following table presents RSU activity for the six months ended June 30, 2020:

	Number of Stock Units		Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2019	766,953	$	63.44
Granted	790,376		50.79
Vested	(243,231)		69.93
Forfeited	(53,690)		61.18
Unvested shares at June 30, 2020	1,260,408	$	54.35

As of June 30, 2020, there was approximately $51.1 million of total unrecognized compensation expense related to RSUs, which we expect to recognize over a weighted-average period of approximately 2.1 years.

Performance-based stock units

The following table presents PSU activity for the six months ended June 30, 2020:

	Number of Stock Units		Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2019	218,143	$	55.64
Granted	20,622		48.49
Vested	(78,920)		54.82
Unvested shares at June 30, 2020	159,845	$	55.13

Stock-based compensation expense associated with these PSUs is recognized if the underlying performance condition is considered probable of achievement using our management’s best estimates.

As of June 30, 2020, there was no unrecognized compensation expense related to PSUs with performance-based vesting criteria that are considered probable of achievement, and $6.9 million of total unrecognized compensation expense related to PSUs with performance-based vesting criteria that are considered not probable of achievement.

Market-based stock units

The following table presents market-based stock unit, or MSU, activity for the six months ended June 30, 2020:

	Number of Stock Units	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2019	42,695	$ 41.50
Granted	—	—
Unvested shares at June 30, 2020	42,695	$ 41.50

The fair value of MSUs are estimated using a Monte Carlo simulation model. Assumptions and estimates utilized in the model include the risk-free interest rate, dividend yield, expected stock volatility and the estimated period to achievement of the market condition. As of June 30, 2020, there was approximately $0.2 million of total unrecognized compensation expense related to MSUs, which we expect to recognize over the remaining derived service period of 0.2 years.

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 and sold 62,694 and 32,410 shares of common stock during the six months ended June 30, 2020 and 2019, respectively, under the 2013 ESPP. The 2013 ESPP provides participating employees with the opportunity to purchase up to an aggregate of 836,363 shares of our common stock. As of June 30, 2020, we had 528,952 shares of common stock 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:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2020	2019	2020	2019
Stock options	$ 11,503	$ 12,467	$ 23,106	$ 25,513
Restricted stock units	7,780	5,243	13,912	9,791
Performance-based stock units	478	—	1,866	186
Employee stock purchase plan	399	392	696	720
Other stock awards	270	445	540	445
Total stock-based compensation expense	$ 20,430	$ 18,547	$ 40,120	$ 36,655

Expenses related to stock options and stock-based awards were allocated as follows in the condensed consolidated statements of operations:

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2020	2019	2020	2019
Research and development expense	$ 10,158	$ 10,067	$ 19,722	$ 20,109
Selling, general and administrative expense	10,272	8,480	20,398	16,546
Total stock-based compensation expense	$ 20,430	$ 18,547	$ 40,120	$ 36,655

12. 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, PSUs and MSUs for which the performance and market vesting conditions, respectively, have been deemed probable, and 2013 ESPP shares are considered to

be common stock equivalents, while PSUs and MSUs with performance and market vesting conditions, respectively, that were not deemed probable as of June 30, 2020 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,	
	2020	2019
Stock options	6,597,951	6,343,294
Restricted stock units	1,260,408	737,510
Performance-based stock units	—	—
Employee stock purchase plan shares	39,997	33,064
Total common stock equivalents	7,898,356	7,113,868

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, 2020 and for the three and six months ended June 30, 2020 and 2019, 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, 2019 filed with the SEC on February 19, 2020. 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, selling, general and administrative expenses, research and development expenses, the sufficiency of our cash for future operations and business activity disruption due to the COVID-19 pandemic. Words such as "anticipate," "believe," "estimate," "expect," "goal," "intend," "may," "plan," "predict," "project," "strategy," "target," "potential," "will," "would," "could," "should," "continue," "vision" 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 for the year ended December 31, 2019. 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 and adjacent areas of biology, with the goal of creating differentiated, small molecule medicines for patients in the areas of hematologic malignancies, solid tumors and rare genetic diseases, or RGDs. To address these focus areas, we take a systems biology approach to deeply understand disease states, drive the discovery and validation of novel therapeutic targets, and define patient selection strategies, thereby increasing the probability that our experimental medicines will have the desired therapeutic effect.

Hematologic malignancies and solid tumors

We are developing ivosidenib for the treatment of IDH1 mutant-positive cancers. Ivosidenib is an orally available, selective, potent inhibitor of the mutated IDH1 protein, making it a highly targeted therapy for the treatment of patients with cancers that harbor IDH1 mutations, including those with acute myeloid leukemia, or AML, myelodysplastic syndromes, or MDS, and cholangiocarcinoma. We hold worldwide development and commercial rights to ivosidenib and have licensed certain development and commercialization rights to ivosidenib to CStone in mainland China, Hong Kong, Macau, Taiwan, and Singapore. We will fund the future development and commercialization costs related to this program with the exception of development and commercialization activities of CStone under the CStone Agreement. The FDA has approved TIBSOVO® (ivosidenib) for the treatment of adult patients with R/R AML and a susceptible IDH1 mutation and for the treatment of patients with newly diagnosed AML with a susceptible IDH1 mutation as detected by an FDA-approved test who are at least 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy. In December 2018, we submitted a marketing authorization application, or MAA to the European Medicines Agency, or EMA for TIBSOVO® for the treatment of adult patients with R/R AML. The FDA granted orphan drug designation for ivosidenib for the treatment of cholangiocarcinoma, granted Breakthrough Therapy designation for ivosidenib in combination with azacitidine for the treatment of newly diagnosed AML with an IDH1 mutation in adult patients who are at least 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy, and granted Breakthrough Therapy designation for ivosidenib for the treatment of adult patients with relapsed or refractory MDS with a susceptible IDH1 mutation as detected by an FDA-approved test.

Celgene, in collaboration with us, is developing enasidenib for the treatment of IDH2 mutant-positive hematologic malignancies. Enasidenib 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. The FDA has granted Celgene approval of IDHIFA® (enasidenib) for the treatment of adult patients with R/R AML and an IDH2 mutation. Celgene has worldwide development and commercialization rights for IDHIFA®, and 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. On June 11, 2020 we sold our tiered, sales-based royalty rights on worldwide net sales of IDHIFA®, as well as our rights to receive up to $55.0 million in outstanding regulatory milestone payments from Bristol Myers Squibb, or BMS, to Royalty Pharma, or RPI, for $255.0 million.

Our pre-commercial clinical cancer product candidates are vorasidenib, AG-270, AG-946, and AG-636.

We are developing vorasidenib for the treatment of IDH mutant-positive low grade glioma. Vorasidenib is an orally available, selective, brain-penetrant, pan-IDH mutant inhibitor.

We are developing AG-270 for the treatment of cancers carrying a methylthioadenosine phosphorylase, or MTAP, deletion, which is present in approximately 15 percent of all cancers. AG-270 is an orally available selective potent inhibitor of MAT2A. On March 25, 2020, Celgene declined to exercise its right to opt into co-development and co-commercialization for the for AG-270, our MAT2A inhibitor development program, under the 2016 Agreement.

We are developing AG-946, a next-generation PKR activator, for the potential treatment of hemolytic anemias.

In the first quarter of 2020, we made the decision to cease the internal development of AG-636 for the treatment of hematologic malignancies, including lymphoma due to limited enrollment in our phase 1 study in lymphoma. AG-636 is an inhibitor of the metabolic enzyme dihydroorotate dehydrogenase, or DHODH, licensed by us from Aurigene Discovery Technologies Limited, or Aurigene.

RGDs

The lead product candidate in our RGD portfolio, mitapivat, targets pyruvate kinase-R, or PKR, for the treatment of pyruvate kinase, or PK, deficiency and other hemolytic anemias. 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. Mitapivat is an orally available small molecule and a potent activator of the wild-type (normal) and mutated PKR enzymes, which has resulted in restoration of adenosine triphosphate levels and a decrease in 2,3-diphosphoglycerate levels in blood sampled from patients with PK deficiency and treated ex-vivo with mitapivat. We are also developing mitapivat for the treatment of patients with thalassemia and sickle cell disease. We have worldwide development and commercial rights to mitapivat and expect to fund the future development and commercialization costs related to this program. The FDA and EMA granted orphan drug designations for mitapivat for the treatment of patients with PK deficiency, and the FDA granted orphan drug designation for mitapivat for the treatment of patients with thalassemia. We are also developing AG-946, our next -generation PKR activator, and plan to initiate a phase 1 study in healthy volunteers in the third quarter of 2020.

In addition to the aforementioned development programs, we are seeking to advance a number of early-stage discovery programs in the areas of hematological malignancies and solid tumors, RGDs.

Collaboration and license agreements

Refer to Note 9, *Collaboration and License Agreements*, of the notes to our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q for a description of the key terms of our arrangements with Celgene and CStone.

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 condensed consolidated financial statements. We have determined that our most critical accounting policies are those relating to revenue recognition, accrued research and development expenses, stock-based compensation, and the liability related to the sale of future revenue. Except those that have been disclosed in Note 2, *Summary of Significant Accounting Policies*, of the notes to our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q, there have been no significant changes to our existing critical accounting policies discussed in our Annual Report on Form 10-K for the year ended December 31, 2019.

Financial Operations Overview

Impact of COVID-19 on our Business

The spread of SARS-CoV-2 and the resulting disease COVID-19 during the first half of 2020 has caused an economic downturn on a global scale, as well as significant volatility in the financial markets. In March 2020 the World Health Organization declared COVID-19 a pandemic. As of June 30, 2020, we have not experienced a significant financial or supply chain impact directly related to the pandemic but have experienced some disruptions to clinical operations, including timelines to complete patient enrollment in some of our clinical trials, as further described below. In this time of uncertainty as a result of

the COVID-19 pandemic, we are continuing to serve our customers while taking precautions to provide a safe work environment for our employees and customers. In March 2020, we established and implemented a work from home policy for our employees. In April 2020, we made internal resource allocation decisions in order to deliver on key business objectives and to increase our financial flexibility, including, pausing the development of certain preclinical research programs, delaying the start of certain longer-term clinical studies, limiting staff hiring, reducing the number of contract workers, and delaying or limiting information technology and facilities infrastructure projects. Lastly, in June 2020, we began implementing Phase 1 of our return to work program, which enables all of our lab-based employees and related support personnel to return to our Cambridge office under strict guidelines as required by federal, state, and local authorities. We have been monitoring our supply chain network for disruptions due to the COVID-19 pandemic, and our third party manufacturers remain largely unaffected, with any campaign delays experienced to date being limited to a few days in duration. Although global shipping continues to be disrupted due to the pandemic, we have not experienced a supply impact and have accrued additional safety stock of TIBSOVO® in order to further mitigate risk.

As the pandemic continues to unfold, the extent of the pandemic's effect on our operational and financial performance will depend in large part on future developments, which cannot be predicted with confidence at this time. Future developments include changes in the duration, scope and severity of the pandemic, the actions taken to contain or mitigate its impact, the impact on governmental programs and budgets, the development of treatments or vaccines, and the resumption of widespread economic activity. Any prolonged material disruption of the Company's employees, suppliers, manufacturing, or customers could negatively impact its consolidated financial position, consolidated results of operations and consolidated cash flows. As a result, we may have to take further actions that we determine are in the best interests of our employees or as required by federal, state, or local authorities.

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, conducting clinical trials and marketing our approved products. To date, we have financed our operations primarily through funding received from our various collaboration agreements discussed above, 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 $130.7 million and $202.9 million for the six months ended June 30, 2020 and 2019, respectively. As of June 30, 2020, we had an accumulated deficit of $1.6 billion. We expect to continue to incur significant expenses and net losses until such time we are able to report profitable results. Our net losses may fluctuate significantly from year to year. We expect that we will continue to incur significant expenses as we continue to advance and expand clinical development activities for our lead programs: ivosidenib, vorasidenib, mitapivat, and AG-270; 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

Our wholly owned product, TIBSOVO®, received approval from the FDA on July 20, 2018 for the treatment of adult patients with R/R AML with susceptible IDH1 mutation. Upon FDA approval of TIBSOVO® in the U.S., we began generating product revenue from sales of TIBSOVO®. We sell TIBSOVO® to a limited number of specialty distributors and specialty pharmacy providers in the U.S., or collectively, the Customers. These Customers subsequently resell TIBSOVO® to pharmacies or dispense directly to patients. In addition to distribution agreements with Customers, we enter into arrangements with healthcare providers and payors that provide for government-mandated and/or privately-negotiated rebates, chargebacks and discounts with respect to the purchase of TIBSOVO®.

We also recognize collaboration revenue from our agreements with Celgene and CStone, and royalty revenue from Celgene on sales of IDHIFA®. On June 11, 2020, we sold our tiered, sales-based royalty rights on worldwide net sales of IDHIFA® (enasidenib), as well as our rights to receive up to $55.0 million in outstanding regulatory milestone payments from Celgene, a wholly-owned subsidiary of BMS, to RPI for $255.0 million. Due to our continued involvement in the generation of these royalties through our co-promote right, we are treating the sale of these royalties as a liability and will continue to recognize royalty revenue on sales of IDHIFA®.

In the future, we expect to continue 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.

Cost of sales

Cost of sales consists primarily of manufacturing costs for sales of TIBSOVO®. Based on our policy to expense costs associated with the manufacturing of our products prior to regulatory approval, certain of the manufacturing costs associated with product shipments of TIBSOVO® recorded during the three and six months ended June 30, 2020 and three and six months ended June 30, 2019, respectively, were expensed prior to July 20, 2018 and, therefore, are not included in costs of sales during the three and six months ended June 30, 2020 and three and six months ended June 30, 2019, respectively.

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 to commercialize these product candidates. We are also unable to positively predict when future net cash inflows will commence from TIBSOVO® (ivosidenib), vorasidenib, mitapivat, AG-270 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 an investigational new drug application, or IND, and/or new drug application, or NDA, enabling toxicology and clinical trials;
- 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 the clinical development activities related to our most advanced programs:

Ivosidenib (mutant IDH1 inhibitor)

- A phase 1b, multicenter, international, open-label clinical trial, to evaluate safety and clinical activity of ivosidenib or enasidenib in combination with induction and consolidation therapy in patients with newly diagnosed AML with an IDH1 or IDH2 mutation who are eligible for intensive chemotherapy. This trial has completed enrollment.
- A phase 1/2 frontline combination clinical trial, conducted by Celgene, of either ivosidenib or enasidenib in combination with VIDAZA® (azacitidine) in newly diagnosed AML patients not eligible for intensive chemotherapy. The trial has completed enrollment.
- AGILE, a global, registration-enabling phase 3 clinical trial, combining ivosidenib and VIDAZA® (azacitidine) in newly diagnosed AML patients with an IDH1 mutation who are ineligible for intensive chemotherapy. The trial is enrolling patients and, due to ongoing disruptions related to the COVID-19 pandemic, we expect to complete enrollment in 2021.
- HOVON150/AMLSG29, an intergroup sponsored, global, registration-enabling phase 3 trial, supported in collaboration with Celgene, combining ivosidenib or enasidenib with standard induction and consolidation chemotherapy in frontline AML patients with an IDH1 or IDH2 mutation. The trial is currently enrolling patients, although disruptions related to the COVID-19 pandemic slowed enrollment compared to our expectations in the first half of 2020.

- 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 hematologic malignancies with an IDH1 mutation. The trial recently reopened enrollment of its relapsed or refractory MDS arm, and due to ongoing disruptions related to the COVID-19 pandemic, we expect to complete enrollment in 2021.
- 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. The trial has completed enrollment.
- ClarIDHy, a registration-enabling phase 3, multicenter, randomized, double-blind, placebo-controlled clinical trial of ivosidenib in previously-treated patients with nonresectable or metastatic cholangiocarcinoma with an IDH1 mutation. The trial has completed enrollment. The primary endpoint of the trial was met and, due to ongoing disruptions related to the COVID-19 pandemic, we expect to file an sNDA with the FDA for TIBSOVO® in cholangiocarcinoma in the first quarter of 2021.
- A phase 1 multi-center, open-label clinical trial of ivosidenib in patients with advanced IDH1 mutant-positive solid tumors, including glioma. The trial has completed enrollment.
- A perioperative study with ivosidenib and vorasidenib in low grade glioma to further investigate their effects on brain tumor tissue. The trial has completed enrollment.

Vorasidenib

- A phase 1 multi-center, open-label clinical trial of vorasidenib in patients with advanced IDH1 or IDH2 mutant-positive solid tumors, including glioma. The trial has completed enrollment.
- The above mentioned perioperative study with ivosidenib and vorasidenib in low grade glioma to further investigate their effects on brain tumor tissue. The trial has completed enrollment.
- INDIGO, a registration-enabling phase 3 clinical trial of vorasidenib in low-grade (grade 2) glioma with an IDH1 or IDH 2 mutation. The trial is enrolling patients although disruptions related to the COVID-19 pandemic slowed enrollment in the first half of 2020.

Mitapivat: PK Activator

- DRIVE PK, a global phase 2, first-in-patient, open-label safety and efficacy clinical trial of mitapivat in adult, transfusion-independent patients with PK deficiency. This trial has completed enrollment.
- ACTIVATE-T, a single arm, global, pivotal trial of mitapivat in regularly-transfused patients with PK deficiency. The trial has completed enrollment. Due to ongoing challenges in accessing clinical sites following completion of dosing as a result of the COVID-19 pandemic, we expect to report topline data from the trial between the end of 2020 and mid-2021.
- ACTIVATE, a 1:1 randomized, placebo-controlled, global, pivotal trial of mitapivat in patients with PK deficiency who do not receive regular transfusions. The trial has completed enrollment. Due to ongoing challenges in accessing clinical sites following completion of dosing as a result of the COVID-19 pandemic, we expect to report topline data from the trial between the end of 2020 and mid-2021.
- A phase 2, open-label safety and efficacy clinical trial of mitapivat in adult patients with non-transfusion-dependent thalassemia. The trial has completed enrollment.
- In collaboration with the National Institutes of Health, or NIH, we are evaluating mitapivat in a phase 1 trial in patients with sickle cell disease pursuant to a cooperative research and development agreement. New enrollment has been paused during the COVID-19 pandemic.

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

- A phase 1 trial in multiple tumor types carrying an MTAP deletion. The first part of the trial, which is complete, is a single agent dose-escalation phase in which cohorts of patients received ascending doses of AG-270 to determine the pharmacokinetics, pharmacodynamics and optimal dose, and schedule. The next phase of development, which was initiated in September 2019, is evaluating AG-270 in combination with taxanes in two areas of high unmet needs. One arm of the study will test AG-270 in combination with docetaxel in MTAP-deleted non-small cell lung cancer and the other arm will test AG-270 in combination with nab-paclitaxel and gemcitabine in MTAP-deleted pancreatic ductal adenocarcinoma. Both combination arms have initiated and are enrolling patients.

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

- A phase 1 dose-escalation trial of AG-636 in subjects with advanced lymphoma. In the first quarter of 2020, we made the decision to halt internal development of AG-636, due to limited enrollment in this study, and will wind down the study during 2020.

AG-946: Next-generation PKR Activator

- We plan to initiate a phase 1 study of AG-946 in healthy volunteers in the third quarter of 2020.

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.

Selling, general and administrative expenses

Selling, 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 selling, general and administrative expenses will increase in the future to support continued research and development, and commercialization activities, including the potential commercialization of our 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

Certain prior-year amounts have been reclassified to conform with current presentation.

Comparison of the three and six months ended June 30, 2020 and 2019

Total Revenue

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2020	2019	2020	2019
Revenues:				
Product revenue, net	$ 27,581	$ 13,727	$ 50,255	$ 22,865
Collaboration revenue – related party	5,735	8,979	65,832	26,898
Collaboration revenue – other	692	812	1,685	1,782
Royalty revenue – related party	3,339	2,703	6,673	4,903
Total revenue	$ 37,347	$ 26,221	$ 124,445	$ 56,448

Total Revenue - Second Quarter of 2020 vs. Second Quarter of 2019 - The increase in total revenue of $11.1 million for the three months ended June 30, 2020 compared to the three months ended June 30, 2019 was primarily due to an increase in product revenue of $13.9 million driven by increased sales volume of TIBSOVO®.

Total Revenue - Six Months ended June 30, 2020 vs. Six Months ended June 30, 2019 - The increase in total revenue of $68.0 million for the six months ended June 30, 2020 compared to the six months ended June 30, 2019 was primarily due to an increase in collaboration revenue - related party of $38.9 million and an increase in product revenue of $27.4 million. The increase in collaboration revenue - related party for the six months ended June 30, 2020 is primarily due to our updated estimate of the future costs that would be incurred from on-going research and development services to complete one of our performance obligations under the 2016 collaboration agreement that is recognized over time using an input method, due to Celgene's decision to decline extending the research term in Q1 2020. The increase in product revenue is primarily the result of increased sales volume of TIBSOVO®.

Total Operating Expenses

(In thousands)	Three Months Ended June 30, 2020	Three Months Ended June 30, 2019	Six Months Ended June 30, 2020	Six Months Ended June 30, 2019
Cost and expenses:				
Cost of sales	$ 675	$ 303	$ 1,208	$ 637
Research and development	90,917	107,389	182,173	202,974
Selling, general and administrative	35,951	32,390	74,452	64,181
Total Operating Expenses	$ 127,543	$ 140,082	$ 257,833	$ 267,792

Total Operating Expenses - Second Quarter of 2020 vs. Second Quarter of 2019 - The decrease in total operating expenses of $12.5 million for the three months ended June 30, 2020 compared to the three months ended June 30, 2019 was primarily due a decrease in research and development expenses of $16.5 million which is described below under Research and Development Expenses. We expect cost of sales to increase moderately in 2020 as we have depleted our finished goods inventory that was expensed prior to receiving FDA approval of TIBSOVO®.

Total Operating Expenses - Six Months ended June 30, 2020 vs. Six Months ended June 30, 2019 - The decrease in total operating expenses of $10.0 million for the six months ended June 30, 2020 compared to the six months ended June 30, 2019 was primarily due to a decrease in research and development expenses of $20.8 million which is described below under Research and Development Expenses partially offset by an increase in selling, general and administrative expense of $10.3 million due to higher personnel costs, including stock-based compensation expense, related to additional hiring for our workforce. We expect cost of sales to increase moderately in 2020 as we have depleted our finished goods inventory that was expensed prior to receiving FDA approval of TIBSOVO®.

Research and Development Expenses

Our research and development expenses, by major program, are outlined in the table below:

(In thousands)	Three Months Ended June 30, 2020	Three Months Ended June 30, 2019	Six Months Ended June 30, 2020	Six Months Ended June 30, 2019
Enasidenib (IDH2 inhibitor)	$ 267	$ 864	$ 625	$ 2,291
Ivosidenib (IDH1 inhibitor)	14,317	20,669	26,842	40,475
Vorasidenib (AG-881) (Pan IDH inhibitor)	4,390	5,741	7,961	8,058
Mitapivat (PKR activator)	11,056	11,718	20,776	21,180
AG-270 (MAT2A inhibitor)	1,243	3,387	3,509	5,853
AG-636 (DHODH inhibitor) discontinued	912	3,782	1,968	5,339
AG-946 (Next-Gen PKR activator)	2,432	1,610	4,838	2,230
Other research and platform programs	7,010	12,007	14,609	20,062
Total direct research and development expenses	41,627	59,778	81,128	105,488
Compensation and related expenses	37,509	35,585	76,148	72,609
Facilities and IT related expenses & other	11,781	12,026	24,897	24,877
Total indirect research and development expenses	49,290	47,611	101,045	97,486
Total research and development expense	$ 90,917	$ 107,389	$ 182,173	$ 202,974

Total Research and development Expenses - Second Quarter of 2020 vs. Second Quarter of 2019 - The decrease in total research and development expenses of $16.5 million for the three months ended June 30, 2020 compared to the three months ended June 30, 2019 was primarily due to a $6.4 million decrease in ivosidenib costs and and a $5.0 million decrease in other research and platform programs, partially offset by a $1.9 million increase in our compensation and related expenses. The decrease in ivosidenib costs was primarily due to decreased trial activities as a result of slowed enrollment due to the COVID-19 pandemic and decreased clinical costs driven by $1.0 million in milestones achieved by HOVON during the three months ended June 30, 2019 for the initiation of the HO150/AMLSG29 trial. The decrease in other research and platform programs was primarily driven by planned decreased activity on various exploratory and discovery activities and a $4.0 million upfront payment for exploratory efforts in the second quarter of 2019. The increase in compensation and related expenses was primarily due to additional hiring during the three months ended June 30, 2020 to support increased clinical program activity, partially offset by reduced employee travel related expenses due to restrictions and reduced industry engagement during the COVID-19 pandemic.

Total Research and development Expenses - Six Months ended June 30, 2020 vs. Six Months ended June 30, 2019 - The decrease in total research and development expenses of $20.8 million for the six months ended June 30, 2020 compared to the six months ended June 30, 2019 was primarily due to a $13.6 million decrease in ivosidenib costs and a $5.5 million decrease in other research and platform programs, partially offset by a $3.5 million increase in our compensation and related expenses. The decrease in ivosidenib costs was primarily due to decreased trial activities as a result of slowed enrollment due to the COVID-19 pandemic and decreased clinical costs driven by $4.2 million in milestones achieved by HOVON during the six months ended June 30, 2019 for the initiation of the HO150/AMLSG29 trial. The decrease in other research and platform programs was primarily driven by planned decreased activity on various exploratory and discovery activities and a $4.0 million upfront payment for exploratory efforts in the second quarter of 2019. The increase in compensation and related expenses was primarily due to additional hiring during the six months ended June 30, 2020 to support increased clinical program activity, partially offset by reduced employee travel related expenses due to restrictions and reduced industry engagement during the COVID-19 pandemic.

Interest Income and Expense

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2020	2019	2020	2019
Interest income, net	$ 1,769	$ 3,990	$ 4,705	$ 8,395
Non-cash interest expense for the sale of future revenue	(2,051)	—	(2,051)	—

Interest Income and Non-cash interest expense for the sale of future revenue- Second Quarter of 2020 vs. Second Quarter of 2019 - The change in interest income, net is primarily attributable to the decrease in our outstanding marketable securities and changes in interest rates earned on our marketable securities recorded in the three months ended June 30, 2020. The change in non-cash interest expense for the sale of future revenue is due to the interest expense associated with the sale of future revenue recorded in the three months ended June 30, 2020.

Interest Income and Non-cash interest expense for the sale of future revenue- Six Months ended June 30, 2020 vs. Six Months ended June 30, 2019 - The change in interest income, net is primarily attributable to the decrease in our outstanding marketable securities and changes in interest rates earned on our marketable securities in the six months ended June 30, 2020. The change in non-cash interest expense for the sale of future revenue is due to the interest expense associated with the sale of future revenue recorded in the six months ended June 30, 2020.

Loss from Operations and Net Loss

	Three Months Ended June 30,		Six Months Ended June 30,	
(In thousands)	2020	2019	2020	2019
Loss from operations	$ (90,196)	$ (113,861)	$ (133,388)	$ (211,344)
Net loss	(90,478)	(109,871)	(130,734)	(202,949)

Loss from Operations and Net Loss – Second Quarter of 2020 vs. Second Quarter of 2019 – The decrease in loss from operations and net loss for the three months ended June 30, 2020 compared to the three months ended June 30, 2019 was primarily driven by higher total revenue as described above in Total Revenue and by lower total expenses as described above in Total Operating Expenses.

Loss from Operations and Net Loss – Six Months ended June 30, 2020 vs. Six Months ended June 30, 2019 – The decrease in loss from operations and net loss for the six months ended June 30, 2020 compared to the six months ended June 30, 2019 was primarily driven by higher total revenue as described above in Total Revenue and by lower total expenses as described above in Total Operating Expenses.

Liquidity and Capital Resources

Sources of liquidity

Since our inception, and through June 30, 2020, we have funded our operations through commercial sales of TIBSOVO®, upfront, milestone, extension, cost reimbursement and royalty payments related to our collaboration agreements, product sales, 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.

On April 30, 2020, we entered into an at-the-market sales agreement, or the 2020 sales agreement, with Cowen & Company LLC, or Cowen, pursuant to which we may offer and sell shares of our common stock having an aggregate offering price of up to $250.0 million through Cowen pursuant to a universal shelf registration statement on Form S-3 filed with the SEC on April

30, 2020. As of June 30, 2020, $250.0 million in common stock remained available for future issuance under the 2020 sales agreement.

On June 11, 2020, we sold our tiered, sales-based royalty rights on worldwide net sales of IDHIFA® (enasidenib), as well as our rights to receive up to $55.0 million in outstanding regulatory milestone payments from BMS, to RPI for $255.0 million. Under the 2010 Agreement, we remain eligible to receive a $25.0 million potential milestone payment for the enasidenib program. The potential milestone payment is a $25.0 million milestone payment upon achievement of a specified ex-U.S. commercial milestone event, as well as reimbursement for costs incurred for our co-commercialization efforts and development activities.

In addition to our existing cash, cash equivalents and marketable securities, which included the $255.0 million proceeds from RPI received in the second quarter of 2020, we are eligible to earn milestone payments, cost reimbursements, and royalty payments under our collaboration agreements with Celgene and CStone. 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, 2020 and 2019:

	Six Months Ended June 30,	
(In thousands)	**2020**	**2019**
Net cash used in operating activities	$ (173,155)	$ (191,422)
Net cash provided by investing activities	130,594	195,832
Net cash provided by financing activities	257,488	8,668
Net change in cash and cash equivalents	$ 214,927	$ 13,078

Net cash used in operating activities. During the six months ended June 30, 2020, we received $52.3 million from sales of TIBSOVO®, $6.3 million in royalty payments and $3.3 million in cost reimbursements and related to our Collaboration Agreements with Celgene, $4.8 million in interest received, and $1.8 million in cost reimbursement related to our Collaboration agreement with CStone. These amounts were offset by decreased operating expenses driven by lower research and development costs described above in Research and Development Expenses partially offset by increased staffing needs due to our expanding operations.

During the six months ended June 30, 2019, we received $22.7 million from sales of TIBSOVO® and $8.8 million in cost reimbursements and royalty payments under 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, commercialization efforts, expanded facilities and increased staffing needs due to our expanding operations.

Net cash provided by investing activities. Cash provided by investing activities for the six months ended June 30, 2020 was primarily the result of higher proceeds from maturities and sales of marketable securities than purchases of marketable securities, offset by $8.7 million in purchases of property and equipment. Cash provided by investing activities for the six months ended June 30, 2019 was primarily the result of higher proceeds from maturities and sales of marketable securities than purchases of marketable securities, offset by $3.3 million in purchases of property and equipment.

Net cash provided by financing activities. Cash provided by financing activities for the six months ended June 30, 2020 was primarily the result of net proceeds of $250.5 million from the sale of our tiered, sales-based royalty rights on worldwide net sales of IDHIFA® (enasidenib) and our ex-US regulatory milestones to RPI in June 2020, and the $7.1 million of proceeds received from stock option exercises and purchases made pursuant to our 2013 ESPP. Cash provided by financing activities for the six months ended June 30, 2019 was primarily the result of the $8.7 million of proceeds received from stock option exercises and purchases made pursuant to our 2013 ESPP.

Funding requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue to 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, CStone or other partners. 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, 2020, together with anticipated product revenue, anticipated interest income and anticipated expense reimbursements under our collaboration and license agreements, but excluding any additional program-specific milestone payments, will enable us to fund our operating expenses and capital expenditure requirements through the end of December 2022. 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;
- commercialization expenses related to approved medicines such as TIBSOVO® and IDHIFA®;
- levels of product revenue from sales of TIBSOVO®;
- the costs associated with preparation for the potential commercial launch of one or more of our product candidates, including the build-out of a limited commercial infrastructure in the EU;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- operational delays due to the ongoing COVID-19 pandemic; and
- the extent to which we acquire or in-license other medicines and technologies.

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 potential 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 CMOs for 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, 2020, except for the minimum rental commitments disclosed in Note 6, *Leases*, to the condensed consolidated financial statements in this Quarterly Report on Form 10-Q, there were no significant changes to our contractual obligations and commitments described under Management's Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the year ended December 31, 2019.

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, 2020 and December 31, 2019, we had cash, cash equivalents and marketable securities of $794.4 million and $717.8 million, respectively, consisting primarily of investments in 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 primarily 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 change 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, and 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, 2020 and December 31, 2019, liabilities denominated in foreign currencies were immaterial.

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, 2020, 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 persons 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.

We entered into the RPI Purchase Agreement as of June 11, 2020. As a result, we made the following modifications to our internal control over financial reporting, including changes to accounting policies and procedures, operational processes, and documentation practices that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting:

- updated our policies and procedures related to liabilities related to the sale of future revenue and added documentation processes related to accounting for the RPI Purchase Agreement;
- added internal controls over the accounting for the RPI Purchase Agreement; and
- added controls to address related disclosures for the RPI Purchase Agreement

Other than the items described above, there were no changes in our internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, that occurred during the fiscal quarter ended June 30, 2020 that have materially affected, or are 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,” “goal,” “intend,” “may,” “plan,” “predict,” “project,” “strategy,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” “vision” 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, 2019.

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 $411.5 million, $346.0 million and $314.7 million for the years ended December 31, 2019, 2018 and 2017, respectively, and $130.7 million for the six months ended June 30, 2020. As of June 30, 2020, we had an accumulated deficit of $1.6 billion. To date, we have generated only modest revenue from sales of TIBSOVO® and prior to our sale to RPI of our royalty rights to IDHIFA® and any other product that contains the compound enasidenib as an active ingredient, which we refer to as the RPI Transaction, royalties on sales of IDHIFA® . Other than the FDA approvals of TIBSOVO® (for the treatment of IDH1 mutant-positive adult patients with R/R AML or newly diagnosed AML who are at least 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy) and IDHIFA® (for the treatment of IDH2 mutant-positive adult patients with R/R AML), we have not obtained marketing approval for any of our product candidates, which are in preclinical or clinical development stages. We have financed our operations primarily through public offerings of our common stock and our collaboration agreements with Celgene and have devoted substantially all of our efforts to research and development. We expect to continue to incur significant expenses and net losses until such time as we are able to report profitable results. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that we will incur significant expenses if and as we:

- initiate and continue clinical trials for our products and product candidates, including: ivosidenib, enasidenib, vorasidenib, mitapivat, AG-270 and AG-946;
- 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 have or may obtain marketing approval;
- 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 one or more 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. Notwithstanding the extent to which we may succeed in these activities, we may never generate revenues 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 to incur significant expenses as we continue to advance our ongoing activities, particularly as we continue the research and development of, initiate and continue clinical trials of, seek marketing approvals for, and potentially commercialize our product candidates, to the extent that such expenses are not the responsibility of Celgene or other collaborators. For example, we have incurred and expect to continue to incur expenses related to the commercialization of TIBSOVO®, and expect to continue to incur expenses in connection with the buildout of a limited commercial infrastructure in the EU. 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, 2020, together with anticipated product revenue, anticipated interest income and anticipated expense reimbursements under our collaboration and license agreements, but excluding any additional program-specific milestone payments, will enable us to fund our operating expenses and capital expenditure requirements through the end of December 2022. Our estimate as to how long we expect our existing cash, cash equivalents, and marketable securities 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;
- commercialization expenses relating to approved medicines such as TIBSOVO® and IDHIFA®;
- levels of product revenue from sales of TIBSOVO®;
- the cost associated with preparation for the potential commercial launch of one or more of our product candidates, including the build-out of a limited commercial infrastructure in the EU;
- our ability to establish and maintain additional collaborations on favorable terms, if at all;
- operational delays due to the COVID-19 pandemic; 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, TIBSOVO®, IDHIFA®, or our current and any future product candidates, if approved, may not achieve or maintain 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 as we can generate positive cash flow, 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 agreements with our collaborators, which are limited in scope and duration. To the extent that we raise additional capital from the issuances and sales of our common stock pursuant to the 2020 sales agreement or through the sale of equity or convertible debt securities, the ownership interests of our common 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 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 commenced operations in late 2008. Our operations to date have been primarily 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 TIBSOVO® and IDHIFA®. 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 process of transitioning from a company with solely a research focus to a company capable of supporting commercial activities and we have not yet demonstrated our ability to conduct large-scale sales and marketing activities. We may not be successful in such a transition.

Our financial condition and operating results to may continue to fluctuate 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.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Recent changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the Tax Cuts and Jobs Act, or the Tax Act, which significantly reformed the U.S. Internal Revenue Code of 1986, as amended, or the Code. The Tax Act, among other things, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for net operating losses arising in taxable years beginning after December 31, 2017 to 80% of current year taxable income and elimination of net operating loss carrybacks for losses arising in taxable years ending after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), the imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

As part of Congress' response to the COVID-19 pandemic, the Families First Coronavirus Response Act, or FFCR Act, was enacted on March 18, 2020, and the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, was enacted on March 27, 2020. Both contain numerous tax provisions. In particular, the CARES Act retroactively and temporarily (for taxable years beginning before January 1, 2021) suspends application of the 80%-of-income limitation on the use of net operating losses, which was enacted as part of the Tax Act. It also provides that net operating losses arising in any taxable year beginning after December 31, 2017, and before January 1, 2021 are generally eligible to be carried back up to five years. The CARES Act also temporarily (for taxable years beginning in 2019 or 2020) relaxes the limitation of the tax deductibility for net interest expense by increasing the limitation from 30 to 50% of adjusted taxable income.

Regulatory guidance under the Tax Act, the FFCR Act and the CARES Act is and continues to be forthcoming, and such guidance could ultimately increase or lessen impact of these laws on our business and financial condition. It is also possible that Congress will enact additional legislation in connection with the COVID-19 pandemic, some of which could have an impact on

our company. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the FFCR Act or the CARES Act.

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

If we do not successfully commercialize TIBSOVO® in current and any additional indications for which it may be approved our 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, and in May 2019, the FDA approved TIBSOVO® for the treatment of adult patients with newly diagnosed AML with a susceptible IDH1 mutation who are at least 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy. In December 2019, the FDA granted Breakthrough Therapy designation for ivosidenib for the treatment of adult patients with relapsed or refractory MDS with a susceptible IDH1 mutation as detected by an FDA-approved test, and we recently reopened enrollment in the MDS arm of our Phase 1 clinical trial of ivosidenib with the goal of generating sufficient data to pursue a regulatory filing in this indication. We are also evaluating ivosidenib in other clinical trials for the treatment of IDH1 mutant-positive cancers. 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® (ivosidenib) 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 operations 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®;
- our efforts to commercialize TIBSOVO® are impeded by the effects of the COVID-19 pandemic;
- we encounter any third-party patent interference, derivation, inter partes review, post-grant review, reexamination or patent infringement claims with respect to ivosidenib;
- 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®;
- new significant safety risks are identified;
- we fail to gain and/or maintain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community;
- ivosidenib 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 and the treatment of adult patients with newly diagnosed AML with a susceptible IDH1 mutation who are at least 75 years old or who have comorbidities that preclude use of intensive induction chemotherapy.

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

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 and adjacent areas of biology in a variety of different types of hematologic malignancies, solid tumors 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 generate incremental product revenue in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

The COVID-19 pandemic, which began in late 2019 and has spread worldwide, may affect our ability to initiate or continue our planned, ongoing and future clinical trials, disrupt regulatory activities, disrupt our ability to maintain a commercial infrastructure for our products or have other adverse effects on our business and operations. In addition, this pandemic has caused substantial disruption in the financial markets and may adversely impact economies worldwide, both of which could result in adverse effects on our business and operations.

The COVID-19 pandemic, which began in December 2019, has spread worldwide, causing many governments to implement measures to slow the spread of the outbreak through quarantines, strict travel restrictions, heightened border scrutiny, and other measures. The outbreak and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the pandemic and its effects on our business and operations are uncertain.

In the event of a continuation of shelter-in-place orders and/or other mandated local travel restrictions, our employees conducting research and development activities may not be able to access our research space, and our core activities may be significant limited or curtailed, possibly for an extended period of time. In light of the pandemic, we may choose to pause certain research programs, delay the start of certain longer-term clinical studies and limit hiring.

We have enrolled, and seek to enroll, patients in our clinical trials at sites located both in the United States and internationally. We face difficulties recruiting or retaining patients in our ongoing clinical trials because of the pandemic. Patients enrolled in our clinical trials may be unable or unwilling to visit clinical trial sites which may impact the collection of important clinical trial data. In addition limitations in the ability to visit sites has affected, and may continue to adversely affect, our enrollment timelines for our clinical trials, and may adversely affect the timing of completion of our clinical trials or our ability to complete clinical trials in a fully compliant manner. For example, due to disruptions related to the COVID-19 pandemic, we have delayed our expectations for completion of enrollment of our phase 3 AGILE clinical trial and the MDS arm of our phase 1 clinical trial of ivosidenib until 2021. Additionally, the potential suspension of clinical trial activity at clinical trial sites may have an adverse impact on our clinical trial plans and timelines.

We may face disruptions in our ability to prepare and submit applications to regulatory authorities for drug approvals and to build and maintain a commercial infrastructure for our products and product candidates. For example, we now expect to submit to the FDA an sNDA for TIBSOVO® for previously treated IDH1 mutant-positive cholangiocarcinoma in the first quarter of 2021, instead of by the end of 2020. We may face disruptions that may affect our ability to initiate and complete clinical trials including disruptions in procuring items that are essential for our research and development activities, including, for example, raw materials used in the manufacturing of our product candidates and laboratory supplies for planned and ongoing clinical trials, in each case, for which there may be shortages because of ongoing efforts to address the outbreak. Site initiation, participant recruitment and enrollment, participant dosing, distribution of clinical trial materials, study monitoring and data analysis may be paused or delayed due to changes in hospital or university policies, federal, state or local regulations, prioritization of hospital resources toward pandemic efforts, or other reasons related to the pandemic. We may face manufacturing disruptions or disruptions related to the ability to obtain necessary institutional review board, or IRB, or other necessary site approvals, as well as other delays at clinical trial sites.

The response to the COVID-19 pandemic may redirect resources with respect to regulatory and intellectual property matters in a way that would adversely impact our ability to progress regulatory approvals and protect our intellectual property. In addition, we may face impediments to regulatory meetings and approvals due to measures intended to limit in-person interactions.

The COVID-19 pandemic has already caused significant disruptions in the financial markets, and may continue to cause such disruptions, which could impact our ability to raise additional funds through public offerings and may also impact the volatility of our stock price and trading in our stock. Moreover, it is possible the pandemic will significantly impact economies worldwide, which could result in adverse effects on our business and operations. We cannot be certain what the overall impact of the COVID-19 pandemic will be on our business and it has the potential to adversely affect our business, financial condition, results of operations, and prospects.

We do not know whether we will be able to develop any additional 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 diseased cells in the laboratory and then using these key enzymes to screen for and identify product candidates targeting cellular metabolism and adjacent areas of biology.

Our focus on using our proprietary technology to screen for and identify product candidates targeting cellular metabolism and adjacent areas of biology may not result in the discovery and development of commercially viable medicines to treat patients with hematologic malignancies, solid tumors 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 and adjacent areas of biology 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 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.

Our ability to generate product revenue will depend heavily on the successful development and eventual commercialization of our current and any future product candidates, including vorasidenib, mitapivat, AG-270 and AG-946.

The success of ivosidenib, vorasidenib, mitapivat, AG-270, and AG-946 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. 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. In June 2018 Celgene submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive AML, which it subsequently withdrew in December 2019. In December 2018, we submitted an MAA to the EMA for TIBSOVO® for the treatment of adult patients with IDH1 mutant-positive R/R AML and we plan to submit an sNDA for TIBSOVO® for previously treated IDH1 mutant-positive cholangiocarcinoma to the FDA in the first quarter of 2021. However, we can provide no assurance that we will successfully submit such sNDA, or any NDA for any of our other product candidates,

or that any MAA, NDA or sNDA 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, 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, 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 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.

Should the COVID-19 pandemic persist and/or spread, our clinical development plans could be affected. Site initiation, participant recruitment and enrollment, participant dosing, distribution of clinical trial materials, study monitoring and data analysis may be paused or delayed due to changes in hospital or university policies, federal, state or local regulations, prioritization of hospital resources toward pandemic efforts, or other reasons related to the pandemic. Some participants and clinical investigators may not be able to comply with clinical trial protocols, for example if quarantines or other travel limitations continue to impede participant movement, affect sponsor access to study sites, or interrupt healthcare services, and we may be unable to conduct our clinical trials. For example, due to disruptions related to the COVID-19 pandemic, we have delayed our expectations for completion of enrollment of our phase 3 AGILE clinical trial and the MDS arm of our phase 1 clinical trial of ivosidenib until 2021. Furthermore, site initiations and patient enrollment may be delayed or suspended by local health authorities considering the COVID-19 outbreak.

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 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. For example, in the first quarter of 2020, we made the decision to halt internal development of AG-636 for the treatment of hematologic malignancies, including lymphoma due to limited enrollment in our phase 1 study in lymphoma. Furthermore, enrollment has been and may continue to be particularly challenging in light of the ongoing COVID-19 pandemic and even more so for some of the orphan diseases we target in our RGD programs. For example, due to disruptions related to the COVID-19 pandemic, we have delayed our expectations for completion of enrollment of our phase 3 AGILE clinical trial and the MDS arm of our phase 1 clinical trial of ivosidenib until 2021. 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 generally 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 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 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, or Forma, with FT-2102, are conducting clinical trials that are targeted specifically towards patients with IDH1 mutant positive-cancers and/or include IDH mutant positive populations; Rocket Pharma LTD is in the preclinical stages of development for a gene therapy targeting PK deficiency; Forma is developing a PKR activator for the treatment of hemolytic anemias; and IDEAYA Biosciences, Inc., or IDEAYA, is developing a MAT2A inhibitor for the treatment of MTAP-deleted cancers. As these companies and others initiate and conduct clinical trials, they may compete for eligible patients with our clinical trials of our product candidates. Competition for these patients may make it particularly difficult for us to enroll enough patients to complete our clinical trials for our product candidates in a timely and cost-effective manner.

We rely on 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 TIBSOVO® and IDHIFA®, 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 or any 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 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, 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, 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 any 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 Abbott Laboratories for the development of the FDA approved diagnostic for TIBSOVO®, and may in the future depend on 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, sNDA or MAA that we and/or Celgene submit for our product candidates, 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 applications 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 applications 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 applications. For example, Celgene withdrew its MAA with the EMA for IDHIFA® for IDH2 mutant-positive AML in December 2019. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us or Celgene from commercializing our product candidates, 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.

Infections and deaths related to the COVID-19 pandemic may disrupt U.S. or international healthcare and regulatory systems. Such disruptions could divert healthcare resources away from, or materially delay review and/or decision making with respect to marketing approvals for our product candidates. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could materially affect the development and study of our product candidates.

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 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 collaborators, 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 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 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 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.

TIBSOVO® and IDHIFA®, or any of our product candidates that receive marketing approval in the future, may fail to gain and/or maintain 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 limited experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for approved medicines 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 our sales of TIBSOVO®, we will 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, including, for example, to support the potential approval of one or more product candidates in the EU.

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 products and 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.), Novartis International AG, Pfizer, Inc. and Astellas Pharma Inc. are each marketing therapies to treat AML, Acceleron Pharma Inc. and bluebird bio, Inc. are each marketing therapies to treat beta thalassemia, and a number of other biotechnology companies have product candidates in clinical development in similar indications as ours. 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 our product candidates, if approved, will be priced at a significant premium over competitive generic products, as is the case with TIBSOVO® and IDHIFA®. 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 hematologic malignancies, solid tumors and RGDs by targeting similar mechanisms of action as our product candidates. These companies include large pharmaceutical companies, such as AstraZeneca plc, Bayer, Daiichi Sankyo, Eli Lilly and Company, Roche and its subsidiary Genentech, Inc., GlaxoSmithKline plc, Merck, and Pfizer, as well as biotechnology companies of various sizes, such as Forma, IDEAYA and Rocket Pharma. In addition, there are several companies developing immunotherapies, including metabolic immunotherapies, targeting cancer, including AstraZeneca; BeiGene, Ltd.; Bristol-Myers Squibb Company; GlaxoSmithKline; Genentech; and Merck. 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 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 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 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 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 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 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 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 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 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 third parties with which we contract, 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 computer viruses, worms and other destructive or disruptive software, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyber attacks by malicious third parties. Cyber incidents are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber incidents could include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber incidents also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient. 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.

System failures, accidents, cyber attacks 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, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from completed or future trials 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, our competitive position could be harmed 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.

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.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to EU General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to: processing health and other sensitive data; obtaining consent of individuals to whom the personal health data relates; providing information to individuals regarding data processing activities; implementing safeguards to protect the security and confidentiality of personal data; providing notification of data breaches; and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States and, as a result, increases the scrutiny that clinical trial sites located in the EEA should apply to transfers of personal data from such sites to countries that are considered to lack an adequate level of data protection, such as the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and it also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of GDPR. In addition, the GDPR provides that EU member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Given the breadth and depth of changes in data protection obligations, preparing for and complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or transfer personal data collected in the EU. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations. Similarly, failure to comply with federal and state laws regarding privacy and security of personal information could expose us to fines and penalties under such laws. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Similar privacy and data security requirements are either in place or underway in the United States. There are a broad variety of data protection laws that are applicable to our activities, and a wide range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act, which went into effect on January 1, 2020, is creating similar risks and obligations as those created by GDPR, though the California Consumer Privacy Act does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states are considering similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with current and any future federal and state laws regarding privacy and security of personal information could expose us to fines and penalties. We also face a threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Risks Related to Our Dependence on Third Parties

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 with Celgene, pursuant to which we and Celgene are evaluating enasidenib in specified clinical trials, and the CStone Agreement, pursuant to which we have granted rights to CStone for the development and commercialization of ivosidenib, either as monotherapy or in combination with other therapies, in the CStone Territory. These collaborations involve complex allocations of rights. Furthermore, in specified cases these collaborations 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, and the CStone Agreement, development and commercialization plans and strategies for licensed programs, such as enasidenib, or in the CStone Territory, ivosidenib, 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.

- 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, in March 2020, Celgene notified us of its decision to decline its option to enter into a development and commercialization agreement with respect to MAT2A and provided notice of its decision to decline its right to extend the research term of the 2016 Agreement. Further, in April 2020, Celgene notified us that BMS has declined to elect any program for continued development and opt-in rights under the 2016 Agreement.
- 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, 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 enasidenib 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, in September 2018, we and Celgene agreed to terminate the AG-881 Agreements effective as of September 4, 2018, as a result of which we will be responsible for future development costs of vorasidenib, other than certain agreed-up costs which we and Celgene had split until December 31, 2018. Celgene can terminate its remaining agreements with us, in their entirety or with respect to enasidenib under the 2010 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 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. For example, BMS may not retain and motivate key personnel who are important to the continued development of the programs under our agreements with Celgene. In addition, BMS could determine to reprioritize Celgene's development programs such that it ceases to diligently pursue the development of our programs, and/or cause the agreements between Celgene and us to terminate.

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 prospects in the CStone Territory.

In June 2018, we entered into the CStone Agreement, for the development and commercialization of ivosidenib, either as monotherapy or in combination with other therapies, in the CStone Territory. Pursuant to the CStone Agreement, CStone will be responsible for the development and commercialization of ivosidenib 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 ivosidenib in the CStone Territory, including:

- CStone may fail to comply with applicable regulatory guidelines with respect to developing, manufacturing or commercializing ivosidenib, which could adversely impact future development or potential sales of ivosidenib 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 ivosidenib 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, significant changes in CStone's business strategy, or the impact of public health epidemics, such as the COVID-19 pandemic, 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 CStone Agreement is terminated early, we may not be able to find another collaborator for the further development and commercialization of ivosidenib in the CStone Territory on acceptable terms, or at all, and we may be unable to pursue continued development and commercialization of ivosidenib in the CStone Territory on our own.

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.

We have been monitoring our supply chain network for any disruptions due to the COVID-19 pandemic, and our CDMO manufacturers have remained largely unaffected, with any campaign delays experienced to date being limited to a few days in duration. Although global shipping continues to be disrupted due to the pandemic, we have not yet experienced a supply impact and we have accrued additional safety stock of TIBSOVO® in order to further mitigate risk. While we have not yet experienced disruptions to our supply chain due to the COVID-19 pandemic, if either we or any third parties on which we rely are adversely impacted by restrictions resulting from the COVID-19 pandemic, our supply chain may be disrupted, limiting our ability to manufacture our product candidates for our clinical trials and research and development operations.

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.

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. 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. 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.

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 in which we intend to commercialize but we continue to actively pursue patent protection for our assets around the world.

The patent prosecution process is costly 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 and/or file patent applications on every aspect of our research and development output that is or may be eligible for patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who may 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. There is also the possibility that loss or theft of data or records may jeopardize the ability to seek patent protection or impede the progress or drafting of patent applications.

We have licensed patent rights, and in the future may license additional patent rights, from third parties. Such licenses may be accompanied by milestone and/or royalty payment obligations. 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 pre-issuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, 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 the patent or in one or more patent claims being narrowed or invalidated, 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 significant amount of time required for the discovery, development, preclinical and clinical testing and regulatory review and approval 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. In such circumstances we would be relying primarily on regulatory or marketing exclusivity to exclude others from commercializing a generic version of our products.

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.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. 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. 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 opposition, derivation, revocation, reexamination, post-grant and inter partes review or interference proceedings before the USPTO or other patent offices around the world. 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 organization.

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 confidential information related to our proprietary platforms and technology, our business and competitive position could be harmed.

In addition to seeking patents for some of our technology and medicines, we also rely on maintaining the confidentiality of unpatented know-how, technology and other proprietary information, to maintain our competitive position. For example, we consider the confidential information and know-how related to our cellular metabolism technology platform to be our primary intellectual property assets in this space. Unpatented proprietary technical information and know-how can be difficult to protect.

We seek to protect this proprietary technical information and know-how, 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, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated proprietary information is difficult, expensive and time-consuming, and the outcome is unpredictable. If any of our proprietary technical information and know-how 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. Moreover, we anticipate that with respect to this platform, at least some of this technical information 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.

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 the FDA approvals 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. For example, Celgene submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive AML which it subsequently withdrew in December 2019. Although we have an MAA under review by the EMA for TIBSOVO® for the treatment of adult patients with IDH1 mutant-positive R/R AML failure to obtain marketing approval for TIBSOVO® or any other 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 EU 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. Celgene submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive AML, which it subsequently withdrew in December 2019 and we have an MAA under review by the EMA for TIBSOVO® for the treatment of adult patients with IDH1 mutant-positive R/R AML. 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 EU, commonly referred to as Brexit. Following protracted negotiations, the United Kingdom left the EU on January 31, 2020. Under the withdrawal agreement, there is a transitional period until December 31, 2020 (extendable up to two years). Discussions between the United Kingdom and the EU have so far mainly focused on finalizing withdrawal issues and transition agreements but have been extremely difficult to date. To date, only an outline of a trade agreement has been reached. Much remains open but the Prime Minister has indicated that the United Kingdom will not seek to extend the transitional period beyond the end of 2020. If no trade agreement has been reached before the end of the transitional period, there may be significant market and economic disruption. The Prime Minister has also indicated that the United Kingdom will not accept high regulatory alignment with the EU.

Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety, and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales, and distribution of pharmaceutical products is derived from EU directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of our product candidates in the United Kingdom. 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 EU 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 EU for our product candidates, which could significantly and materially harm our business.

Furthermore, other European countries may seek to conduct referenda with respect to continuing membership with the EU. We do not know to what extent Brexit or other comparable initiatives, or any resulting changes, would affect our ability to conduct clinical trials or obtain marketing approval in these jurisdictions, and each could materially impact our ability to conduct clinical trials or obtain marketing approval on a timely basis, or at all.

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, enasidenib and ivosidenib 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 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 or 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 or 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 market our medicines for uses other than their respective 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, which violations may result in the imposition of significant administrative, civil and criminal penalties.

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 other notice of violation 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 EU 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 EU 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;
- 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.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the EU. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of EU Member States, such as the U.K. Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain EU Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual EU Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the EU Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Under 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.

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.

For example, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, which required 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 required 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 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 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 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 ACA 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.

Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. One Executive Order directs 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. The second Executive Order terminates the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. The loss of the cost share reduction payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. Further, on June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

In addition, the Centers for Medicare & Medicaid Services, or CMS, has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. On November 30, 2018, CMS announced a proposed rule that would amend the Medicare Advantage and Medicare Part D prescription drug benefit regulations to reduce out of pocket costs for plan enrollees and allow Medicare plans to negotiate lower rates for certain drugs. Among other things, the proposed rule changes would allow Medicare Advantage plans to use pre authorization (PA) and step therapy (ST) for six protected classes of drugs, with certain exceptions, permit plans to implement PA and ST in Medicare Part B drugs; and change the definition of "negotiated prices" while a definition of "price concession" in the regulations. It is unclear whether these proposed changes we be accepted, and if so, what effect such changes will have on our business. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results. We continue to evaluate the effect that the ACA and its possible repeal and replacement has on our business.

While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA. For example, with enactment of the Tax Cuts and Jobs Act of 2017 or TCJA, 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, became 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.

On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The Trump Administration and CMS have both stated that the

ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. The Trump Administration thereafter represented to the Court of Appeals considering this judgment that it does not oppose the lower court's ruling. On July 10, 2019, the Court of Appeals for the Fifth Circuit heard oral argument in this case. In those arguments, the Trump Administration argued in support of upholding the lower court decision. On December 18, 2019, that court affirmed the lower court's ruling that the individual mandate portion of the ACA is unconstitutional and remanded the case to the district court for reconsideration of the severability question and additional analysis of the provisions of the ACA. On January 21, 2020, the U.S. Supreme Court declined to review this decision on an expedited basis. On March 3, 2020, that court agreed to hear this case. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

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.

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.

Specifically, there have been several recent U.S. congressional inquiries and proposed federal and proposed and enacted state 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. At the federal level, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. For example, on May 11, 2018, the current administration issued a plan to lower drug prices. Under this blueprint for action, the current administration indicated that the Department of Health and Human Services, or HHS, will take steps to end the gaming of regulatory and patent processes by drug makers to unfairly protect monopolies, advance biosimilars and generics to boost price competition, evaluate the inclusion of prices in drug makers' ads to enhance price competition, speed access to and lower the cost of new drugs by clarifying policies for sharing information between insurers and drug makers, avoid excessive pricing by relying more on value-based pricing by expanding outcome-based payments in Medicare and Medicaid, work to give Medicare Part D plan sponsors more negotiation power with drug makers, examine which Medicare Part B drug prices could be negotiated by Medicare Part D plans, improve the design of the Medicare Part B Competitive Acquisition Program, update Medicare's drug-pricing dashboard to increase transparency, prohibit Medicare Part D contracts that include "gag rules" that prevent pharmacists from informing patients when they could pay less out-of-pocket by not using insurance, and require that Medicare Part D plan members be provided with an annual statement of plan payments, out-of-pocket spending, and drug price increases. In addition, on December 23, 2019, the Trump Administration published a proposed rulemaking that, if finalized, would allow states or certain other non-federal government entities to submit importation program proposals to the FDA for review and approval. Applicants would be required to demonstrate that their importation plans pose no additional risk to public health and safety and will result in significant cost savings for consumers. At the same time, the FDA issued draft guidance that would allow manufacturers to import their own FDA-approved drugs that are authorized for sale in other countries (multi-market approved products).

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to

encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

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 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, 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, fires and the impact of public health epidemics, such as the ongoing COVID-19 pandemic.

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. Although we have managed recent executive transitions, including of our chief executive officer and chief scientific officer, we cannot predict the likelihood, timing or effect of future departures among our executive leadership.

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.

In response to the COVID-19 pandemic, we have been required to close our facilities except for a limited number of essential facilities and laboratory staff. In the event of a continuation of shelter-in-place orders and other mandated local travel restrictions, our employees conducting research and development activities may not be able to access our research space, and our core activities may be significantly limited or curtailed, possibly for an extended period of time.

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 continue to experience growth in the number of our employees and the scope of our operations, including 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. 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, 2015 the price of our common stock on the Nasdaq Global Select Market has ranged from $27.77 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 COVID-19 pandemic, which has had a broad impact globally, including restrictions on travel and quarantine policies put into place by businesses and governments, may have a material effect on our business. While the full extent of the economic impact and the duration of the pandemic may be difficult to assess or predict, it has already caused, and is likely to result in further, significant disruption of global financial markets, which may reduce our ability to access capital either at all or on favorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the COVID-19 pandemic could materially and adversely affect our business and the value of our common stock.

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 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;
- the societal and economic impact of public health epidemics, such as the ongoing COVID-19 pandemic;
- 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 or upon vesting of restricted stock units, performance-based stock units or market-based stock units 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, 2020, 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 Code and corresponding provisions of state law, if a company undergoes an “ownership change,” generally defined as a greater than 50% change (by value) in its equity ownership by certain stockholders 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 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, 2019, and determined that we did not have a qualified ownership change since our last review as of December 31, 2018. 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.

There is also a risk that due to regulatory changes, such as suspensions on the use of net operating losses, or other unforeseen reasons, our existing net operating losses could expire or otherwise become unavailable to offset future income tax liabilities. As described above in “Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition,” the Tax Act, as amended by the CARES Act, includes changes to U.S. federal tax rates and the rules governing net operating loss carryforwards that may significantly impact our ability to utilize our net operating losses to offset taxable income in the future. In addition, state net operating losses generated in one state cannot be used to offset income generated in another state. For these reasons we may be unable to use a material portion of our net operating losses and other tax attributes.

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 as a result of 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 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 devote, and will need to continue 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 5. 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	Sales Agreement, dated April 30, 2020, by and between the Registrant and Cowen and Company, LLC	S-3ASR	333-237930	April 30, 2020	1.2	
10.2†	Royalty Purchase Agreement, dated as of June 11, 2020, by and between the Registrant and RPI 2019 Intermediate Finance Trust					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 has been granted as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission

* This certification will not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, or otherwise subject to the liability of that section. Such certification will not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except to the extent specifically incorporated by reference into such filing

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.

July 30, 2020 By: /s/ Jacqualyn A. Fouse

Jacqualyn A. Fouse, Ph.D.
Chief Executive Officer
(principal executive officer)

July 30, 2020 By: /s/ Andrew Hirsch

Andrew Hirsch
Chief Financial Officer and Head of Corporate Development
(principal financial officer)

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) would likely cause competitive harm to the Company, if publicly disclosed. Double asterisks denote omissions.

Royalty Purchase Agreement

by and between

Agios Pharmaceuticals, Inc.

and

RPI 2019 Intermediate Finance Trust

Dated as of June 11, 2020

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ROYALTY PURCHASE AGREEMENT

THIS ROYALTY PURCHASE AGREEMENT (this "Agreement") is made as of June 11, 2020, by and between Agios Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and RPI 2019 Intermediate Finance Trust, a Delaware statutory trust (the "Purchaser").

RECITALS

WHEREAS, pursuant to the License Agreement, the Company granted to Licensee a royalty-bearing license in the Field under the Company's rights in Agios Intellectual Property and Agios Collaboration Intellectual Property to, among other things, commercialize the Licensed Product in the Field on an exclusive basis in the Territory, subject to Agios' right to conduct certain commercialization activities in the US Territory pursuant to the Commercialization Plan; and

WHEREAS, pursuant to terms set forth in this Agreement, the Company desires to sell to the Purchaser, and the Purchaser desires to purchase from the Company, the Royalty.

NOW, THEREFORE, in consideration of the premises and mutual covenants herein contained, and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto agree as follows:

SECTION 1

Defined Terms and Rules of Construction

1.1 ***Definitions***
. As used in this Agreement, the following terms shall have the following meanings:

"Affiliate" means, with respect to any particular Person, any other Person directly or indirectly controlling, controlled by or under common control with such particular Person.

"Agios Collaboration Intellectual Property" shall have the meaning ascribed thereto in Section 1.3 of the License Agreement.

"Agios Collaboration Patent Right" shall have the meaning ascribed thereto in Section 1.3 of the License Agreement.

"Agios Intellectual Property" shall have the meaning ascribed thereto in Section 1.4 of the License Agreement.

"Agios Inventors" is defined in Section 4.10(d).

"Agios Reverted Product" shall have the meaning ascribed thereto in Section 1.8 of the License Agreement.

"Agreement" is defined in the Preamble.

"Annual Net Sales" shall have the meaning ascribed thereto in Exhibit A to the License Agreement.

"Bankruptcy Laws" means, collectively, bankruptcy, insolvency, reorganization, moratorium, fraudulent conveyance, fraudulent transfer or other similar laws affecting the enforcement of creditors' rights generally.

"Bill of Sale" means that certain bill of sale evidencing the sale, transfer, assignment and conveyance of the Royalty, substantially in the form attached hereto as Exhibit A (the "Bill of Sale").

"Board of Directors" means the board of directors of the Company.

"Business Day" means any day other than (i) a Saturday or Sunday or (ii) a day on which banking institutions located in New York are permitted or required by applicable law or regulation to remain closed.

"Buy-In Product" shall have the meaning ascribed thereto in Section 1.15 of the License Agreement.

"Celgene Collaboration Intellectual Property" shall have the meaning ascribed thereto in Section 1.19 of the License Agreement.

"Celgene Program Option" shall have the meaning ascribed thereto in Section 3.2 of the License Agreement.

"Celgene Reverted Product" shall have the meaning ascribed thereto in 1.24 of the License Agreement.

"Closing" is defined in Section 3.1.

"Closing Date" is defined in Section 3.1.

"Co-Commercialized Product" has the meaning ascribed thereto in Section 1.28 of the License Agreement.

"Commercialization Plan" shall have the meaning ascribed thereto in Section 6.2(a)(i) of the License Agreement.

"Commercialize" means any and all activities directed to the manufacture, distribution, marketing, detailing, promotion, selling and securing of reimbursement of Licensed Product (including the making, using, importing, selling and offering for sale of the Licensed Product), and shall include post-marketing approval studies, post-launch marketing, promoting, detailing, marketing research, distributing, customer service, selling the Licensed Product, importing,

exporting or transporting the Licensed Product for sale, and regulatory compliance with respect to the foregoing.

"Commission" means the U.S. Securities and Exchange Commission.

"Commission Documents" means the reports, schedules, forms, statements and other documents required to be filed by the Company during the past twelve (12) months with the Commission pursuant to the reporting requirements of the Exchange Act, including filings incorporated by reference therein and material filed pursuant to Section 13(a) or 15(d) of the Exchange Act.

"Committee" shall have the meaning ascribed thereto in Section 2.1 of the License Agreement.

"Company" is defined in the Preamble.

"Competitive Infringement" means any infringement, unauthorized use or misappropriation by a third party of the Licensed IP that is competitive with the Licensed Product.

"Confidential Information" is defined in Section 7.1.

"Control" shall have the meaning ascribed thereto in Section 1.42 of the License Agreement. For the avoidance of doubt, where used in this Agreement, Control of applicable intellectual property by the Company is subject to the licenses granted by the Company to Licensee under the License Agreement.

"Cover" shall have the meaning ascribed thereto in Section 1.44 of the License Agreement.

"Credit Event" means any insolvency, bankruptcy, receivership, assignment for the benefit of creditors, or similar proceeding, following or as a result of which the Licensee fails to pay amounts owing under the License Agreement in respect of the Royalty as a result of the Licensee's financial distress, creditworthiness, or insolvency.

"Development" shall have the meaning ascribed thereto in Section 1.46 of the License Agreement.

"Development Plan" shall have the meaning ascribed thereto in Section 3.9(a) of the License Agreement.

"DGCL" means the Delaware General Corporation Law.

"Disclosed Information" means, collectively, (i) any Royalty Reports, (ii) any commercialization reports, marketing reports, or similar materials that the Licensee is required to deliver, to the Company pursuant to the License Agreement and (iii) all notices that relate to

the Licensed Product sent by the Licensee to the Company, whether pursuant to the License Agreement or otherwise.

"Disclosing Party" is defined in Section 7.1.

"Disclosure Schedule" means the Disclosure Schedule, attached hereto as Exhibit B and dated as of the date hereof and delivered by the Company to the Purchaser.

"Excess Amount" is defined in Section 6.2(d).

"Exchange Act" means the Securities Exchange Act of 1934, as amended.

"Existing Third Party Agreements" shall have the meaning ascribed thereto in Section 1.53 of the License Agreement.

"Failed Product" shall have the meaning ascribed thereto in Section 9.6(a)(iv) of the License Agreement.

"Field" shall have the meaning ascribed thereto in Section 1.56 of the License Agreement.

"Governmental Entity" means any: (i) nation, principality, republic, state, commonwealth, province, territory, county, municipality, district or other jurisdiction of any nature; (ii) federal, state, local, municipal, foreign or other government; (iii) governmental or quasi-governmental authority of any nature (including any governmental division, subdivision, department, agency, bureau, branch, office, commission, council, board, instrumentality, officer, official, representative, organization, unit, body or other entity and any court, arbitrator or other tribunal); (iv) multi-national organization or body; or (v) individual, body or other entity exercising, or entitled to exercise, any executive, legislative, judicial, administrative, regulatory, police, military or taxing authority or power of any nature.

"Indemnified Party" is defined in Section 8.1.

"Indemnifying Party" is defined in Section 8.1.

"Independent Program" shall have the meaning ascribed thereto in Section 1.67 of the License Agreement.

"JCC" shall have the meaning ascribed thereto in Section 2.1 of the License Agreement.

"Joint Patent" shall have the meaning ascribed thereto in Section 10.1(c) of the License Agreement.

"Knowledge of the Company" means the actual knowledge of [**] after due inquiry.

"License Agreement" means that certain Discovery and Development Collaboration and License Agreement, dated as of April 14, 2010, by and between the Company and the Licensee,

as amended by that certain Amendment No. 1, dated October 3, 2011, by and between the Company and the Licensee, that certain Amendment No. 2, dated October 3, 2011, by and between the Company and the Licensee, and that certain Amendment No. 3, dated July 14, 2014, by and between the Company and the Licensee.

"Licensed Agios Patents" means the Agios Patent Rights and the Agios Collaboration Patent Rights, as each such capitalized term is defined in the License Agreement, that Cover or are otherwise necessary or useful for the Development, Manufacture and/or Commercialization of the Licensed Product.

"Licensed IP" means the Agios Intellectual Property and the Agios Collaboration Intellectual Property, in each case that is necessary or useful for the Development, Manufacture and/or Commercialization of the Licensed Product.

"Licensed Product" means, collectively, (a) the product known as IDHIFA (enasidenib) that is approved by the U.S. Food and Drug Administration for marketing in the U.S. Territory pursuant to NDA No. 209606, and (b) any other product that contains the compound enasidenib as an active ingredient, alone or in combination with another active component, in each case of (a) and (b), in any strengths, forms, formulations, administrations or delivery routes.

"Licensee" means Celgene Corporation and any successor thereof, as permitted pursuant to the terms of this Agreement and the License Agreement.

"Licensee Consent" means that certain letter agreement, dated May 12, 2020, by and between the Company and Licensee, attached hereto as Exhibit C-1, as supplemented by that certain letter agreement, dated June 8, 2020, by and among the Company, the Licensee and the Purchaser, attached hereto as Exhibit C-2.

"Licensee Instruction Letter" is defined in Section 3.7.

"Lien" means any mortgage, lien, pledge, charge, adverse claim, security interest, encumbrance or restriction of any kind, including any restriction on use, transfer or exercise of any other attribute of ownership of any kind.

"Losses" is defined in Section 8.1.

"Manufacture" shall have the meaning ascribed thereto in Section 1.79 to the License Agreement.

"Material Adverse Effect" means (i) a material adverse effect on the legality, validity or enforceability of the Transaction Documents, (ii) a material adverse effect on the ability of the Company to perform any of its obligations thereunder, (iii) a material adverse effect on the rights of the Company under the License Agreement with respect to the Royalty, other than as a result of a Permitted Reduction or Credit Event, (iv) a material adverse effect on the validity or enforceability of any of the Licensed Agios Patents that would reasonably be expected to adversely affect in any material respect the timing, amount or duration of the payments to be

made to the Purchaser in respect of the Royalty, or (v) an adverse effect in any material respect on the timing, amount or duration of the payments to be made to the Purchaser in respect of the Royalty or the right of the Purchaser to receive such payments, other than as a result of a Permitted Reduction or Credit Event.

"Net Sales" shall have the meaning ascribed thereto in Exhibit A to the License Agreement.

"New Arrangement" is defined in Section 6.10(c).

"New Licensee " is defined in Section 6.10(b).

"[**]" is defined in Section 4.10(d).

"Permitted Liens" means any (i) mechanic's, materialmen's, and similar liens for amounts not yet due and payable, (ii) statutory liens for taxes not yet due and payable or for taxes that the taxpayer is contesting in good faith and (iii) other liens and encumbrances not incurred in connection with the borrowing of money that do not materially and adversely affect the use or value of the affected assets.

"Permitted Reduction" means a Royalty Reduction pursuant to Sections 9.7(f)(ii), 9.7(g)(iii) or 9.11(a) of the License Agreement with respect to the Licensed Product.

"Person" means any individual, firm, corporation, company, partnership, limited liability company, trust, joint venture, association, estate, trust, Governmental Entity or other entity, enterprise, association or organization.

"Picked Product" shall have the meaning ascribed thereto in Section 1.99 of the License Agreement.

"Prime Rate" means the prime rate published by the Wall Street Journal, from time to time, as the prime rate.

"Proceeds" means any amounts actually recovered by the Company as a result of any settlement or resolution of any actions, suits, proceedings, claims or disputes related to the Royalty.

"Program" shall have the meaning ascribed thereto in Section 1.102 of the License Agreement.

"Purchase Price" means Two Hundred and Fifty-Five Million Dollars ($255,000,000).

"Purchaser" is defined in the Preamble.

"Q2 Company Share" is defined in Section 6.2(c).

"Receiving Party" is defined in Section 7.1.

"Representative" means, with respect to any Person, (i) any member or partner of such Person and (ii) any manager, director, officer, employee, agent, advisor or other representative (including attorneys, accountants, consultants, bankers, financial advisors and actual and potential lenders and investors) of such Person.

"Reversionary Rights" is defined in Section 6.10(a).

"ROW Territory" shall have the meaning ascribed thereto in Section 1.112 of the License Agreement.

"Royalty" means, collectively, (a) for the period commencing April 1, 2020 and thereafter, all of the Company's right, title and interest in and to (i) all payments payable to the Company by Licensee under Section 9.7 of the License Agreement with respect to all Net Sales of the Licensed Product in the Territory, (ii) without duplication of any payments described in clause (a)(i), any payments payable to the Company by Licensee under Section 14.3(b)(ii) of the License Agreement, (iii) any payments payable to the Company under the License Agreement in lieu of such payments described in clause (a)(i) and clause (a)(ii), (iv) any payments payable to the Company under Section 10.3(e) of the License Agreement to the extent related to the Licensed Product (other than for any unreimbursed costs payable to Company thereunder) and (v) any payments payable to the Company under Section 9.13 of the License Agreement in respect of the payments described in clauses (a)(i) to (iv); and (b) all of the Company's right, title and interest in and to (i) the [**] Dollar ($[**]) payment payable to the Company by Licensee upon achievement of the milestone event that is set forth in the third row of the table contained in Section 9.6(a) of the License Agreement, (ii) the [**] Dollar ($[**]) payment payable to the Company by Licensee upon achievement of the milestone event that is set forth in the fourth row of the table contained in Section 9.6(a) of the License Agreement and (iii) any payments payable to the Company under Section 9.13 of the License Agreement in respect of the payments described in clauses (b)(i) and (ii); provided that, notwithstanding Section 9.6(a)(iii)(B) of the License Agreement, the portion of the Royalty set forth in this clause (b) shall only include the payment payable to the Company by Licensee upon the first achievement of each of the milestone events referenced in the foregoing clauses (b)(i) and (b)(ii).

"Royalty-Bearing Product" shall have the meaning ascribed thereto in Section 1.113 of the License Agreement.

"Royalty Reduction" is defined in Section 4.8(l).

"Royalty Reports" means the quarterly reports deliverable by Licensee to the Company pursuant to Section 9.8 of the License Agreement.

"Sales Milestone" means the milestone payable to the Company pursuant to Section 9.6(c) of the License Agreement.

"Second Generation Product" shall have the meaning ascribed thereto in Section 9.6(a)(iv) of the License Agreement.

"Shortfall Amount" is defined in Section 6.2(d).

"Specified Financing Statements" is defined in Section 2.4.

"Split Product" shall have the meaning ascribed thereto in Section 1.115 of the License Agreement.

"Subsidiary" means, with respect to any Person, any corporation, partnership, joint venture or other entity, whether or not incorporated, of which at least 50% of the securities having, by their terms, ordinary voting power to elect members of the board of directors, or other bodies performing similar functions with respect to such entity, is directly or indirectly owned by such Person.

"Terminated Program" shall have the meaning ascribed thereto in Section 1.121 of the License Agreement.

"Territory" shall have the meaning ascribed thereto in Section 1.122 of the License Agreement.

"Transaction Documents" means this Agreement, the Licensee Consent, the Licensee Instruction Letter and the Bill of Sale.

"UCC" means the New York Uniform Commercial Code as in effect from time to time.

"US Territory" shall have the meaning ascribed thereto in Section 1.126 of the License Agreement.

1.2 ***Certain Interpretations***
. Except where expressly stated otherwise in this Agreement, the following rules of interpretation apply to this Agreement:

(a) "either" and "or" are not exclusive and "include," "includes" and "including" are not limiting and shall be deemed to be followed by the words "without limitation;"

(b) "extent" in the phrase "to the extent" means the degree to which a subject or other thing extends, and such phrase does not mean simply "if;"

(c) "hereof," "hereto," "herein" and "hereunder" and words of similar import when used in this Agreement refer to this Agreement as a whole and not to any particular provision of this Agreement;

(d) references to a Person are also to its permitted successors and assigns;

(e) definitions are applicable to the singular as well as the plural forms of such terms;

(f) unless otherwise indicated, references to an "Article", "Section" or "Exhibit" refer to an Article or Section of, or an Exhibit to, this Agreement, and references to a "Schedule" refer to the corresponding part of the Disclosure Schedule;

(g) references to "$" or otherwise to dollar amounts refer to the lawful currency of the United States; and

(h) references to a law include any amendment or modification to such law and any rules and regulations issued thereunder, whether such amendment or modification is made, or issuance of such rules and regulations occurs, before or after the date of this Agreement.

1.3 ***Headings***. The table of contents and the descriptive headings of the several Articles and Sections of this Agreement and the Exhibits and Schedules are for convenience only, do not constitute a part of this Agreement and shall not control or affect, in any way, the meaning or interpretation of this Agreement.

SECTION 2

Purchase and Sale of Royalty

2.1 ***Sale of Royalty***. Subject to the terms and conditions hereof, at the Closing, the Company shall sell, transfer, assign and convey to the Purchaser, and the Purchaser shall purchase, acquire and accept from the Company, free and clear of all Liens, all of the Company's right, title and interest in and to all of the Royalty.

2.2 ***Purchase Price***. The purchase price to be paid to the Company for the sale, transfer, assignment and conveyance of the Company's right, title and interest in and to the Royalty to the Purchaser, is the Purchase Price.

2.3 ***No Assumed Obligations***. Notwithstanding any provision in this Agreement to the contrary, the Purchaser is purchasing, acquiring and accepting only the Royalty, and is not assuming any liability or obligation of the Company of whatever nature, whether presently in existence or arising or asserted hereafter, under the License Agreement or otherwise. Except as specifically set forth herein in respect of the Royalty purchased, acquired and accepted hereunder, the Purchaser does not, by such purchase, acquisition and acceptance, acquire any other contract rights of the Company under the License Agreement or any other assets of the Company.

2.4 ***True Sale of Royalty***. It is the intention of the parties hereto that the sale, transfer, assignment and conveyance of the Royalty contemplated by this Agreement constitute a sale of the Royalty from the Company to the Purchaser and not a financing transaction, borrowing or loan. Following the Closing, the Purchaser will be the owner of the Royalty, the Purchaser will have no right to return the Royalty to the Company, and the Company will have no right to repurchase the Royalty from the Purchaser. The sole recourse of the Purchaser against the Company in respect of the Royalty will be (a) for Royalty Reductions, only to the

extent permitted under Section 6.3 hereof, and (b) indemnification for Losses, only to the extent permitted under Section 8 hereof; provided, however, that nothing in this Section 2.4 shall otherwise limit the Company's obligations under its covenants in Section 6 and elsewhere in this Agreement or the Company's liability for failure to perform such obligations. Accordingly, the Company shall treat the sale, transfer, assignment and conveyance of the Royalty as a sale of an "account" or a "payment intangible" (as appropriate) in accordance with the UCC for legal and tax purposes, and the Company hereby authorizes the Purchaser to file financing statements (and continuation statements with respect to such financing statements when applicable) naming the Company as the debtor and the Purchaser as the secured party in respect of the Royalty (the "Specified Financing Statements"). Not in derogation of the foregoing statement of the intent of the parties hereto in this regard, and for the purposes of providing additional assurance to the Purchaser in the event that, despite the intent of the parties hereto, the sale, transfer, assignment and conveyance contemplated hereby is hereafter held not to be a sale, the Company does hereby grant to the Purchaser, as security for the obligations of the Company hereunder, a first priority security interest in and to all right, title and interest of the Company, in, to and under the Royalty and any "proceeds" (as such term is defined in the UCC) thereof, and the Company does hereby authorize the Purchaser, from and after the Closing, to file such financing statements (and continuation statements with respect to such financing statements when applicable) as are necessary to perfect such security interest.

SECTION 3

Closing; Payment of Purchase Price

3.1 ***Closing***. The purchase and sale of the Royalty shall take place remotely via the exchange of documents and signatures (the "Closing") on the date hereof, or at such other time as agreed by both parties (the "Closing Date"). At the Closing, the Purchaser shall pay the Purchase Price by wire transfer of immediately available funds to the account specified by the Company on Exhibit D.

3.2 ***Closing Certificates***.

(a) *Company's Closing Certificate*. At the Closing, the Company shall deliver to the Purchaser a certificate of the Secretary of the Company, dated as of the Closing Date, certifying (i) as to the incumbency of the officer of the Company executing this Agreement and (ii) as to the attached copies of Company's certificate of incorporation, bylaws and resolutions adopted by the Board of Directors authorizing the execution and delivery by the Company of this Agreement and the consummation by the Company of the transactions contemplated hereby.

(b) *Purchaser's Incumbency Certificate*. At the Closing, the Purchaser shall deliver to the Company a certificate of an authorized person of the owner trustee of the Purchaser certifying as to the incumbency of the authorized person executing this Agreement on behalf of Purchaser.

3.3 ***Bill of Sale***. At the Closing, upon confirmation of the receipt of the Purchase Price by the Company, the Company shall deliver to the Purchaser the duly executed Bill of Sale.

3.4 ***Form W-9***. At the Closing, the Company shall deliver to the Purchaser a valid, properly executed IRS Form W-9 certifying that the Company is exempt from U.S. federal withholding tax and "backup" withholding tax.

3.5 ***Form W-8BEN-E***. At the Closing, the Purchaser shall deliver to the Company a valid, properly executed IRS Form W-8BEN-E certifying that the Purchaser is exempt from U.S. federal withholding tax with respect to any and all payments of and in respect of the Royalty.

3.6 ***Data Room***. At the Closing, the Company shall deliver to the Purchaser an electronic copy of all the information and documents posted to the virtual data room in the folder titled "IDHIFA" or that otherwise specifically relate to the Licensed Product, Licensed IP or Royalty established by the Company as of the date hereof and made available to the Purchaser via Intralinks, for archival purposes only and to be held in escrow in the event of a future dispute regarding its contents.

3.7 ***Licensee Instruction Letter***. At the Closing, the Company shall deliver to the Purchaser a duly executed counterpart to the instruction letter, in substantially the form attached hereto as Exhibit E (the "Licensee Instruction Letter"), notifying Licensee of the Closing and instructing Licensee to pay the Royalty to the account specified by the Purchaser, which the Purchaser shall deliver to the Licensee promptly following the Closing.

SECTION 4

Representations and Warranties of the Company

Except as set forth on the Disclosure Schedule, the Company hereby represents and warrants the following as of the date hereof:

4.1 ***Organization and Good Standing and Qualifications***. The Company is an entity duly incorporated or otherwise organized, validly existing and in good standing under the laws of the jurisdiction of its incorporation or organization (as applicable), and has all requisite corporate power and authority to own or lease, as the case may be, and to operate its properties and conduct its business as now being conducted. The Company is not in violation or default of any of the provisions of its respective certificate of incorporation, bylaws, or other organizational documents. The Company is duly qualified as a foreign corporation to do business and is in good standing in every jurisdiction in which the nature of the business conducted or property owned or leased by it makes such qualification necessary, other than those in which the failure so to qualify or be in good standing would not reasonably be expected to have a Material Adverse Effect.

4.2 ***Authorization***.

(a) The Company has the requisite corporate power and authority to enter into and perform its obligations under the Transaction Documents.

(b) The execution, delivery and performance of the Transaction Documents by the Company, the consummation by the Company of the transactions contemplated thereby have been duly authorized by all necessary corporate action and no further consent or authorization of the Company, its Board of Directors and its stockholders is required.

(c) The Agreement has been duly executed and delivered and constitutes a valid and binding obligation of the Company enforceable against the Company in accordance with its terms, except as such enforceability may be limited by applicable Bankruptcy Laws or by other equitable principles of general application.

4.3 ***No Conflicts***.

(a) The execution, delivery and performance of this Agreement and any other document or instrument contemplated hereby by the Company and the consummation by the Company of the transactions contemplated hereby, do not:

(i)violate any provision of the certificate of incorporation or bylaws of the Company;

(ii)violate any provision of any judgment, decree, order or obligation to which it is a party or by which it or any of its properties or assets are bound;

(iii)violate, to its Knowledge, any federal, state or local statute, rule or governmental regulation;

(iv)conflict with, or constitute a default (or an event which with notice or lapse of time or both would become a default) under, or give to others any rights of termination, amendment, acceleration or cancellation of, any material agreement, mortgage, deed of trust, indenture, note, bond, license, lease agreement, instrument or obligation to which the Company is a party where such default or conflict would reasonably be expected to result in a Material Adverse Effect;

(v)create or impose a Lien on any property or assets of the Company under any agreement or any commitment to which the Company is a party or by which the Company is bound, which would reasonably be expected to result in a Material Adverse Effect;

(vi)result in a violation of any federal, state, local or foreign statute, rule, regulation, order, writ, judgment or decree (including federal and state securities laws and regulations) applicable to the Company or any of its Subsidiaries or by which any property or asset of the Company are bound or affected where such violation would reasonably be expected to result in a Material Adverse Effect; or

(vii) require any consent of any third-party that has not been obtained pursuant to any material contract to which the Company is subject or to which any of its assets, operations or management may be subject, where the failure to obtain any such consent would reasonably be expected to result in a Material Adverse Effect.

(b) Assuming the accuracy of the relevant representations and agreements of the Purchaser set forth herein, the Company is not required to obtain any consent, waiver, authorization or order of, give any notice to, or make any filing or registration with, any court or other federal, state, local or other governmental agency or other Person in connection with the execution, delivery or performance of any of its obligations under the Transaction Documents, other than any required filings pursuant to the Exchange Act or the rules of the Commission.

4.4 ***No Undisclosed Liabilities***. To the Company's Knowledge, neither the Company nor any of its Subsidiaries has any liabilities, obligations, claims or losses (whether liquidated or unliquidated, secured or unsecured, absolute, accrued, contingent or otherwise) that would be required to be disclosed on a balance sheet of the Company or any of its Subsidiaries (including the notes thereto) in conformity with GAAP and are not disclosed in the Commission Documents, other than those incurred in the ordinary course of the Company's or its Subsidiaries' respective businesses since March 31, 2020.

4.5 ***No Undisclosed Events or Circumstances***. Except for the transactions contemplated by the Transaction Documents, no event or circumstance has occurred or exists with respect to the Company, its Subsidiaries or their respective businesses, properties, operations or financial condition, which, under applicable law, rule or regulation, requires public disclosure or announcement by the Company but which has not been so publicly announced or disclosed and which, individually or in the aggregate, would reasonably be expected to result in a Material Adverse Effect.

4.6 ***Actions Pending***. There is no action, suit, claim, investigation or proceeding pending or, to the Knowledge of the Company, threatened against the Company which questions the validity of this Agreement or the transactions contemplated hereby or any action taken or to be taken pursuant hereto. There is no action, suit, claim, investigation or proceeding pending or, to the Knowledge of the Company, threatened, against or involving the Company, any Subsidiary, or any of their respective properties or assets that would reasonably be expected to result in a Material Adverse Effect. No judgment, order, writ, injunction or decree or award has been issued by or, to the Knowledge of the Company, requested of any court, arbitrator or governmental agency which would reasonably be expected to result in a Material Adverse Effect.

4.7 ***Compliance with Law***. The business of the Company has been and is presently being conducted in accordance with all applicable federal, state and local governmental laws, rules, regulations and ordinances, except as would not reasonably be expected to cause a Material Adverse Effect. The Company holds all franchises, permits, licenses, consents and other governmental or regulatory authorizations and approvals necessary for the conduct of its business as now being conducted by it, except for such franchises, permits, licenses, consents

and other governmental or regulatory authorizations and approvals, the failure to possess which, individually or in the aggregate, would not reasonably be expected to result in a Material Adverse Effect.

4.8 ***License Agreement***

(a) *Agreements*. Attached hereto as Exhibit F-1 is a true, correct and complete copy of the License Agreement, including any plans, budgets, schedules, exhibits, ancillary agreements, instruments, certificates or other documents attached thereto. Attached hereto as Exhibit F-2 and Exhibit F-3, respectively, are true, correct and complete copies of that certain letter agreement, dated May 17, 2016, by and between the Company and Licensee, that certain letter agreement, dated September 4, 2018, by and between the Company, Licensee, Agios International SARL and Celgene International II SARL, [**]. The Company has delivered to the Purchaser true, correct and complete copies of the following communications under the License Agreement since January 1, 2018: Royalty Reports, commercialization reports, commercialization plans and marketing reports that Licensee has delivered to the Company pursuant to the License Agreement and all written minutes of, and written documents delivered to participants at meetings of the JCC and of any subcommittees thereof. [**].

(b) *No Other Agreements*.

(i) Except for the Licensee Consent and the Licensee Instruction Letter, the License Agreement is the only agreement or instrument between the Company (or any predecessor or Affiliate thereof), on the one hand, and Licensee (or any predecessor or Affiliate thereof), on the other hand, relating, directly or indirectly, to the Licensed Product, the Licensed IP or the Royalty.

(ii) (1) Except for the License Agreement, the Licensee Consent and the Licensee Instruction Letter, and as set forth on Schedule 4.8(b)(ii)(1), there are no other agreements, instruments, arrangements or understandings between the Company (or any predecessor or any Affiliate thereof), on the one hand, and Licensee (or any predecessor or Affiliate thereof), on the other hand, including any Existing Third Party Agreements, that relate to the Licensed Product (including the development or commercialization thereof, including under any Commercialization Plan or any Development Plan or any related budgets), the Licensed IP, or the Royalty. (2) Except as set forth on Schedule 4.8(b)(ii)(2), there are no other amendments, supplements, modifications of, to or under the License Agreement as of the date hereof.

(iii) The Company has not waived or amended any provision of the License Agreement since July 14, 2014 that would reasonably be expected to result in a Material Adverse Effect. The Company has not, in the [**] prior to the date of this Agreement, proposed or received any proposal to waive or amend any provision of the License Agreement, except as set forth in the Licensee Consent (and drafts thereof exchanged between the Company and the Licensee). The Company does not have any plans to further amend or waive any provision of the License Agreement.

(c) *Licenses/Sublicenses*. The Company has not granted or consented to any license or sublicense in respect of the Company's rights and obligations under the License Agreement relating to the Licensed IP in the Territory and, to the Knowledge of the Company, there are no licenses or sublicenses entered into by Licensee or any other Person (or any predecessor or Affiliate thereof) in respect of Licensee's rights and obligations under the License Agreement relating to the Licensed IP in the Territory.

(d) *Validity and Enforceability*. The License Agreement is a valid and binding obligation of the Company and Licensee in accordance with its terms. The License Agreement is enforceable against the Company and Licensee in accordance with its terms, except as may be limited by applicable Bankruptcy Laws or by general principles of equity (whether considered in a proceeding in equity or at law) or by any Credit Event. The Company has not received any notice in connection with the License Agreement challenging the validity, enforceability or interpretation of any provision of such agreement, including Licensee's obligation to pay any portion of the Royalty without set-off of any kind.

(e) *Licensed Product*. The Licensed Product (i) is a Co-Commercialized Product and a Royalty-Bearing Product and (ii) is not a Failed Product, a Second Generation Product, a Split Product, a Buy-In Product, a Picked Product, a Celgene Reverted Product, an Agios Reverted Product or part of a Terminated Program or an Independent Program, in each case, under the License Agreement, and Licensee has validly exercised its Celgene Program Option under the License Agreement with respect to the Licensed Product. Licensee is contractually obligated under the License Agreement to pay royalties in accordance with Section 9.7(a) thereof on aggregate worldwide Annual Net Sales of the Licensed Product in the Territory, subject to Permitted Reductions. To the Knowledge of the Company, no development, regulatory, or commercial activities are being conducted for any "Licensed Product" (as such term is defined in the License Agreement) under the License Agreement except for the Licensed Product (as such term is defined herein).

(f) *No Liens or Assignments by the Company*. The Company has not, except for Permitted Liens or as contemplated hereby, conveyed, assigned or in any other way transferred or granted any Liens upon or with respect to all or any portion of its right, title and interest in and to the Royalty, the Licensed Product or the Licensed IP, nor has the Company consented to any such assignment, transfer or Lien.

(g) *No Waivers or Releases*. The Company has not granted any material waiver under the License Agreement with respect to the Royalty, the Licensed Product or the Licensed IP and has not released Licensee, in whole or in part, from any of its material obligations under the License Agreement with respect to the Royalty, the Licensed Product or the Licensed IP, including under any applicable Commercialization Plan for the Licensed Product or Development Plan for the Licensed Product or related budgets.

(h) *No Termination*. (i) The Company has not (1) given Licensee any notice of termination of the License Agreement in whole or any notice expressing any intention to terminate the License Agreement with respect to the Royalty, the Licensed Product or the

Licensed IP or as a whole or (2) received any notice of termination of the License Agreement in whole or any notice expressing any intention to terminate the License Agreement with respect to the Royalty, the Licensed Product or the Licensed IP or as a whole. (ii) To the Knowledge of the Company, no event has occurred that would give rise to the expiration or termination of the License Agreement with respect to the Royalty, the Licensed Product or the Licensed IP or as a whole. (iii) Except as set forth on Schedule 4.8(h), the Company has not (1) given Licensee any notice of termination of the License Agreement in part or (2) received any notice of termination of the License Agreement in part, and none of such notices of termination set forth on Schedule 4.8(h) relate to the Royalty, the Licensed Product or the Licensed IP.

(i) *No Breaches or Defaults*. There is and has been no material breach or default under any provision of the License Agreement either by the Company (or any predecessor or Affiliate thereof) or, to the Knowledge of the Company, by Licensee (or any predecessor or Affiliate thereof), and there is no event that upon notice or the passage of time, or both, would reasonably be expected to give rise to any material breach or default either by the Company or, to the Knowledge of the Company, by Licensee.

(j) *Payments Made*. To the Knowledge of the Company, the Company has received from Licensee the full amount of the payments due and payable under the License Agreement by Licensee to the Company.

(k) *No Indemnification Claims*. The Company has not notified Licensee or any other Person of any claims for indemnification under the License Agreement nor has the Company received any claims for indemnification under the License Agreement, whether pursuant to Article 13 thereof or otherwise. To the Knowledge of the Company, no event exists that would give rise to a claim for indemnification under the License Agreement with respect to the Licensed Product, the Licensed IP or the Royalty.

(l) *No Royalty Reductions*. The amount of the Royalty paid under Section 9.7 of the License Agreement has not been and, to the Knowledge of the Company, the amount of the Royalty due and payable under Section 9.7 of the License Agreement is not, as of the date hereof, subject to any claim against the Company pursuant to any right of set-off, counterclaim, or credit, by contract or otherwise, including any Permitted Reduction (a "Royalty Reduction"). To the Knowledge of the Company, no event or condition currently exists that, upon notice or otherwise, would permit Licensee to make, or have the right to make, any Royalty Reduction in respect of the Royalty.

(m) *No Notice of Infringement*. The Company has not received any written notice from, or given any written notice to, Licensee pursuant to Section 10.3(a) or Section 10.4(a) of the License Agreement.

(n) *Audits*. Since April 14, 2010, neither the Company nor Licensee has initiated, pursuant to Section 9.10 of the License Agreement, any inspection or audit of books of accounts or other records pertaining to Net Sales of the Licensed Product or the Royalty or other amounts payable by Licensee to the Company under the License Agreement related to the

Licensed Product or the Licensed IP, including any applicable Commercialization Plans or Development Plans or related budgets.

4.9 ***Title to Royalty***. The Company has good and marketable title to the Royalty free and clear of all Liens (other than Permitted Liens). Upon payment of the Purchase Price to the Company by the Purchaser at the Closing, the Purchaser will acquire, subject to the terms and conditions set forth in this Agreement and the License Agreement, good and marketable title to the Royalty, free and clear of all Liens (other than Liens created by the Purchaser).

4.10 ***Intellectual Property***.

(a) Schedule 4.10(a)(i) of the Disclosure Schedule lists all Licensed Agios Patents. The Company Controls all of the Licensed Agios Patents. To the Knowledge of the Company, the Company and Licensee collectively are the sole owners of, and collectively have the sole interest in, the Joint Patents, and the Company is the sole owner of, and has the sole interest in, its undivided half interest in each of the Joint Patents. Schedule 4.10(a)(i) of the Disclosure Schedule specifies as to each of the Licensed Agios Patents, as applicable, the jurisdictions by or in which each such patent has issued as a patent or such patent application has been filed, including the respective patent numbers and application numbers and issue and filing dates, and, solely with respect to the Licensed Agios Patents for which the Company controls prosecution and maintenance, the record owner of each such patent or patent application.

(b) To the Knowledge of the Company, there are no pending or threatened litigations, interferences, reexamination, oppositions or like procedures involving any Licensed Agios Patent.

(c) All of the issued Licensed Agios Patents for which the Company controls prosecution and maintenance, and to the Knowledge of the Company all of the issued Licensed Agios Patents for which the Company does not control prosecution and maintenance, are in full force and effect and have not lapsed, expired or otherwise terminated. To the Knowledge of the Company all of the issued Licensed Agios Patents are valid and enforceable. The Company has not received any written notice relating to the lapse, expiration or other termination of any of the issued Licensed Agios Patents, or any written legal opinion that alleges that any of the issued Licensed Agios Patents is invalid or unenforceable.

(d) There is no Person who is, or claims to be, an inventor under any of the (i) owned Licensed Agios Patents that are not Joint Patents or [**].

(e) The Company has not, and, to the Knowledge of the Company, Licensee has not, received any written notice of any claim by any Person challenging inventorship or ownership of, the rights of the Company or Licensee, as applicable, in and to, or the patentability, validity or enforceability of, any Licensed Agios Patent, or asserting that the development, manufacture, importation, sale, offer for sale or use of the Licensed Product infringes any patent or other intellectual property rights of such Person.

(f) To the Knowledge of the Company, the discovery and development of the Licensed Product did not and has not infringed, violated or misused any patent or other intellectual property rights owned by any third party. The Company has not, and, to the Knowledge of the Company, Licensee has not, in-licensed any intellectual property right covering the manufacture, use, sale, offer for sale or import of the Licensed Product.

(g) To the Knowledge of the Company, the manufacture, use, marketing, sale, offer for sale, importation or distribution of the Licensed Product does not infringe, misappropriate or otherwise violate any patent rights or other intellectual property rights owned by any other Person.

(h) To the Knowledge of the Company there has been no Competitive Infringement of the Licensed Agios Patents by any third party.

(i) All required maintenance fees, annuities and like payments with respect to the Licensed Agios Patents for which Company controls the prosecution and maintenance in accordance with Section 10.2 of the License Agreement, and to the Knowledge of the Company, with respect to all other Licensed Agios Patents, have been timely paid.

4.11 ***UCC Representation and Warranties***. The Company's exact legal name is, and for the immediately preceding ten years has been, "Agios Pharmaceuticals, Inc.". The Company is, and for the prior ten years has been, incorporated under the laws of the State of Delaware.

4.12 ***Brokers***. Other than Cowen and Company, LLC, there is no investment banker, broker, finder, financial advisor or other intermediary who has been retained by or is authorized to act on behalf of the Company who might be entitled to any fee or commission in connection with the transactions contemplated by this Agreement.

SECTION 5

Representations and Warranties of the Purchaser

The Purchaser hereby represents and warrants the following as of the date hereof:

5.1 ***Experience***. The Purchaser is experienced in evaluating companies such as the Company, has such knowledge and experience in financial and business matters that the Purchaser is capable of evaluating the merits and risks of the Purchaser's prospective investment in the Company, and has the ability to bear the economic risks of the investment. The Purchaser has sufficient cash to pay the Purchase Price at the Closing and acknowledges that its obligations under this Agreement are not contingent on obtaining financing.

5.2 ***Access to Information***. The Purchaser has received and reviewed information about the Company and has had an opportunity to discuss the Company's business, management and financial affairs with its management and to review the Company's facilities. The Purchaser has had a full opportunity to ask questions of and receive answers from the

Company, or any person or persons acting on behalf of the Company, concerning the terms and conditions of the purchase of the Royalty. The Purchaser is not relying upon, and has not relied upon, any statement, representation or warranty made by any person, except for the statements, representations and warranties contained in this Agreement.

5.3 ***Enforceability***. This Agreement when executed and delivered by the Purchaser will constitute a valid and legally binding obligation of the Purchaser, enforceable in accordance with its terms, subject to: (i) judicial principles respecting election of remedies or limiting the availability of specific performance, injunctive relief, and other equitable remedies; and (ii) Bankruptcy Laws.

5.4 ***Authorization***. The Purchaser has the requisite trust power and authority to enter into and perform its obligations under the Transaction Documents. The execution, delivery and performance of the Transaction Documents by the Purchaser and the consummation by the Purchaser of the transactions contemplated thereby have been duly authorized by all necessary corporate action on the part of its owner trustee and no further consent or authorization of the Purchaser and its owner trustee is required.

5.5 ***No Conflicts***.

(a) The execution, delivery and performance of this Agreement, and any other document or instrument contemplated hereby, by the Purchaser and the consummation by the Purchaser of the transactions contemplated hereby, do not and will not:

(i)violate any provision of the organizational documents of the Purchaser;

(ii)conflict with, or constitute a default (or an event which with notice or lapse of time or both would become a default) under, or give to others any rights of termination, amendment, acceleration or cancellation of, any material agreement, mortgage, deed of trust, indenture, note, bond, license, lease agreement, instrument or obligation to which the Purchaser is a party;

(iii)result in a violation of any federal, state, local or foreign statute, rule, regulation, order, writ, judgment or decree (including federal and state securities laws and regulations) applicable to the Purchaser or any of its Subsidiaries; or

(iv)require any consent of any third-party that has not been obtained pursuant to any material contract to which the Purchaser is subject.

(b) Assuming the accuracy of the relevant representations and agreements of the Company set forth herein, the Purchaser is not required to obtain any consent, waiver, authorization or order of, give any notice to, or make any filing or registration with, any court or other federal, state, local or other governmental agency or other Person in connection with the execution, delivery or performance of any of its obligations under the Transaction Documents,

other than any required filings or approvals under the Exchange Act or the rules of the Commission.

SECTION 6

Covenants

6.1 ***Disclosures***. Except for a press release previously approved in form and substance by the Company and the Purchaser, or any other public announcement using substantially the same text as such press release, neither the Company nor the Purchaser shall, and each party hereto shall cause its respective Representatives, Affiliates and Affiliates' Representatives not to, issue a press release or other public announcement or otherwise make any public disclosure with respect to the Transaction Documents or the subject matter hereof without the prior written consent of the other party hereto (which consent shall not be unreasonably withheld, conditioned or delayed), except as may be required by applicable law or stock exchange rule (in which case the party hereto required to make the press release or other public announcement or disclosure shall allow the other party hereto reasonable time to comment on such press release or other public announcement or disclosure in advance of such issuance).

6.2 ***Payments Received in Error; Interest***.

(a) Commencing on the Closing Date and at all times thereafter, if any payment of any portion of the Royalty is made to the Company, the Company shall pay such amount to the Purchaser, promptly (and in any event within [**] after the date on which the Company is notified of such payment) after the receipt thereof, by wire transfer of immediately available funds to an account designated in writing by the Purchaser, without any deduction, recoupment or offset for any reason whatsoever. The Company shall notify the Purchaser of such wire transfer and provide reasonable details regarding the Royalty payment so received by the Company. The Company agrees that, in the event any portion of the Royalty is paid to the Company, the Company (i) until paid to the Purchaser, shall hold such payment received in trust for the benefit of the Purchaser, and (ii) shall have no right, title or interest in such payment and shall not pledge or otherwise grant any Lien on such payment.

(b) Commencing on the Closing Date and at all times thereafter, if any payment due under the License Agreement that does not constitute the Royalty is made to the Purchaser, the Purchaser shall pay such amount to the Company, promptly (and in any event within [**] after the date on which the Purchaser is notified of such payment) after the receipt thereof, by wire transfer of immediately available funds to an account designated in writing by the Company, without any deduction, recoupment or offset for any reason whatsoever. The Purchaser shall notify the Company of such wire transfer and provide reasonable details regarding the erroneous payment so received by the Purchaser. The Purchaser agrees that, in the event any payment due under the License Agreement that does not constitute the Royalty is paid to the Purchaser, the Purchaser (i) until paid to the Company, shall hold such payment received

in trust for the benefit of the Company, and (ii) shall have no right, title or interest in such payment and shall not pledge or otherwise grant any Lien on such payment.

(c) Promptly (and in any event within [**]) after the date on which the Purchaser receives payment of the Royalty in respect of Net Sales for the period commencing April 1, 2020 and ending June 30, 2020, the Purchaser shall pay to the Company (by wire transfer of immediately available funds to an account designated in writing by the Company, without any deduction, recoupment or offset for any reason whatsoever) an amount equal to [**] percent ([**]%) of the amount of such payment of the Royalty received by the Purchaser for such period (the "Q2 Company Share"). The Purchaser shall notify the Company of such wire transfer. Until paid to the Company, the Purchaser shall hold the Q2 Company Share for the benefit of the Company and shall have no right, title or interest in the Q2 Company Share and shall not pledge or otherwise grant any Lien on the Q2 Company Share.

(d) If the Royalty paid for any period commencing on April 1, 2020 or later is reduced (other than as a result of a Permitted Reduction) by Licensee in a manner permitted by the License Agreement due to an overestimate by the Licensee of Net Sales for any period prior to April 1, 2020 to less than the amount that would have been received by the Purchaser had such overestimate not occurred (the amount of such reduction in the Royalty, the "Shortfall Amount"), then the Company shall promptly pay the Purchaser the Shortfall Amount (or, in the case of the period from April 1, 2020 to June 30, 2020, [**] percent ([**]%) of the Shortfall Amount). If the Royalty paid for any period commencing on April 1, 2020 or later is increased by Licensee in a manner permitted by the License Agreement due to an underestimate by the Licensee of Net Sales for any period prior to April 1, 2020 to more than the amount that would have been received by the Purchaser had such underpayment underestimate not occurred (the amount of such increase in the Royalty, the "Excess Amount"), then the Purchaser shall promptly pay the Company the Excess Amount (or, for the period from April 1, 2020 to June 30, 2020, [**] percent ([**]%) of the Excess Amount.

(e) A late fee of [**]% over the Prime Rate shall accrue on all unpaid amounts with respect to any sum payable under Section 6.2(a), 6.2(b), 6.2(c) or 6.2(d) beginning [**] after payee's receipt of notice from the other party hereto of such erroneous payment.

6.3 ***Royalty Reduction***. If Licensee exercises any Royalty Reduction against any payment of the Royalty other than a Permitted Reduction, and if such Royalty Reduction reduces any amount paid to the Purchaser in respect of the Royalty to less than the amount that would have been received by the Purchaser in respect of the Royalty had such Royalty Reduction not been exercised by Licensee, then the Company shall promptly (and in any event within [**] following the Company's receipt of notice from the Purchaser of the payment of the Royalty affected by such Royalty Reduction) make a true-up payment to the Purchaser such that the Purchaser receives the full amount of such Royalty payment that would have been payable to the Purchaser had such Royalty Reduction not occurred. For the avoidance of doubt, any nonpayment by Licensee as a result of a Credit Event shall not constitute a Royalty Reduction

for purposes of this Section 6.3 and shall not obligate the Company to make any payment under this Section 6.3.

6.4 ***Royalty Reports and Other Information; Plans***. Promptly (and in any event within [**]) following the receipt by the Company of any IDHIFA Confidential Information (as defined in the Licensee Consent) or any Disclosed Information that the Licensee has not provided to the Purchaser directly, the Company shall furnish a true, correct and complete copy of the same to the Purchaser. On a calendar quarterly basis, the Company shall deliver to the Purchaser an updated copy of Schedule 4.10(a)(i).

6.5 ***Notices to the Licensee***. The Company and the Purchaser shall consult prior to the Company sending any material written notice to Licensee relating to, directly or indirectly, the Licensed Product, the Licensed IP, the Royalty or the License Agreement. The Company shall not send any such notice without the prior written consent of the Purchaser (which consent shall not be unreasonably withheld, conditioned or delayed). The Company shall send to the Licensee such notices as the Purchaser shall reasonably request.

6.6 ***Inspections and Audits***.

(a) At the written request of the Purchaser, the Company shall, to the extent permitted under Section 9.10 of the License Agreement, cause an inspection or audit by an internationally recognized independent accounting firm to be made for the purpose of determining the correctness of, or to ensure compliance with the License Agreement that would reasonably be expected to impact, the Royalty payments made under the License Agreement. With respect to any inspection requested by the Purchaser, the Company shall, for purposes of Section 9.10 of the License Agreement, select such independent accounting firm as the Purchaser shall select for such purpose (subject to the Licensee's right of reasonable objection to such firm as provided in Section 9.10 of the License Agreement). The Company shall not, without the Purchaser's prior written consent, cause an inspection or audit to be made under Section 9.10 of the License Agreement with respect to the Royalty. The Purchaser shall pay the Company the expenses of any inspection or audit (including the fees and expenses of such independent public accounting firm designated for such purpose) undertaken at the Purchaser's request that would otherwise be borne by the Company pursuant to the License Agreement (if and as such expenses are actually incurred by the Company). Notwithstanding the foregoing, in the event that the Company desires to exercise its audit right in a given Calendar Year with respect to the Sales Milestone, the Company shall notify the Purchaser and the parties shall reasonably cooperate on the Company's exercise of its audit right under the License Agreement for such Calendar Year.

6.7 ***Amendment or Assignment of License Agreement***. The Company shall not, without the Purchaser's prior written consent, assign, amend, modify, supplement or restate (or consent to any assignment, amendment, modification, supplement or restatement of) any provision of the License Agreement that directly or indirectly relates to or could reasonably be expected to impact the Licensed Product, the Licensed IP or the Royalty, including the overall effectiveness of the License Agreement or the Company's ability to satisfy its obligations

thereunder. Subject to the foregoing, promptly, and in any event within [**], following receipt by the Company of any final assignment, amendment, modification, supplement or restatement of the License Agreement, the Company shall furnish a copy of the same to the Purchaser.

6.8 ***Maintenance of Agreements***. The Company shall comply in all material respects with its obligations under the License Agreement, including any Commercialization Plan and Development Plan and related budgets pertaining directly or indirectly to the Licensed Product, and shall not take any action or forego any action that would reasonably be expected to constitute a material breach thereof or default thereunder by the Company. The Company may exercise its rights under Section 2.11 or Section 6.3(g) of the License Agreement without the prior written consent of the Purchaser, provided that the Company provides prior written notice to the Purchaser of its intention to exercise such rights. Promptly, and in any event within [**], after receipt of any (written or oral) notice from Licensee of an alleged breach or default by the Company under the License Agreement, the Company shall give notice thereof to the Purchaser, including delivering to the Purchaser a copy of any such written notice. The Company shall use its reasonable best efforts to cure any breaches or defaults by it under the License Agreement and shall give written notice to the Purchaser upon curing any such breach or default. The Company shall consult with the Purchaser as to any action the Company proposes to take to dispute or cure any alleged breach or default under the License Agreement, and in connection with any dispute regarding an alleged breach or default under the License Agreement, shall employ such counsel, reasonably acceptable to the Company, as the Purchaser may select. The Company shall not, without the prior consent of the Purchaser, (a) forgive, release or compromise any amount owed to or becoming owed to the Company under the License Agreement in respect of the Royalty or (b) waive any obligation of, or grant any consent to, Licensee under, in respect of or related to the Royalty, provided that neither the occurrence of a Credit Event nor any automatic effect of a Credit Event under the License Agreement without an affirmative action of the Company shall itself be deemed any forgiving, release, compromise, waiver or consent by the Company. The Company shall not exercise or enforce its applicable rights under the License Agreement in any manner that would be reasonably be expected to result in a Material Adverse Effect.

6.9 ***Enforcement of Agreements***.

(a) Notice of Breaches by Licensee. Promptly (and in any event within [**]) after the Company becomes aware of, or comes to believe in good faith that there has been, a breach of the License Agreement by Licensee, the Company shall provide notice of such breach to the Purchaser. In addition, the Company shall provide to the Purchaser a copy of any written notice of breach or alleged breach of the License Agreement delivered by the Company to Licensee as soon as practicable and in any event not less than [**] following such delivery.

(b) Enforcement of License Agreement. In the case of any breach by Licensee referred to in Section 6.9(a), the Company shall consult with the Purchaser regarding the timing, manner and conduct of any enforcement of Licensee's obligations under the License Agreement. The Company shall, (i) if requested in writing by the Purchaser, within [**] after receipt of such request, exercise such rights and remedies relating to any such breach related

directly or indirectly to the Licensed Product, the Licensed IP or the Royalty as shall be available to the Company, whether under the License Agreement or by operation of law, as instructed by the Purchaser, and (ii) if requested by the Purchaser, the Company shall employ such counsel reasonably acceptable to the Company as the Purchaser shall recommend for such purpose; provided, however, that nothing herein shall limit the Company's exercise of its rights under the License Agreement (in its sole discretion and at its own cost and expense) related to the Company's rights, and the Licensee's obligations, with respect to the Sales Milestone or achievement thereof.

(c) Allocation of Proceeds and Costs of Enforcement. The Purchaser shall pay all costs and expenses incurred by the Purchaser and the Company (including the fees and expenses of attorneys engaged jointly or separately by the Purchaser and the Company) of any enforcement pursuant to this Section 6.9 undertaken at the Purchaser's request, as they are incurred and paid. All Proceeds resulting from any enforcement of Licensee's obligations under the License Agreement that relate to the Royalty and are undertaken at the Purchaser's request shall be paid to the Purchaser net of any such costs and expenses then remaining unpaid. The Company hereby assigns and, if not presently assignable, agrees to assign to the Purchaser the amount of Proceeds due to the Purchaser in accordance with this Section 6.9(c).

6.10 ***Termination of Agreements***.

(a) The Company shall not exercise any right to terminate the License Agreement, agree with Licensee to terminate the License Agreement, or take, or permit any Affiliate or sublicensee to take, any action that would reasonably be expected to give Licensee the right to terminate the License Agreement, under Article 14 of the License Agreement, in each case, except with the prior written consent of the Purchaser, provided that in no event shall the Company be obligated to prevent any termination of the License Agreement as a result of a Credit Event so long as such termination is not also a result of any affirmative action of the Company.

(b)

(i) If the License Agreement is terminated in whole or in part by Licensee pursuant to Section 14.2(a) of the License Agreement or by the Company pursuant to Section 14.2(b) of the License Agreement, then the Company shall (i) act as reasonably instructed by the Purchaser in pursuing and otherwise exercising the non-exclusive license to the Celgene Collaboration Intellectual Property granted to it under Section 14.3(a)(iv)(B) of the License Agreement and to obtain receipt of the summary report provided for in Section 14.3(a)(iv)(A) of the License Agreement (and promptly, and in any event within [**] after receipt by the Company thereof, deliver such report to the Purchaser) and (ii) if requested in writing by the Purchaser and at the Purchaser's cost and expense, act as reasonably instructed by the Purchaser in exercising such other rights provided to it under Section 14.3 of the License Agreement to effectuate the grant of the licenses and other rights provided for under Section 14.3 of the License Agreement with respect to the Licensed IP and the Celgene Collaboration

Intellectual Property (those rights provided in the foregoing clauses (i) and (ii) collectively, the "Reversionary Rights").

(ii) The Purchaser shall have the exclusive right to negotiate one or more licenses or sublicenses to Commercialize the Licensed Product with one or more third parties (each, a "New Licensee") under the Reversionary Rights (each such license or sublicense, a "New Arrangement"). Notwithstanding such exclusive right, during the [**] period following any such termination of the License Agreement, the Company may submit a reasonably detailed written offer to the Purchaser to Commercialize the Licensed Product under a New Arrangement and for [**] thereafter the Purchaser shall negotiate a New Arrangement exclusively with the Company. The Company shall reasonably cooperate with the Purchaser, at the Purchaser's direction, cost and expense, in connection with the negotiation, execution and delivery of any New Arrangement. Any New Arrangement shall not include terms, conditions and limitations that are, in the aggregate, more burdensome to the Company than those contained in the License Agreement. The Company's rights and obligations under this Agreement in respect of the License Agreement shall apply to any New Arrangement *mutatis mutandis* (as applicable to such New Arrangement). The Purchaser shall reimburse the Company for any reasonable and documented third party expenses (including attorneys' fees) incurred by the Company in connection with the pursuit, negotiation or execution of any New Arrangement with a third party. As soon as practicable following the execution of any New Arrangement by each party thereto, the Purchaser and the Company shall cooperate with one another to enter into new agreements (or to make amendments to this Agreement, the Bill of Sale, the Licensee Instruction Letter and such other documents and the Purchaser may reasonably request) to effect the foregoing.

6.11 ***Preservation of Rights***. The Company shall not hereafter sell, transfer, hypothecate, assign or in any manner convey or mortgage, pledge or grant a security interest or other encumbrance of any kind in any portion of the Licensed Agios Patents or the License Agreement, except that the Company may transfer all or substantially all of its assets and business to which the Licensed Agios Patents and the License Agreement relate as long as (i) in connection therewith the counterparty thereto assumes the obligations of the Company hereunder in a writing in form and substance reasonably satisfactory to the Purchaser and (ii) such transaction does not require the Licensee to deduct or withhold from payments of the Royalty any additional taxes pursuant to Section 9.11 of the License Agreement. The Company shall not hereafter subject to a Lien (other than a Permitted Lien), sell, transfer, assign, convey title (in whole or in part), grant any right to, or otherwise dispose of any portion of the Royalty.

6.12 ***Enforcement; Infringement Claims***.

(a) The Company shall promptly inform the Purchaser of any known or alleged infringement by a third party of any of the Licensed Agios Patents. The Company shall provide to the Purchaser a copy of any written notice of any known or alleged infringement in the Territory of any of the Licensed Agios Patents delivered or received under Section 10.3(a) of the License Agreement or otherwise as soon as practicable and in any event not less than [**] following such delivery.

(b) If the Company has the right to initiate an enforcement action with respect to Competitive Infringement as set forth in Section 10.3(b) or 10.3(c) of the License Agreement, the Company shall, if requested in writing by the Purchaser, promptly after receipt of such request (and, provided that the Purchaser provides such request at least [**] prior to the deadline provided for in Section 10.3(c) of the License Agreement, no later than such deadline), exercise such right as instructed by the Purchaser and, if requested by the Purchaser, the Company shall employ such counsel reasonably acceptable to the Company as the Purchaser shall recommend for such purpose. The Purchaser shall pay all fees and expenses of such counsel. The Company shall not commence or join any action for Competitive Infringement under Section 10.3(b) or 10.3(c) of the License Agreement without the Purchaser's prior written consent.

(c) The Company shall use commercially reasonable efforts to, or shall cause another Person to, in each case at the sole expense of the Company, (i) take any and all actions, and prepare, execute, deliver and file any and all agreements, documents and instruments, that are reasonably necessary or desirable to diligently prosecute, preserve and maintain the Licensed Agios Patents for which it controls the prosecution and maintenance in accordance with Section 10.2 of the License Agreement that are necessary or useful to develop, make, have made, use, sell, have sold, import or export the Licensed Product, including payment of maintenance fees or annuities on any such Licensed Agios Patents, (ii) prosecute any corrections, substitutions, reissues, reviews and reexaminations of the Licensed Agios Patents for which it controls the prosecution and maintenance in accordance with Section 10.2 of the License Agreement and any other forms of patent term restoration in any applicable jurisdiction in accordance with Section 10.5 of the License Agreement, (iii) diligently defend the Licensed Agios Patents for which it controls the defense in accordance with Section 10.4 of the License Agreement against interference or like proceedings by any other Person, and against any claims of invalidity or unenforceability, in any jurisdiction (including by bringing any legal action for infringement or defending any counterclaim of invalidity or action of a third party for declaratory judgment of non-infringement or non-interference), and (iv) not disclaim or abandon, or fail to take any action necessary or desirable to prevent the disclaimer or abandonment (including through lack of enforcement against third party infringers), of the Licensed Agios Patents for which it controls the prosecution and maintenance in accordance with Section 10.2 of the License Agreement. For purposes of compliance with this Section 6.12(c), the Company shall reasonably consider the Purchaser's recommendations of counsel for such purpose. Notwithstanding the foregoing, to the extent the Company decides not to file any such Licensed Agios Patent in the Territory or intends to allow such Licensed Agios Patent to lapse or become abandoned without having first filed a substitute and Licensee does not exercise its step-in rights under Section 10.2(a) of the License Agreement in respect of such Licensed Agios Patent, the Company shall notify and consult with the Purchaser on such decision or intention at least [**] prior to the date upon which such Licensed Agios Patent shall lapse or become abandoned, and, to the extent the Licensee has declined to step-in to assume, as applicable, the filing, prosecution or maintenance of such Licensed Agios Patent in accordance with Section 10.2(a) of the License Agreement, the Purchaser shall thereupon have the right (but not the obligation) to assume the same at its own expense with counsel of its own choice.

In such case, the Company shall use commercially reasonable efforts to transfer such prosecution and maintenance to the Purchaser, at the sole cost of the Purchaser.

6.13 ***Further Assurances***. From and after the Closing, each of the Company and the Purchaser shall execute and deliver such additional documents (including the Specified Financing Statements, other financing statements and continuation statements in respect thereof), certificates and instruments, and perform such additional acts, as may be reasonably requested and necessary or appropriate to carry out all of the provisions of this Agreement and to give full effect to and consummate the transactions contemplated by this Agreement, including to (a) perfect the sale, assignment, transfer and conveyance of the Royalty to the Purchaser pursuant to this Agreement, (b) perfect, more fully evidence and vest in the Purchaser good, valid and marketable right and interest in and to the Royalty free and clear of all Liens (other than those contemplated by this Agreement) and (c) create, evidence and perfect the security interest granted to the Purchaser pursuant to Section 2.4. The Company shall not (i) liquidate or dissolve, (ii) initiate any bankruptcy or insolvency proceeding relating to the Company, or (iii) without at least [**] prior written notice to the Purchaser (A) change its jurisdiction of organization, (B) change its organizational structure or type, (C) change its legal name or (D) change any organizational number (if any) assigned by its jurisdiction of organization.

SECTION 7

Confidentiality

7.1 ***Confidentiality***. Except as provided in this Section 7 or otherwise agreed in writing by the parties, the parties hereto agree that, during the term of this Agreement and for [**] thereafter, each party (the "Receiving Party") shall keep confidential and shall not publish or otherwise disclose and shall not use for any purpose other than as provided for in this Agreement (which includes the exercise of any rights or the performance of any obligations hereunder) any information furnished to it by or on behalf of the other party (the "Disclosing Party") pursuant to this Agreement (such information, "Confidential Information" of the Disclosing Party), except for that portion of such information that:

(a) was already known to the Receiving Party, other than under an obligation of confidentiality, at the time of disclosure by the Disclosing Party;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the Receiving Party in breach of this Agreement;

(d) is independently developed by the Receiving Party or any of its Affiliates, as evidenced by written records, without the use of or reference of the Confidential Information; or

(e) is subsequently disclosed to the Receiving Party on a non-confidential basis by a third party without obligations of confidentiality with respect thereto.

7.2 ***Authorized Disclosure***.

(a) Either party may disclose Confidential Information to the extent such disclosure is reasonably necessary in the following situations:

(i)prosecuting or defending litigation;

(ii)complying with applicable laws and regulations, including regulations promulgated by securities exchanges;

(iii)complying with a valid order of a court of competent jurisdiction or other Governmental Entity;

(iv)for regulatory, tax or customs purposes;

(v)for audit purposes, provided that each recipient of Confidential Information must be bound by customary obligations of confidentiality and non-use prior to any such disclosure;

(vi)disclosure to its Affiliates and Representatives on a need-to-know basis, provided that each recipient of Confidential Information must be bound by customary obligations of confidentiality and non-use prior to any such disclosure;

(vii)upon the prior written consent of the Disclosing Party; or

(viii)disclosure to its actual or potential investors and co-investors, and other sources of funding, including debt financing, or potential partners, collaborators or acquirers, and their respective accountants, financial advisors and other professional representatives, provided, that such disclosure shall be made only to the extent (A) that the Disclosing Party determines in good faith that the information to be disclosed is material to an investment in the Disclosing Party and is customarily required to consummate such investment, financing transaction partnership, collaboration or acquisition and that each recipient of Confidential Information must be bound by customary obligations of confidentiality and non-use prior to any such disclosure, or (B) that the information is the sales of the Licensed Product and such information is to be included in the Purchaser’s financial reports to its investors.

(b) Notwithstanding the foregoing, in the event the Disclosing Party is required to make a disclosure of the Receiving Party’s Confidential Information pursuant to Sections 7.2(a)(i), (ii), (iii) or (iv), it will, except where impracticable, give reasonable advance notice to the Receiving Party of such disclosure and use reasonable efforts to secure confidential treatment of such information and to avoid and/or minimize the extent of such disclosure. In any event, the Purchaser shall not file any patent application based upon or using the Confidential Information of Company provided hereunder.

SECTION 8

Indemnification

8.1 ***Indemnification***. Each party (an "Indemnifying Party") hereby indemnifies and holds harmless the other party, such other party's respective officers, directors, employees, consultants, representatives and advisers, and any and all Affiliates of the foregoing (each of the foregoing, an "Indemnified Party") from and against all losses, liabilities, costs, damages and expense (including reasonable legal fees and expenses) (collectively, "Losses") suffered or incurred by any such Indemnified Party to the extent arising from, connected with or related to (a) breach of any representation or warranty of such Indemnifying Party in this Agreement; (b breach of any covenant or undertaking of any Indemnifying Party in this Agreement; and (c) in the case of Purchaser or its respective other Indemnified Parties, Licensee exercising its right under Section 14.2(b)(ii) to terminate the License Agreement and any related reduction in the amount of the Royalty pursuant to Section 14.3(b)(ii)) of the License Agreement; provided that, with respect to clauses (a), (b) and (c), in no event shall the Company be liable for any Losses as a result of any Credit Event or any Permitted Reduction. Notwithstanding anything herein to the contrary, if Licensee exercises its right under Section 14.2(b)(ii) of the License Agreement to terminate the License Agreement: (i) the Losses which the Purchaser shall be entitled to recover under clause (c) of the immediately preceding sentence shall be equal to [**] percent ([**]%) of then projected net present value of the Royalty (the "Reduced Royalty Value"); (ii) the Company and the Purchaser agree that the Reduced Royalty Value shall be determined based upon (1) a discount rate equal to the then applicable federal rate (AFR), based upon the then projected duration of the Royalty, and (2) consensus Wall Street analyst projections of Net Sales of the Licensed Product; and (iii) Company will automatically owe the Purchaser the Reduced Royalty Value within [**] of Licensee exercising its right under Section 14.2(b)(ii) to terminate the License Agreement (without any requirement for notice from, or other action by, the Purchaser). In calculating Losses of the Purchaser under clause (a) or clause (b) of the first sentence of this Section 8.1, all such Losses shall be reduced by the projected net present value of any amounts payable to the Purchaser under any New Arrangement, with net present value determined in accordance with the immediately preceding sentence. If an event or omission (including, without limitation, any claim asserted or action or proceeding commenced by a third party) occurs which an Indemnified Party asserts to be an indemnifiable event pursuant to this Section 8, the Indemnified Party will provide written notice to the Indemnifying Party, setting forth the nature of the claim and the basis for indemnification under this Agreement. The Indemnified Party will give such written notice to the Indemnifying Party promptly after it becomes aware of the existence of any such event or occurrence. Such notice will be a condition precedent to any obligation of the Indemnifying Party to act under this Agreement but will not relieve it of its obligations under the indemnity except to the extent that the failure to provide prompt notice as provided in this Agreement prejudices the Indemnifying Party with respect to the transactions contemplated by this Agreement and to the defense of the liability. In case any such action is brought by a third party against any Indemnified Party and it notifies the Indemnifying Party of the commencement thereof, the Indemnifying Party will be entitled to participate therein and, to the extent that it wishes, to assume the defense and settlement thereof with counsel reasonably selected by it and, after notice from the Indemnifying Party to the

Indemnified Party of such election so to assume the defense and settlement thereof, the Indemnifying Party will not be liable to the Indemnified Party for any legal expenses of other counsel or any other expenses subsequently incurred by such Indemnified Party in connection with the defense thereof, provided, however, that an Indemnified Party shall have the right to employ separate counsel at the expense of the Indemnifying Party if (i) the employment thereof has been specifically authorized in writing by the Indemnifying Party; or (ii) representation of both parties by the same counsel would be inappropriate due to actual or potential conflicts of interests between such parties (which such judgment shall be made by counsel to the Indemnified Party in good faith). The Indemnified Party agrees to cooperate fully with (and to provide all relevant documents and records and make all relevant personnel available to) the Indemnifying Party and its counsel, as reasonably requested, in the defense of any such asserted claim at no additional cost to the Indemnifying Party. No Indemnifying Party will consent to the entry of any judgment or enter into any settlement with respect to any such asserted claim without the prior written consent of the Indemnified Party, not to be unreasonably withheld or delayed, (a) if such judgment or settlement does not include as an unconditional term thereof the giving by each claimant or plaintiff to each Indemnified Party of a release from all liability in respect to such claim or (b) if, as a result of such consent or settlement, injunctive or other equitable relief would be imposed against the Indemnified Party or such judgment or settlement would materially and adversely affect the business, operations or assets of the Indemnified Party. No Indemnified Party will consent to the entry of any judgment or enter into any settlement with respect to any such asserted claim without the prior written consent of the Indemnifying Party, not to be unreasonably withheld or delayed. If an Indemnifying Party makes a payment with respect to any claim under the representations or warranties set forth herein and the Indemnified Party subsequently receives from a third party or under the terms of any insurance policy a sum in respect of the same claim, the receiving party will repay to the other party such amount that is equal to the sum subsequently received.

8.2 ***Limitations on Liability***. No party hereto shall be liable for any punitive or special damages under this Section 8 (and no claim for indemnification hereunder shall be asserted) as a result of any breach or violation of any covenant or agreement of such party (including under this Section 8) in or pursuant to this Agreement. For the avoidance of doubt, and notwithstanding anything to the contrary in this Agreement, the Purchaser shall have no recourse against the Company as a result of any Credit Event or any Permitted Reduction.

8.3 ***Exclusive Remedy***. Except as set forth in Section 10.7, the rights of the parties hereto pursuant to (and subject to the conditions of) this Section 8 shall be the sole and exclusive remedy of the parties hereto and their respective Affiliates with respect to any Losses (whether based in contract, tort or otherwise) resulting from or relating to any breach of the representations, warranties covenants and agreements made under this Agreement or any certificate, document or instrument delivered hereunder, and each party hereto hereby waives, to the fullest extent permitted under applicable law, and agrees not to assert after Closing, any other claim or action in respect of any such breach. Notwithstanding the foregoing, claims for common law fraud shall not be waived or limited in any way by this Section 8.

SECTION 9

Termination

9.1 ***Automatic Termination***. This Agreement shall continue in full force and effect until sixty (60) days after such time as Licensee is no longer obligated to make any payments of the Royalty, at which point this Agreement shall automatically terminate, except with respect to any rights that shall have accrued prior to such termination.

9.2 ***Survival***. Notwithstanding anything to the contrary in this Section 9, the following provisions shall survive termination of this Agreement: Section 6.1 (Disclosures), Section 6.2 (Payments Received in Error; Interest), Section 6.6 (Inspections and Audits), Section 7 (Confidentiality), Section 8 (Indemnification), Section 9.2 (Survival) and Section 10 (Miscellaneous). Termination of the Agreement shall not relieve any party of liability in respect of breaches under this Agreement by any party on or prior to termination.

SECTION 10

Miscellaneous

10.1 ***Governing Law***. This Agreement shall be governed in all respects by the laws of the State of New York as applied to agreements entered into and performed entirely in the State of New York by residents thereof.

10.2 ***Successors, Assigns***. Except as otherwise provided herein, the provisions hereof shall inure to the benefit of, and be binding upon, the successors, assigns, heirs, executors and administrators of the parties hereto. Unless such assignment is made in accordance with Section 6.11, the Company may not assign (a) this Agreement, in part or in whole, (b) all or any portion of its interest in the Licensed IP or (c) all or any of its interest in the License Agreement without the prior written consent of the Purchaser. The Purchaser may assign this Agreement in part or in whole, provided that the Purchaser promptly thereafter notifies the Company and any such assignee promptly thereafter agrees in writing to be bound by all of the obligations of the Purchaser contained in this Agreement (if assigned in whole) or such of the Purchaser's obligations contained in this Agreement that are assigned (if assigned in part).

10.3 ***Notices***. All notices and other communications required or permitted hereunder shall be in writing and shall be sent by facsimile (receipt confirmed) or mailed by registered or certified mail, postage prepaid, return receipt requested, or otherwise delivered by hand or by messenger, addressed

if to the Purchaser, at the following address:

RPI Finance Trust
c/o RP Management, LLC
110 East 59th St, 33rd Floor
New York, NY 10022

Attention: [**]
Telephone: [**]
E-mail: [**]
Facsimile: [**]

with a copy, which shall not constitute notice, to:

Goodwin Procter LLP
100 Northern Avenue
Boston, Massachusetts 02210
Attention: Arthur McGivern and Robert Crawford
Telephone: (617) 570-1971; (617) 570-1255
Facsimile: (617) 523-1231
E-mail: AMcGivern@goodwinlaw.com; RCrawford@goodwinlaw.com

if to the Company, at the following address:

Agios Pharmaceuticals, Inc.
88 Sidney Street
Cambridge, MA, 02139
Attention: [**]
Telephone: [**]
E-mail: [**]

with a copy, which shall not constitute notice, to:

WilmerHale
Attention: Steven D. Barrett and George Shuster
Telephone: (617) 526-6000
Facsimile: (617) 526-5000
E-mail: steven.barrett@wilmerhale.com; george.shuster@wilmerhale.com

or at such other address as one party shall have furnished to the other party in writing. All notices and communications under this Agreement shall be deemed to have been duly given (i) when delivered by hand, if personally delivered, (ii) when received by a recipient, if sent by email, (iii) when sent, if sent by facsimile, with an acknowledgement of sending being produced by the sending facsimile machine or (iv) one Business Day following sending within the United States by overnight delivery via commercial one-day overnight courier service.

10.4 ***Expenses***. Each of the Company and the Purchaser shall bear its own expenses and legal fees incurred on its behalf with respect to this Agreement and the transactions contemplated hereby.

10.5 ***Finder's Fees***. Each of the Company and the Purchaser shall indemnify and hold the other harmless from any liability for any commission or compensation in the nature of

a finder's fee, placement fee or underwriter's discount (including the costs, expenses and legal fees of defending against such liability) for which the Company or the Purchaser, or any of its respective partners, employees, or representatives, as the case may be, is responsible.

10.6 ***Counterparts***. This Agreement may be executed in counterparts, each of which shall be enforceable against the party actually executing the counterpart, and all of which together shall constitute one instrument.

10.7 ***Specific Performance***. Each of the parties hereto acknowledges and agrees that the other party hereto would be damaged irreparably in the event any of the provisions of this Agreement are not performed in accordance with their specific terms or are otherwise breached or violated. Accordingly, notwithstanding Section 8.3, each of the parties hereto agrees that, without posting bond or other undertaking, the other party hereto shall be entitled to an injunction or injunctions to prevent breaches or violations of the provisions of this Agreement and to enforce specifically this Agreement and the terms and provisions hereof in any action, suit or other proceeding instituted in any court of the United States or any state thereof having jurisdiction over the parties and the matter in addition to any other remedy to which it may be entitled, at law or in equity. Each party further agrees that, in the event of any action for specific performance in respect of such breach or violation, it shall not assert the defense that a remedy at law would be inadequate.

10.8 ***Severability***. In the event that any provision of this Agreement becomes or is declared by a court of competent jurisdiction to be illegal, unenforceable or void, this Agreement shall continue in full force and effect without said provision; provided that no such severability shall be effective if it materially changes the economic benefit of this Agreement to any party.

10.9 ***Entire Agreement***. This Agreement, including the exhibits and schedules attached hereto and thereto, constitutes the full and entire understanding and agreement among the parties with regard to the subjects hereof and thereof, and this Agreement shall supersede any existing confidentiality agreements between the parties, including that certain Confidentiality Agreement by and between the Company and RP Management LLC, dated as of May 15, 2020, with all Confidential Information exchanged thereunder deemed Confidential Information hereunder and subject to the confidentiality and non-use restrictions set forth in Section 7. No party shall be liable or bound to any other party in any manner with regard to the subjects hereof or thereof by any warranties, representations or covenants except as specifically set forth herein or therein. Neither the Company, on the one hand, nor the Purchaser or any applicable Affiliate of the Purchaser, on the other hand, shall have any right to deduct or offset any amount owing to the other under this Agreement, or under any other agreement between the Company and the Purchaser or any Affiliate of the Purchaser.

10.10 ***Waiver***. The failure of either party to assert a right hereunder or to insist upon compliance with any term or condition of this Agreement shall not constitute a waiver of that right or excuse a similar subsequent failure to perform any such term or condition by the other

party. None of the terms, covenants and conditions of this Agreement can be waived except by the written consent of the party waiving compliance.

10.11 ***Trustee Capacity of Wilmington Trust***. Notwithstanding anything contained herein to the contrary, it is expressly understood and agreed by the parties hereto that (i) this Agreement is executed and delivered by Wilmington Trust, National Association, not individually or personally but solely in its trustee capacity, in the exercise of the powers and authority conferred and vested in it under the trust deed of the Purchaser, (ii) each of the representations, undertakings and agreements herein made on the part of the Purchaser is made and intended not as a personal representation, undertaking and agreement by Wilmington Trust, National Association but is made and intended for the purpose of binding only the Purchaser and (iii) under no circumstances shall Wilmington Trust, National Association be personally liable for the payment of any indebtedness or expenses of the Purchaser or be liable for the breach or failure of any obligation, representation, warranty or covenant made or undertaken by the Purchaser under this Agreement or any related documents.

[SIGNATURE PAGES FOLLOW]

IN WITNESS WHEREOF, the parties have executed this Royalty Purchase Agreement as of the date first set forth above.

AGIOS PHARMACEUTICALS, INC.

By: /s/ Andrew Hirsch
Name: Andrew Hirsch
Title: Chief Financial Officer

RPI 2019 INTERMEDIATE FINANCE TRUST

By: Wilmington Trust, National Association, not in its individual capacity but solely in its capacity as owner trustee

By: /s/ Cynthia Major
Name: Cynthia Major
Title: Banking Officer

Exhibit F-1

License Agreement

Incorporated by reference to Exhibits 10.11 and 10.12 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 filed with the Securities and Exchange Commission

Exhibit 31.1

CERTIFICATION

I, Jacqualyn A. Fouse, 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: July 30, 2020

/s/ Jacqualyn A. Fouse, Ph.D.

Jacqualyn A. Fouse, Ph.D.
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: July 30, 2020

/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, 2020, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Jacqualyn A. Fouse, Chief Executive Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to her 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: July 30, 2020

/s/ Jacqualyn A. Fouse, Ph.D.

Jacqualyn A. Fouse, Ph.D.
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, 2020, 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: July 30, 2020

/s/ Andrew Hirsch
Andrew Hirsch
Chief Financial Officer and Head of Corporate Development
(principal financial officer)