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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, 2019
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 26, 2019: 58,752,886

AGIOS PHARMACEUTICALS, INC.

FORM 10-Q

FOR THE THREE AND SIX MONTHS ENDED JUNE 30, 2019

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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements (Unaudited)

AGIOS PHARMACEUTICALS, INC.

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

	June 30, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 83,580	$ 70,502
Marketable securities	411,810	514,800
Accounts receivable, net	7,147	5,076
Collaboration receivable – related party	2,524	2,462
Collaboration receivable – other	2,222	670
Royalty receivable – related party	2,700	2,234
Inventory	4,659	869
Prepaid expenses and other current assets	19,063	17,167
Total current assets	533,705	613,780
Marketable securities	128,649	220,119
Operating lease assets	98,500	—
Property and equipment, net	23,016	24,320
Other non-current assets	—	238
Total assets	$ 783,870	$ 858,457
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 15,435	$ 17,880
Accrued expenses	49,218	42,147
Deferred revenue – related party	18,454	32,710
Operating lease liabilities	6,397	—
Deferred rent	—	766
Total current liabilities	89,504	93,503
Deferred revenue, net of current portion – related party	51,616	59,809
Operating lease liabilities, net of current portion	110,073	—
Deferred rent, net of current portion	—	17,608
Total liabilities	251,193	170,920
Stockholders' equity:		
Preferred stock, $0.001 par value; 25,000,000 shares authorized; no shares issued or outstanding at June 30, 2019 and December 31, 2018	—	—
Common stock, $0.001 par value; 125,000,000 shares authorized; 58,749,186 and 58,218,653 shares issued and outstanding at June 30, 2019 and December 31, 2018, respectively	59	58
Additional paid-in capital	1,839,710	1,794,283
Accumulated other comprehensive income (loss)	490	(2,171)
Accumulated deficit	(1,307,582)	(1,104,633)
Total stockholders' equity	532,677	687,537
Total liabilities and stockholders' equity	$ 783,870	$ 858,457

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	**2018**	**2019**	**2018**
Revenues:				
Product revenue, net	$ 13,727	$ —	$ 22,865	$ —
Collaboration revenue – related party	8,979	26,401	26,898	33,746
Collaboration revenue – other	812	12,440	1,782	12,440
Royalty revenue – related party	2,703	1,573	4,903	2,990
Total revenue	26,221	40,414	56,448	49,176
Cost and expenses:				
Cost of sales	303	—	637	—
Research and development	107,389	86,730	202,974	164,954
Selling, general and administrative	32,390	26,633	64,181	51,183
Total cost and expenses	140,082	113,363	267,792	216,137
Loss from operations	(113,861)	(72,949)	(211,344)	(166,961)
Interest income	3,990	4,204	8,395	7,391
Net loss	$ (109,871)	$ (68,745)	$ (202,949)	$ (159,570)
Net loss per share – basic and diluted	$ (1.87)	$ (1.19)	$ (3.46)	$ (2.81)
Weighted-average number of common shares used in computing net loss per share – basic and diluted	58,722,244	57,721,786	58,589,167	56,713,795

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	**2018**	**2019**	**2018**
Net loss	$ (109,871)	$ (68,745)	$ (202,949)	$ (159,570)
Other comprehensive income (loss)				
Unrealized gain (loss) on available-for-sale securities	974	245	2,661	(1,009)
Comprehensive loss	$ (108,897)	$ (68,500)	$ (200,288)	$ (160,579)

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

Condensed Consolidated Statements of Stockholders' Equity
(in thousands, except share amounts)
(Unaudited)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
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

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2017	48,826,153	$ 49	$ 1,174,904	$ (1,389)	$ (798,061)	$ 375,503
Issuance of common stock for follow-on offering	8,152,986	8	516,198	—	—	516,206
Common stock issued under stock incentive plan and ESPP	562,474	1	12,331	—	—	12,332
Stock-based compensation expense	—	—	14,522	—	—	14,522
Other comprehensive loss	—	—	—	(1,254)	—	(1,254)
Cumulative effect of ASC 606	—	—	—	—	39,456	39,456
Net loss	—	—	—	—	(90,825)	(90,825)
Other	—	—	(346)	—	—	(346)
Balance at March 31, 2018	57,541,613	$ 58	$ 1,717,609	$ (2,643)	$ (849,430)	$ 865,594
Common stock issued under stock incentive plan and ESPP	391,423	$ —	$ 9,638	$ —	$ —	$ 9,638
Stock-based compensation expense	—	—	16,455	—	—	16,455
Other comprehensive income	—	—	—	245	—	245
Net loss	—	—	—	—	(68,745)	(68,745)
Other	—	—	(45)	—	—	(45)
Balance at June 30, 2018	57,933,036	$ 58	$ 1,743,657	$ (2,398)	$ (918,175)	$ 823,142

See accompanying Notes to Condensed Consolidated Financial Statements.

AGIOS PHARMACEUTICALS, INC.

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

	Six Months Ended June 30,	
	2019	**2018**
Operating activities		
Net loss	$ (202,949)	$ (159,570)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	4,042	3,464
Stock-based compensation expense	36,655	30,977
Net accretion of premium and discounts on investments	(2,019)	(1,291)
(Gain) loss on disposal of property and equipment	—	(20)
Non-cash operating lease expense	4,208	—
Changes in operating assets and liabilities:		
Accounts receivable, net	(2,071)	—
Collaboration receivable – related party	(62)	(16,878)
Collaboration receivable – other	(1,552)	(440)
Royalty receivable – related party	(466)	(351)
Inventory	(3,790)	—
Prepaid expenses and other current and non-current assets	(2,517)	2,413
Accounts payable	(1,874)	(6,198)
Accrued expenses	7,071	(7,841)
Deferred revenue – related party	(22,449)	(10,644)
Operating lease liabilities	(3,649)	—
Deferred rent	—	(16)
Net cash used in operating activities	(191,422)	(166,395)
Investing activities		
Purchases of marketable securities	(144,231)	(592,664)
Proceeds from maturities and sales of marketable securities	343,372	331,666
Purchases of property and equipment	(3,309)	(2,793)
Net cash provided by (used in) investing activities	195,832	(263,791)
Financing activities		
Payment of public offering costs, net of reimbursements	—	(391)
Proceeds from public offering of common stock, net of commissions	—	516,206
Net proceeds from stock option exercises and employee stock purchase plan	8,668	21,970
Net cash provided by financing activities	8,668	537,785
Net change in cash and cash equivalents	13,078	107,599
Cash and cash equivalents at beginning of the period	70,502	102,724
Cash and cash equivalents at end of the period	$ 83,580	$ 210,323
Supplemental disclosure of non-cash investing and financing transactions		
Additions to property and equipment in accounts payable and accrued expenses	$ 535	$ 1,365
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 making transformative, first- or best-in-class medicines for the treatment of cancer and rare genetic diseases, or RGDs. To address both cancer and RGDs, 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, 2019, the condensed consolidated statements of operations, comprehensive loss and stockholders' equity for the three and six months ended June 30, 2019 and 2018, and the condensed consolidated statements of cash flows for the six months ended June 30, 2019 and 2018 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, 2019, our results of operations and stockholders' equity for the three and six months ended June 30, 2019 and 2018, and cash flows for the six months ended June 30, 2019 and 2018. 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, 2019 are not necessarily indicative of the results to be expected for the year ending December 31, 2019 or for any other future annual or interim period. The year-end condensed consolidated balance sheet data was derived from our audited financial statements, but does not include all disclosures required by U.S. generally accepted accounting principles, or U.S. GAAP. Accordingly, the condensed consolidated interim financial statements should be read in conjunction with the audited consolidated financial statements and notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 2018 that was filed with the Securities and Exchange Commission, or the SEC, on February 14, 2019.

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.

Liquidity

As of June 30, 2019, we had cash, cash equivalents and marketable securities of $624.0 million. Although we have incurred recurring losses and expect to continue to incur losses for the foreseeable future, we expect our cash, cash equivalents and marketable securities will be sufficient to fund current operations for at least the next twelve months from the issuance date of these financial statements.

2. Summary of Significant Accounting Policies

Leases

In February 2016, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2016-02, *Leases (Topic 842)*, which was codified as Accounting Standards Codification, or ASC, 842, *Leases*, and amended through subsequent ASUs. We adopted ASC 842 effective January 1, 2019 using the modified retrospective transition approach and elected the package of practical expedients, both provided for under ASU 2018-11, *Leases (Topic 842): Targeted Improvements*. The package of practical expedients allows us not to reassess whether contracts are or contain leases, lease classification, and whether initial direct costs qualify for capitalization. Additionally, as an accounting policy, we have chosen not to separate the non-lease components from the lease components for our building leases and, instead, accounted for non-lease and lease components as a single component.

Impact of Adoption of ASC 842

Upon adoption of ASC 842 on January 1, 2019, we recorded operating lease assets of $59.9 million and operating lease liabilities of $77.3 million. The adoption of ASC 842 did not have a material impact on our condensed consolidated statements of operations. Prior periods are presented in accordance with ASC 840, *Leases*.

Leases Accounting Policy

We determine if an arrangement is a lease at inception. An arrangement is determined to contain a lease if the contract conveys the right to control the use of an identified property, plant, or equipment for a period of time in exchange for consideration. If we can benefit from the various underlying assets of a lease on their own or together with other resources that are readily available, or if the various underlying assets are neither highly dependent on nor highly interrelated with other underlying assets in the arrangement, they are considered to be a separate lease component. In the event multiple underlying assets are identified, the lease consideration is allocated to the various components based on each of the component's relative fair value.

Operating lease assets represent our right to use an underlying asset for the lease term and operating lease liabilities represent our obligation to make lease payments arising from the leasing arrangement. Operating lease assets and liabilities are recognized at commencement date based on the present value of lease payments over the lease term. As most of our leases do not provide an implicit rate, in determining the operating lease liabilities we use an estimate of our incremental borrowing rate. The incremental borrowing rate is determined using two alternative credit scoring models to estimate our credit rating, adjusted for collateralization. The calculation of the operating lease assets includes any lease payments made and excludes any lease incentives. Our lease terms may include options to extend or terminate the lease when it is reasonably certain that we will exercise that option.

For operating leases, we record operating lease assets and liabilities in our consolidated balance sheets. Lease expense for lease payments is recognized on a straight-line basis over the lease term. Short-term leases, or leases that have a lease term of 12 months or less at commencement date, are excluded from this treatment and are recognized on a straight-line basis over the term of the lease.

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. 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, 2019 (in thousands):

	Level 1	Level 2	Level 3	Total
Cash equivalents	$ 27,012	$ 10,995	$ —	$ 38,007
Marketable securities:				
Certificates of deposit	—	240	—	240
U.S. Treasuries	—	186,449	—	186,449
Government securities	—	87,368	—	87,368
Corporate debt securities	—	266,402	—	266,402
Total cash equivalents and marketable securities	$ 27,012	$ 551,454	$ —	$ 578,466

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, 2019.

There have been no changes to the valuation methods during the six months ended June 30, 2019. We evaluate transfers between levels at the end of each reporting period. There were no transfers between Level 1 and Level 2 during the six months ended June 30, 2019. We have no financial assets or liabilities that were classified as Level 3 at any point during the six months ended June 30, 2019.

4. Marketable Securities

Our marketable securities are classified as available-for-sale pursuant to ASC 320, *Investments – Debt and Equity Securities*, and are recorded at fair value, with unrealized gains and losses included as a component of accumulated other comprehensive income (loss) 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. 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, 2019 and 2018.

Marketable securities at June 30, 2019 consisted of the following (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
Certificates of deposit	$ 240	$ —	$ —	$ 240
U.S. Treasuries	186,295	211	(57)	186,449
Government securities	54,836	20	(34)	54,822
Corporate debt securities	170,255	148	(104)	170,299
Non-current:				
Government securities	32,575	19	(48)	32,546
Corporate debt securities	95,657	491	(45)	96,103
Total marketable securities	$ 539,858	$ 889	$ (288)	$ 540,459

Marketable securities at December 31, 2018 consisted of the following (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Current:				
Certificates of deposit	$ 960	$ —	$ (4)	$ 956
U.S. Treasuries	231,101	7	(228)	230,880
Government securities	75,335	—	(121)	75,214
Corporate debt securities	208,233	—	(483)	207,750
Non-current:				
U.S. Treasuries	12,202	4	(125)	12,081
Government securities	70,177	10	(188)	69,999
Corporate debt securities	139,082	12	(1,055)	138,039
Total marketable securities	$ 737,090	$ 33	$ (2,204)	$ 734,919

As of June 30, 2019 and December 31, 2018, 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, 2019 and December 31, 2018, we held 79 and 242 debt securities, respectively, that were in an unrealized loss position for less than one year. The aggregate fair value of debt securities in an unrealized loss position at June 30, 2019 and December 31, 2018 was $175.5 million and $639.3 million, respectively. There were no individual securities that were in a significant unrealized loss position as of June 30, 2019 and December 31, 2018. 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 other-than-temporarily impaired as of June 30, 2019 and December 31, 2018.

5. Inventory

Inventory, which consists of commercial supply of TIBSOVO® (ivosidenib), consists of the following (in thousands):

	June 30, 2019	December 31, 2018
Raw materials	$ 180	$ —
Work-in-process	4,392	788
Finished goods	87	81
Total inventory	$ 4,659	$ 869

6. Leases

On April 11, 2019, we entered into an agreement to lease approximately 13,000 square feet of office space located at 38 Sidney Street, Cambridge, Massachusetts, or the 38 Sidney Lease, with Thirty-Eight Sidney Street, LLC. The initial term of the 38 Sidney Lease commenced on May 1, 2019 and expires on February 29, 2028. At the end of the lease term, we have the option to extend the 38 Sidney Lease for two consecutive terms of five years at fair market rent at the time of the extension. The 38 Sidney Lease provides us with the right to lease additional space within the 38 Sidney Street building and also includes rent escalation clauses and a tenant improvement allowance of $1.0 million.

In connection with the 38 Sidney Lease, we also amended our existing building leases at 88 Sidney Street, Cambridge, Massachusetts and at 64 Sidney Street, Cambridge, Massachusetts to extend the initial terms of those leases by approximately three years through February 29, 2028. The amendments also provide us with the right to lease additional space at the 64 Sidney Street building. Our existing extension options for the 88 Sidney Street building and 64 Sidney Street building continue as set forth in the existing leases for those buildings.

Our building leases are comprised of office and laboratory space under non-cancelable operating leases. These lease agreements have remaining lease terms of nine 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, 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, 2019.

As of June 30, 2019, undiscounted minimum rental commitments under non-cancelable leases, for each of the next five years and total thereafter were as follows (in thousands):

Remaining 2019	$ 5,695
2020	14,015
2021	14,380
2022	16,773
2023	18,126
2024	18,660
Thereafter	63,891
	$ 151,540

In arriving at the operating lease liabilities as of June 30, 2019, we applied the weighted-average incremental borrowing rate of 5.7% over a weighted-average remaining lease term of 8.7 years.

As of June 30, 2019, the following represents the difference between the remaining undiscounted minimum rental commitments under non-cancelable leases and the operating lease liabilities (in thousands):

Undiscounted minimum rental commitments	$	151,540
Present value adjustment using incremental borrowing rate		(35,070)
Operating lease liabilities	$	116,470

As of December 31, 2018, minimum rental commitments under non-cancelable leases, for each of the next five years and total thereafter were as follows (in thousands):

2019	$	12,759
2020		13,135
2021		13,473
2022		15,552
2023		17,145
Thereafter		19,223
	$	91,287

7. Accrued Expenses

Accrued expenses consist of the following (in thousands):

	June 30, 2019	December 31, 2018
Accrued compensation	$ 10,541	$ 20,843
Accrued research and development costs	30,189	14,777
Accrued professional fees	6,357	5,441
Accrued other	2,131	1,086
Total accrued expenses	$ 49,218	$ 42,147

8. Product Revenue

We sell TIBSOVO®, our wholly owned product, to a limited number of specialty distributors and specialty pharmacy providers in the U.S., 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.

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.

Total net product revenue from U.S. sales of TIBSOVO®, which is our only source of product revenue, was $13.7 million and $22.9 million for the three and six months ended June 30, 2019, respectively. We did not record any product revenues during the three and six months ended June 30, 2018. The following table summarizes balances and activity in each of the product revenue allowance and reserve categories for the six months ended June 30, 2019 (in thousands):

	Contractual Adjustments	Government Rebates	Returns	Total
Balance at December 31, 2018	$ 592	$ 325	$ 334	$ 1,251
Current provisions relating to sales in the current year	3,145	820	586	4,551
Adjustments relating to prior years	8	—	—	8
Payments/returns relating to sales in the current year	(2,450)	(355)	—	(2,805)
Payments/returns relating to sales in the prior years	(598)	(230)	—	(828)
Balance at June 30, 2019	$ 697	$ 560	$ 920	$ 2,177

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

	June 30, 2019	December 31, 2018
Reduction of accounts receivable	$ 416	$ 326
Component of accrued expenses	1,761	925
Total revenue-related reserves	$ 2,177	$ 1,251

The following table presents changes in our contract assets during the six months ended June 30, 2019 (in thousands):

	December 31, 2018	Additions	Deductions	June 30, 2019
Contract assets (1)				
Accounts receivable, net	$ 5,076	$ 27,395	$ (25,324)	$ 7,147

(1) Additions to contract assets relate to amounts billed to Customers for product sales during the reporting period. 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, 2018, 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, 2018.

Collaboration revenue

On January 1, 2018 we adopted ASC 606, *Revenue from Contracts with Customers,* under the modified retrospective method. Prior to January 1, 2018, we accounted for collaboration agreements under ASC 605-25, *Multiple Element Arrangements.* In determining the appropriate amount of revenue to be recognized under ASC 606, we performed the following steps: (i) identified the promised goods or services in the contract; (ii) determined whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measured the transaction price, including the constraint on variable consideration; (iv) allocated the transaction price to the performance obligations; and (v) recognized revenue when (or as) we satisfied each performance obligation.

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 not considered probable of being achieved 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 Corporation, or Celgene, 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. Under the remaining terms of the 2010 Agreement, we are eligible to receive up to $80.0 million in potential milestone payments for the enasidenib program. The potential milestone payments are comprised of: (i) up to $55.0 million in milestone payments upon achievement of specified ex-U.S. regulatory milestone events, and (ii) a $25.0 million milestone payment upon achievement of a specified ex-U.S. commercial milestone event, as well as royalties at tiered, low-double digit to mid-teen percentage rates on net sales of IDHIFA®.
- 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. The initial four-year research term of the 2016 Agreement may be extended for up to two, or in specified cases, up to four additional one-year terms by paying a $40.0 million per year extension fee. Celgene has designated AG-270, our methionine adenosyltransferase 2a, or MAT2A, inhibitor, as a development candidate under the 2016 Agreement, and has the option, upon payment of an option exercise fee of at least $30.0 million, to participate in a worldwide 50/50 cost and profit share with us for AG-270, under which we are eligible for up to $169.0 million in potential milestone payments for the program, comprised of: (i) a $20.0 million milestone-based payment upon achievement of a specified clinical development event and (ii) up to $149.0 million in milestone-based payments upon achievement of specified regulatory milestone events. We are also eligible to receive designation, option exercise and milestone and royalty payments for other programs that may be designated for further development under the 2016 Agreement.

Collaboration revenue

During the three and six months ended June 30, 2019 and 2018, we recognized the following collaboration revenue (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Services performed that were considered performance obligations as of the modification dates				
Licenses	$ —	$ 15,000	$ —	$ 15,000
On-going research and development services	8,155	9,830	25,220	16,194
Services performed that were not considered performance obligations as of the modification dates				
Development activities	—	590	—	590
Commercialization activities	824	981	1,678	1,962
Total collaboration revenue - related party	$ 8,979	$ 26,401	$ 26,898	$ 33,746

The following table presents changes in our contract assets and liabilities during the six months ended June 30, 2019 (in thousands):

	December 31, 2018	Additions	Deductions	June 30, 2019
Contract assets (1)				
Collaboration receivable – related party	$ 2,462	$ 4,452	$ (4,390)	$ 2,524
Royalty receivable – related party	2,234	4,900	(4,434)	2,700
Contract liabilities (2)				
Deferred revenue – related party, current and net of current portions	92,519	3,705	(26,154)	70,070

(1) Additions to contract assets relate to amounts billed to Celgene during the reporting period. Deductions to contract assets relate to collection of receivables during the reporting period.
(2) Additions to contract liabilities relate to consideration from Celgene during the reporting period. Deductions to contract liabilities relate to deferred revenue recognized as revenue during the reporting period.

During the three and six months ended June 30, 2019 and 2018, we recognized the following as revenue due to changes in the contract liability balances (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Amounts included in the contract liability at the beginning of the period	$ 8,009	$ 9,932	$ 24,419	$ 15,917
Performance obligations satisfied in previous periods	—	220	—	543

As of June 30, 2019, the aggregate amount of the transaction price allocated to performance obligations that are partially unsatisfied was $75.5 million. This amount is expected to be recognized as performance obligations are satisfied through March 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, 2019 and 2018, we recognized the following as royalty revenue (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Royalty revenue – related party	$ 2,703	$ 1,573	$ 4,903	$ 2,990

Milestone revenue

During the three months ended June 30, 2018, Celgene submitted a marketing authorization application, or MAA, to the European Medicines Agency, or EMA, for IDHIFA® for isocitrate dehydrogenase 2, or IDH2, mutant-positive relapsed or

refractory, or R/R, acute myeloid leukemia, or AML. As a result of the filing, we recognized a $15.0 million milestone payment as collaboration revenue - related party. No other milestones were achieved during the three and six months ended June 30, 2019 or 2018. The next potential milestone expected to be achieved under our Collaboration Agreements is the first regulatory approval in any of China, Japan or a major European country, which would result in a milestone payment of $35.0 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. Pursuant to the CStone Agreement, CStone will initially be responsible for the development and commercialization of ivosidenib in 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 $412.0 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, 2019 and 2018, we recognized the following collaboration revenue - other (in thousands):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Services performed that were considered performance obligations as of the inception date				
License	$ —	$ 12,440	$ —	$ 12,440
Services performed that were not considered performance obligations as of the inception date				
Other Services	812	—	1,782	—
Total collaboration revenue - other	$ 812	$ 12,440	$ 1,782	$ 12,440

The following table presents changes in our contract assets during the six months ended June 30, 2019 (in thousands):

	December 31, 2018	Additions	Deductions	June 30, 2019
Contract assets (1)				
Collaboration receivable - other	$ 670	$ 1,782	$ (230)	$ 2,222

(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, 2019, the aggregate amount of the transaction price allocated to performance obligations that are partially unsatisfied was $0.7 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, 2019 and 2018. The next potential milestone expected to be achieved under the CStone Agreement is the dosing of the first patient in a local study in a hematological indication in mainland China. Achievement of this event will result in a milestone payment of $5.0 million.

10. 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 stock options and other stock-based awards. Following the adoption of the 2013 Plan, we granted no further stock options or other stock-based awards under the 2007 Stock Incentive Plan, or the 2007 Plan. Any stock options or stock-based awards outstanding under the 2007 Plan at the time of adoption of the 2013 Plan remained outstanding and effective. As of June 30, 2019, the total number of shares reserved under the 2007 Plan and the 2013 Plan was 9,475,602, and we had 2,194,806 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, 2019:

	Number of Stock Options	Weighted-Average Exercise Price
Outstanding at December 31, 2018	5,416,069	$ 60.10
Granted	1,464,728	57.08
Exercised	(181,010)	38.59
Forfeited/Expired	(356,493)	66.38
Outstanding at June 30, 2019	6,343,294	$ 59.66
Exercisable at June 30, 2019	3,414,953	$ 58.63
Vested and expected to vest at June 30, 2019	6,343,294	$ 59.66

At June 30, 2019, there was approximately $114.6 million of total unrecognized compensation expense related to unvested stock option awards, which we expect to recognize over a weighted-average period of approximately 2.8 years.

Restricted stock units

The following table presents restricted stock unit, or RSU, activity for the six months ended June 30, 2019:

	Number of Stock Units	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2018	532,144	$ 75.45
Granted	408,707	58.46
Vested	(150,082)	69.29
Forfeited	(53,259)	72.24
Unvested shares at June 30, 2019	737,510	$ 67.52

As of June 30, 2019, there was approximately $37.5 million of total unrecognized compensation expense related to RSUs, which we expect to recognize over a weighted-average period of approximately 2.0 years.

Performance-based stock units

The following table presents performance-based stock unit, or PSU, activity for the six months ended June 30, 2019:

	Number of Stock Units	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2018	169,031	$ 52.67
Granted	155,297	61.93
Vested	(167,031)	52.36
Unvested shares at June 30, 2019	157,297	$ 62.15

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, 2019, there was approximately $9.8 million of total unrecognized compensation expense related to PSUs with performance-based vesting criteria that are not considered 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, 2019:

	Number of Stock Units	Weighted-Average Grant Date Fair Value
Unvested shares at December 31, 2018	—	$ —
Granted	42,695	41.50
Unvested shares at June 30, 2019	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, 2019, there was approximately $1.3 million of total unrecognized compensation expense related to MSUs, which we expect to recognize over the remaining derived service period of 1.2 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 32,410 shares and 27,377 shares during the six months ended June 30, 2019 and 2018, respectively, under the 2013 ESPP. The 2013 ESPP provides participating employees with the opportunity to purchase up to an aggregate of 327,272 shares of our common stock. As of June 30, 2019, we had 128,126 shares available for future issuance under the 2013 ESPP.

Stock-based compensation expense

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Stock options	$ 12,467	$ 13,311	$ 25,513	$ 25,783
Restricted stock units	5,243	2,805	9,791	4,602
Employee stock purchase plan	392	339	720	592
Other stock awards	445	—	631	—
Total stock-based compensation expense	$ 18,547	$ 16,455	$ 36,655	$ 30,977

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Research and development expense	$ 10,067	$ 9,667	$ 20,109	$ 18,307
Selling, general and administrative expense	8,480	6,788	16,546	12,670
Total stock-based compensation expense	$ 18,547	$ 16,455	$ 36,655	$ 30,977

11. 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 met, 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 met as of June 30, 2019 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,	
	2019	2018
Stock options	6,343,294	5,706,476
Restricted stock units	737,510	438,892
Employee stock purchase plan	33,064	21,205
Total common stock equivalents	7,113,868	6,166,573

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, 2019 and for the three and six months ended June 30, 2019 and 2018, 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, 2018 filed with the SEC on February 14, 2019. 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, and the sufficiency of our cash for future operations. Words such as "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar statements or variation of these terms or the negative of those terms and similar expressions are intended to identify these forward-looking statements. Readers are cautioned that these forward-looking statements are predictions and are subject to risks, uncertainties and assumptions that are difficult to predict. Therefore, actual results may differ materially and adversely from those expressed in any forward-looking statements. Among the important factors that could cause actual results to differ materially from those indicated by our forward-looking statements are those discussed under the heading "Risk Factors" in Part II, Item 1A. and elsewhere in this report, and in our Annual Report on Form 10-K for the year ended December 31, 2018. 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 making transformative, first- or best-in-class medicines for the treatment of cancer and RGDs. To address both cancer and RGDs, 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.

Oncology

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 AML or cholangiocarcinoma. We hold worldwide development and commercial rights to ivosidenib and have licensed certain development and commercialization rights to ivosidenib to CStone. 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. In July 2018, the FDA granted us approval of TIBSOVO® for the treatment of adult patients with R/R AML with a susceptible IDH1 mutation as detected by an FDA-approved test. In December 2018, we submitted an MAA to the EMA for TIBSOVO® for the treatment of adult patients with R/R AML. In May 2019, the FDA approved our supplemental new drug application, or sNDA, to update the U.S. Prescribing Information for TIBSOVO® to include 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. The FDA granted us fast track designation for ivosidenib for treatment of patients with previously treated, unresectable or metastatic cholangiocarcinoma with an IDH1 mutation, granted orphan drug designation for ivosidenib for the treatment of cholangiocarcinoma, and 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.

Celgene, in collaboration with us, is developing enasidenib for the treatment of IDH2 mutant-positive hematologic cancers. Enasidenib is an orally available, selective, potent inhibitor of the mutated IDH2 protein, making it a highly targeted therapy for the treatment of patients with cancers that harbor IDH2 mutations, including those with AML. In August 2017, the FDA granted Celgene approval of IDHIFA® for the treatment of adult patients with R/R AML and an IDH2 mutation. In June 2018, Celgene submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive AML. Celgene 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.

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

We are developing vorasidenib for the treatment of IDH mutant-positive 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% of all cancers. AG-270 is an orally available selective potent inhibitor of MAT2A. Celgene has designated AG-270 as a development candidate under the 2016 Agreement, and has the option to participate in a worldwide 50/50 cost and profit share with us for the program, under which we are eligible for clinical and regulatory milestone payments.

We are developing AG-636 for the treatment of hematologic malignancies, including lymphoma. AG-636 is an inhibitor of the metabolic enzyme dihydroorotate dehydrogenase, or DHODH, licensed by us from Aurigene Discovery Technologies Limited, or Aurigene. In October 2018, we submitted an investigational new drug application, or IND, for AG-636 for the treatment of hematologic malignancies, which was accepted by the FDA in December 2018.

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. 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 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. We have worldwide development and commercial rights to mitapivat and expect to fund the future development and commercialization costs related to this program.

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

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, and stock-based compensation. 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, 2018.

Financial Operations Overview

General

Since inception, our operations have primarily focused on organizing and staffing our company, business planning, raising capital, assembling our core capabilities in cellular metabolism, identifying potential product candidates, undertaking preclinical studies and conducting clinical trials. Beginning in 2018, we also began to increase our commercial activities in connection with the FDA approval of TIBSOVO® and we will continue to build out our commercial capabilities to support potential approvals of our other product candidates. To date, we have financed our operations primarily through funding received from our various collaboration agreements, 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 $202.9 million and $159.6 million for the six months ended June 30, 2019 and 2018, respectively. As of June 30, 2019, we had an accumulated deficit of $1.3 billion. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from year to year. We anticipate that our expenses will increase significantly as we continue to advance and expand clinical development activities for our lead programs: ivosidenib, vorasidenib, mitapivat, AG-270, and AG-636; continue to discover and validate novel targets and drug product candidates; expand and protect our intellectual property portfolio; and hire additional commercial, development and scientific personnel.

Revenue

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. and these Customers subsequently resell TIBSOVO® to pharmacies or dispense directly to patients. In addition to distribution agreements with these 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 revenue from our collaborations with Celgene and CStone, and 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®.

Research and development expenses

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as our product candidate development programs progress. However, the successful development of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development and commercialize these product candidates.

We are also unable to predict when, if ever, material net cash inflows will commence from sales of our product candidates. This is due to the numerous risks and uncertainties associated with developing medicines, including the uncertainty of:

- establishing an appropriate safety profile in enabling toxicology and clinical studies to support IND, and/or new drug application, or NDA;
- 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

- 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.

- 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.
- 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.
- HO150/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, which initiated sites and is currently screening patients.
- 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.
- 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.
- 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 primary endpoint of the trial was met and we plan to submit an sNDA to the FDA for TIBSOVO® for second-line or later IDH1 mutant-positive cholangiocarcinoma by the end of 2019.

Enasidenib

- In addition to the clinical trials discussed above, enasidenib is also being evaluated by Celgene in IDHENTIFY, an international phase 3, multi-center, open-label, randomized clinical trial designed to compare the efficacy and safety of enasidenib versus conventional care regimens in patients 60 years or older with IDH2 mutant-positive AML that is refractory to or relapsed after second- or third-line therapy.

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.
- A perioperative study with ivosidenib and vorasidenib in low grade glioma to further investigate their effects on brain tumor tissue.
- A registration-enabling phase 3 study of vorasidenib in low-grade glioma with an IDH1 or IDH2 mutation is expected to initiate by the end of 2019.

Mitapivat

- 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.
- ACTIVATE-T, a single arm, global, pivotal trial of mitapivat in up to 40 regularly-transfused patients with PK deficiency.
- ACTIVATE, a 1:1 randomized, placebo-controlled, global, pivotal trial of mitapivat in approximately 80 patients with PK deficiency who do not receive regular transfusions.
- A phase 2, open-label safety and efficacy clinical trial of mitapivat in approximately 20 adult patients with non-transfusion-dependent thalassemia.

AG-270

- A phase 1 trial in multiple tumor types carrying an MTAP deletion. The first part of the trial is a single agent dose-escalation phase in which cohorts of patients will receive ascending doses of AG-270 to determine the pharmacokinetics, pharmacodynamics, and optimal dose and schedule. The next phase of development will evaluate AG-270 in combination with taxanes in two areas of high unmet need. One arm of the study will test AG-270 in combination with docetaxel in MTAP-deleted non-small cell lung cancer and another arm will test AG-270 in combination with nab-paclitaxel and gemcitabine in MTAP-deleted pancreatic ductal adenocarcinoma.

AG-636

- A phase 1 study of AG-636 in subjects with advanced lymphoma.

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 activities related to the commercialization of TIBSOVO®, the potential commercialization of our product candidates, and the build-out of a limited commercial infrastructure in the European Union, or EU. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses.

Results of Operations

Comparison of the three and six months ended June 30, 2019 and 2018

The following table summarizes our results of operations for the three and six months ended June 30, 2019 and 2018 ($ in thousands):

	Three Months Ended June 30				Six Months Ended June 30			
($ in thousands)	**2019**	**2018**	**$ Change**	**% Change**	**2019**	**2018**	**$ Change**	**% Change**
Product revenue, net	$ 13,727	$ —	$ 13,727	N/A	$ 22,865	$ —	$ 22,865	N/A
Collaboration revenue – related party	8,979	26,401	(17,422)	(66) %	26,898	33,746	(6,848)	(20) %
Collaboration revenue – other	812	12,440	(11,628)	(93) %	1,782	12,440	(10,658)	(86) %
Royalty revenue – related party	2,703	1,573	1,130	72 %	4,903	2,990	1,913	64 %
Total revenue	26,221	40,414	(14,193)	(35) %	56,448	49,176	7,272	15 %
Cost and expenses:								
Cost of sales	303	—	303	N/A	637	—	637	N/A
Research and development	107,389	86,730	20,659	24 %	202,974	164,954	38,020	23 %
Selling, general and administrative	32,390	26,633	5,757	22 %	64,181	51,183	12,998	25 %
Loss from operations	(113,861)	(72,949)	(40,912)	56 %	(211,344)	(166,961)	(44,383)	27 %
Interest income	3,990	4,204	(214)	(5) %	8,395	7,391	1,004	14 %
Net loss	$ (109,871)	$ (68,745)	$ (41,126)	60 %	$ (202,949)	$ (159,570)	$ (43,379)	27 %

Product Revenue. Product revenue for the three and six months ended June 30, 2019 was due to the recognition of net product revenue from the sale of our first commercial product, TIBSOVO®, which was approved for sale in the U.S. on July 20, 2018.

Collaboration Revenue. The decrease in collaboration revenue - related party for the three months ended June 30, 2019 is primarily due to recognition of a milestone payment of $15.0 million in 2018. The decrease in collaboration revenue - related party for the six months ended June 30, 2019 is primarily related to the recognition of the milestone payment in 2018, offset by revenue recognized in 2019 upon satisfaction of our research and development activities under our Collaboration Agreements with Celgene.

Collaboration revenue - other consists of revenue generated under the CStone Agreement. The decrease is collaboration revenue - other is primarily due to revenue recognized in June 2018 relating to the delivery of the license to CStone. Revenue recognized for the three and six months ended June 30, 2019 consists of revenue recognized upon satisfaction of other services under the CStone Agreement.

Royalty Revenue. In addition to product revenue and collaboration revenue, we recognized royalty revenue on Celgene's net sales of IDHIFA® under the 2010 Agreement.

Cost of Sales. Cost of sales for the three and six months ended June 30, 2019 relate to manufacturing costs associated with TIBSOVO® sales. Based on our policy to expense costs associated with the manufacture of our products prior to regulatory approval, certain of the TIBSOVO® costs were expensed prior to July 20, 2018, and therefore are not included in costs of sales during the current period.

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

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

	Three Months Ended June 30				Six Months Ended June 30			
	2019	2018	$ Change	% Change	2019	2018	$ Change	% Change
Ivosidenib (IDH1m inhibitor)	$ 35,367	$ 34,716	$ 651	2 %	$ 71,439	$ 65,223	$ 6,216	10 %
Enasidenib (IDH2m inhibitor)	1,181	3,108	(1,927)	(62) %	2,966	5,647	(2,681)	(47) %
Vorasidenib (Brain-penetrant IDHm inhibitor)	9,114	3,797	5,317	140 %	14,461	7,478	6,983	93 %
Mitapivat (PKR activator)	20,837	14,604	6,233	43 %	40,193	27,719	12,474	45 %
AG-270 (MAT2A inhibitor)	6,541	5,908	633	11 %	12,034	11,936	98	1 %
AG-636 (DHODH inhibitor)	5,879	3,204	2,675	83 %	9,638	3,204	6,434	201 %
Other research and platform programs	28,470	21,393	7,077	33 %	52,243	43,747	8,496	19 %
Total research and development expenses, net	$ 107,389	$ 86,730	$ 20,659	24 %	$ 202,974	$ 164,954	$ 38,020	23 %

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

- Ivosidenib costs for the six months ended June 30, 2019 increased primarily as a result of increased clinical costs related to the initiation of the HO150/AMLSG29 trial, which was initiated in the first quarter of 2019, and our AGILE study.
- Vorasidenib costs for the three and six months ended June 30, 2019 increased due to start-up costs related to our planned phase 3 study of vorasidenib in low-grade glioma with an IDH1 mutation, which is expected to initiate by the end of 2019.
- Mitapivat costs for the three and six months ended June 30, 2019 increased as a result of continuing enrollment in the ACTIVATE-T trial, which we initiated in April 2018, the ACTIVATE trial, which we initiated in June 2018, and the phase 2 study of mitapivat in thalassemia, which we initiated in December 2018.
- AG-636 costs for the six months ended June 30, 2019 increased primarily as a result of a $2.0 million milestone due to Aurigene upon first patient dosing within the phase 1 lymphoma study.
- The increase in the costs of other research and platform programs include activities related to exploratory efforts, target validation and lead optimization for our discovery and follow-on programs, and our proprietary metabolomics platform.

Selling, General and Administrative Expense. Selling, general and administrative expense increased during the three and six months ended June 30, 2019 primarily due to commercial costs for TIBSOVO®, including costs related to the sNDA, and personnel costs, including stock-based compensation expense, related to our workforce.

Interest Income. The change in interest income is primarily attributable to the change in our outstanding marketable securities and changes in interest rates earned on our marketable securities.

Liquidity and Capital Resources

Sources of liquidity

Since our inception, and through June 30, 2019, we have funded our operations through commercial sales of TIBSOVO®, upfront, milestone, extension, cost reimbursement and royalty payments related to our collaboration agreements, proceeds received from our issuance of preferred stock, our initial public offering and concurrent private placement of common stock to an affiliate of Celgene, and our follow-on public offerings.

In addition to our existing cash, cash equivalents and marketable securities, we are eligible to earn a significant amount of milestone payments, cost reimbursements, and royalty payments under our Collaboration Agreements with Celgene and the

CStone Agreement, and designation fees, license option fees and extension fees under our Collaboration Agreements with Celgene. Our ability to earn the milestone payments, cost reimbursements and royalty payments, and the timing of earning these amounts are dependent upon the timing and outcome of our development, regulatory and commercial activities, and is uncertain at this time. Our right to payments under our collaboration agreements with Celgene and CStone are our only committed potential external source of funds.

Cash flows

The following table provides information regarding our cash flows for the six months ended June 30, 2019 and 2018 (in thousands):

	Six Months Ended June 30,	
	2019	2018
Net cash used in operating activities	$ (191,422)	$ (166,395)
Net cash provided by (used in) investing activities	195,832	(263,791)
Net cash provided by financing activities	8,668	537,785
Net change in cash and cash equivalents	$ 13,078	$ 107,599

Net cash used in operating activities. 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 that relate to increases in clinical study costs due to advancements in our most advanced product candidates, commercialization efforts, expanded facilities and increased staffing needs due to our expanding operations.

During the six months ended June 30, 2018, we received $8.9 million in cost reimbursements related to our Collaboration Agreements with Celgene. This amount was offset by increased operating expenses which relate to increases in clinical study costs due to advancements in our most advanced product candidates, expanded facilities and increased staffing needs due to our expanding operations.

Net cash provided by (used in) investing activities. 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. Cash used in investing activities for the six months ended June 30, 2018 was primarily the result of higher purchases of marketable securities than proceeds from maturities and sales of marketable securities, and $2.8 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, 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. Cash provided by financing activities for the six months ended June 30, 2018 was the result of the $516.2 million of net proceeds received from our January 2018 follow-on public offering, after underwriting discounts and commissions, as well as $22.0 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 or other collaborators. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations.

We expect that our existing cash, cash equivalents and marketable securities as of June 30, 2019 together with anticipated product and royalty revenue, anticipated interest income and anticipated expense reimbursements under our collaboration agreements, but excluding any additional program-specific milestone payments, will enable us to fund our operating expenses and capital expenditure requirements through at least the end of 2020. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the success of, and developments regarding, our collaborations;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;

- the costs, timing and outcome of regulatory review of our product candidates;
- 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;
- commercialization expenses relating to approved medicines such as TIBSOVO® and IDHIFA®;
- the levels of product revenue from sales of TIBSOVO® or royalties on sales of IDHIFA®;
- our ability to establish and maintain additional collaborations on favorable terms, if at all; and
- the extent to which we acquire or in-license other medicines and technologies.

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

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

Off-balance Sheet Arrangements

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

Contractual Obligations

We have entered into agreements in the normal course of business with CROs for clinical trials and 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, 2019, 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 the Annual Report on Form 10-K for the year ended December 31, 2018.

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, 2019 and December 31, 2018, we had cash, cash equivalents and marketable securities of $624.0 million and $805.4 million, respectively, consisting primarily of investments in certificates of deposit, U.S. Treasuries, government securities and corporate debt securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are 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, 2019 and December 31, 2018, we had minimal or no liabilities denominated in foreign currencies.

Item 4. Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of the end of the period covered by this Quarterly Report on Form 10-Q, the effectiveness of our disclosure controls and procedures.

Based on that evaluation of our disclosure controls and procedures as of June 30, 2019, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports it files or submits under the Exchange Act is accumulated and communicated to its management, including its principal executive officer and principal financial officer, or person performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

No change in our internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, occurred during the fiscal quarter ended June 30, 2019 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

Item 1A. Risk Factors

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained herein, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of our management are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. You should read this Quarterly Report on Form 10-Q completely and with the understanding that our actual future results may be materially different from what we expect. The risks described are not the only risks facing our company. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition and/or operating results. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law. These risk factors restate and supersede the risk factors set forth under the heading "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2018.

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 $346.0 million, $314.7 million and $198.5 million for the years ended December 31, 2018, 2017, and 2016, respectively, and $202.9 million for the six months ended June 30, 2019. As of June 30, 2019, we had an accumulated deficit of $1.3 billion. To date, we have generated only modest revenue from sales of TIBSOVO® and royalties on sales of IDHIFA®. The FDA approved IDHIFA® for the treatment of adult patients with R/R AML and an IDH2 mutation, and approved TIBSOVO® 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.. We have not obtained marketing approval for any of our other product candidates, which are in preclinical or clinical development stages. We have financed our operations primarily through private placements of our preferred stock, our initial public offering and the concurrent private placement, our follow-on public offerings and our collaboration agreements with Celgene focused on cancer metabolism and metabolic immuno-oncology. We have devoted substantially all of our efforts to research and development. Although we may from time to time report profitable results, we expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

- initiate and continue clinical trials for our products and product candidates, including: enasidenib, ivosidenib, vorasidenib, mitapivat, AG-270 and AG-636;
- continue our research and preclinical development of our product candidates;
- seek to identify additional product candidates;
- seek marketing approvals for our product candidates that successfully complete clinical trials;
- establish and maintain a sales, marketing and distribution infrastructure to commercialize any medicines for which we 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 our expenses to increase in connection with our ongoing activities, particularly as we continue the research and development of, initiate and continue clinical trials of, 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 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, 2019, together with anticipated product and royalty revenue, anticipated interest income and anticipated expense reimbursements under our collaboration agreements, but excluding any additional program-specific milestone payments, will enable us to fund our operating expenses and capital expenditure requirements through at least the end of 2020. Our estimate as to how long we expect our existing cash and cash equivalents to be available to fund our operations is based on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;
- the success of, and developments regarding, our collaborations;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims;
- commercialization expenses relating to approved medicines such as TIBSOVO® and IDHIFA®;
- levels of product revenue from sales of TIBSOVO® and royalties on sales IDHIFA®;
- 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; 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 other product candidates, if approved, may not achieve commercial success. Even if we succeed in developing and commercializing one or more of our product candidates, we may never achieve sufficient sales revenue to achieve or maintain profitability. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds, other than our collaborations, which are limited in scope and duration. To the extent that we raise additional capital through the sale of equity or convertible debt securities, ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may require us to enter into agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us.

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

We were incorporated in the second half of 2007 and commenced operations in late 2008. Our operations to date have been 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®. We have not yet demonstrated our ability to successfully complete any large-scale or pivotal clinical trials. Typically, it takes about 10 to 15 years to develop one new medicine from the time it is discovered to when it is available for treating patients, assuming that it successfully completes all stages of research and development and achieves marketing approval, all of which is highly uncertain. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors that may adversely affect our ability to successfully commercialize our products and product candidates. We are in the early stages of transitioning from a company with solely a research focus to a company capable of supporting commercial activities and we have not yet demonstrated our ability to conduct large-scale sales and marketing activities necessary for successful commercialization. We may not be successful in such a transition.

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

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

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

Our scientific approach focuses on using our proprietary technology to identify key metabolic enzymes in cancer, RGDs, or other 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. We are also focused on metabolic immuno-oncology, an emerging field of cancer research focused on altering the metabolic state of immune cells to enhance the body's immune response to cancer.

Our focus on using our proprietary technology to screen for and identify product candidates targeting cellular metabolism and adjacent areas of biology may not result in the discovery and development of commercially viable medicines to treat cancer or RGDs. Any medicines that we develop may not effectively correct metabolic pathways or alter the metabolic state of immune cells. If we are able to develop a product candidate that targets cellular metabolism in preclinical studies, we may not succeed in demonstrating safety and efficacy of the product candidate in human clinical trials. In addition, even if we obtain marketing approval for one of our product candidates, we can provide no assurance that commercialization of such product candidate will be successful.

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

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

The development and commercialization of TIBSOVO® (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®;
- 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;
- 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.

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

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

In June 2018, we entered into 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 or significant changes in CStone's business strategy may adversely affect CStone's ability or resources available to perform its obligations under the CStone Agreement.

The CStone Agreement is also subject to early termination, including through CStone's right under certain circumstances to terminate upon advance notice to us. If the 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 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 cancer and RGDs, as well as in immune cells for the treatment of cancer. A significant portion of the research that we are conducting involves new compounds and drug discovery methods, including our proprietary technology. The drug discovery that we are conducting using our proprietary technology may not be successful in identifying compounds that are useful in treating cancer or RGDs. In addition, our efforts in the emerging field of metabolic immuno-oncology may not be as successful as our efforts to date in cancer metabolism and RGDs. Furthermore, our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

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

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

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

We depend heavily on the success of our clinical product candidates. Clinical trials of our product candidates may not be successful. If we or our collaborators are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the identification of our products and most advanced programs, which are TIBSOVO® (ivosidenib), IDHIFA® (enasidenib), and vorasidenib for the treatment of hematological and solid tumors, mitapivat for the treatment of PK deficiency, and AG-270 for the treatment of MTAP deleted cancers. The FDA approved IDHIFA® and TIBSOVO® for the treatment of adult patients with R/R AML with an IDH2 or IDH1 mutation, respectively. In June 2018, Celgene submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive R/R AML. 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. We plan to submit an sNDA for TIBSOVO® for second line or later IDH1 mutant-positive cholangiocarcinoma to the FDA by the end of 2019. Other than TIBSOVO®, IDHIFA®, vorasidenib, mitapivat, AG-270 and AG-636, we have not commenced clinical trials for any of our other product candidates. Our ability to generate product revenue will depend heavily on the successful development and eventual commercialization of our product candidates.

The success of ivosidenib 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. The FDA has approved IDHIFA® and TIBSOVO® for the treatment of adult patients with R/R AML and an IDH2 or IDH1 mutation, respectively. In June 2018 Celgene submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive AML and, 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. We plan to submit an sNDA for TIBSOVO® for second line or later IDH1 mutant-positive cholangiocarcinoma to the FDA by the end of 2019. 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.

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. Enrollment may be particularly challenging for some of the orphan diseases we

target in our RGD programs. In addition, some of our competitors may have ongoing clinical trials for product candidates that would treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Patient enrollment is also affected by other factors including:

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

Utilizing our precision medicine approach, we 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, 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; companies such as ASLAN Pharmaceuticals Limited, or ASLAN, Bayer, Clear Creek Bio and PTC Therapeutics, Inc., or PTC, are clinically evaluating DHODH inhibitors for the treatment of hematologic malignancies; Rocket Pharma LTD is in the preclinical stages of development for a gene therapy targeting PK deficiency; 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.

Furthermore, 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®, all of our most advanced product candidates are still in clinical stage development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. Adverse events or undesirable side effects caused by, or other unexpected properties of, our product candidates could cause us 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 Celgene and Abbott Laboratories for the development of the FDA approved companion diagnostics for IDHIFA® and TIBSOVO®, respectively, and may in the future depend on Celgene or other third parties for the development of other companion diagnostics for our cancer therapeutic product candidates. If any parties, including without

limitation Celgene or us, or any third parties engaged by Celgene or us are unable to successfully develop companion diagnostics for our therapeutic product candidates, or experience delays in doing so:

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

As a result of any of these events, our business would be harmed, possibly materially.

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

It is possible that the FDA or EMA may refuse to accept for substantive review any NDA, 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. 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.

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 nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we

may not generate significant product revenue and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

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

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

We have limited experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any approved medicine for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization or outsource these functions to other third parties. Although we have established sales and marketing capabilities to support our co-promotion efforts for IDHIFA® and the commercial launch of TIBSOVO®, we 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, 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 cancer 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 ASLAN, Clear Creek Bio, IDEAYA, PTC 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 collaborators or contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

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

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company, including personal information of our employees. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our employees or employees of our vendors to disclose sensitive information in order to gain access to our data. Like other companies, we may experience threats to our data and systems, including malicious codes and viruses, and other cyber-attacks. The number and complexity of these threats continue to increase over time. If a material breach of our security or that of our vendors occurs, the market perception of the effectiveness of our security measures could be harmed, we could lose business and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. Although we develop and maintain systems and controls

designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become more sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely.

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.

Risks Related to Our Dependence on Third Parties

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

In August 2017, the FDA approved IDHIFA® for the treatment of adult patients with R/R AML and an IDH2 mutation, on the basis of an NDA submitted by Celgene. Although IDHIFA® has received FDA approval in R/R AML with an IDH2 mutation, we and Celgene are still evaluating enasidenib in other clinical trials. Celgene maintains worldwide development and commercial rights to IDHIFA® and will fund the development and commercialization costs related to this program, although we have certain co-commercialization and co-promotion rights to IDHIFA®. Under the 2010 Agreement, Celgene is responsible for all development costs for enasidenib, and we are eligible to receive up to $80.0 million in milestone payments and a tiered royalty on any net sales of products containing IDHIFA®. Thus, our ability to generate revenue from IDHIFA® will depend heavily on Celgene's successful development and eventual commercialization of the product.

The development and continued commercialization of IDHIFA® (enasidenib) could be unsuccessful if:

- IDHIFA® becomes no longer accepted as safe, efficacious, and cost-effective for the treatment of adult patients with R/R AML and an IDH2 mutation in the medical community and by third-party payors;
- Celgene fails to continue to apply the necessary financial resources and expertise to manufacturing, marketing and selling IDHIFA®;
- Celgene does not continue to develop and implement effective marketing, sales and distribution strategies and operations for development and commercialization of IDHIFA®;
- Celgene does not continue to develop, validate and maintain a commercially viable manufacturing process for IDHIFA® that is compliant with current good manufacturing practices;
- Celgene does not successfully obtain third party reimbursement and generate commercial demand that results in sales of IDHIFA®;
- Celgene fails to provide us with timely and accurate information regarding development, sales and marketing activities;
- we or Celgene encounter any third party patent interference, derivation, inter partes review, post-grant review, reexamination or patent infringement claims with respect to enasidenib;
- Celgene does not comply with regulatory and legal requirements applicable to the sale of IDHIFA®;
- competing drug products are approved for the same indications as IDHIFA®;
- new safety risks are identified;
- enasidenib does not demonstrate acceptable safety and efficacy in current or future clinical trials, or otherwise does not meet applicable regulatory standards for approval in indications other than for the treatment of adult patients with R/R AML and an IDH2 mutation; or
- Celgene does not maintain or defend intellectual property rights associated with enasidenib.

We also face the risk that Celgene could determine to reprioritize its commercial or development programs and reduce or terminate its efforts on the development or commercialization of IDHIFA®. For example, on January 3, 2019, Bristol-Myers Squibb, or BMS, and Celgene announced that they have entered into a definitive merger agreement pursuant to which BMS will acquire Celgene in a transaction that is expected to close in the third quarter of 2019, subject to shareholder approval and the satisfaction of customary closing conditions and regulatory approvals. Celgene's merger with BMS could divert the attention of Celgene's management and adversely affect Celgene's ability to retain and motivate key personnel who are important to the continued development of the programs under our agreements with Celgene. In addition, if the transaction is completed as planned, thereafter 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.

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

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

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

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

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

- Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations. Under the 2010 Agreement, programs under a co-development and co-commercialization agreement pursuant to the 2016 Agreement and the CStone Agreement, development and commercialization plans and strategies for licensed programs, such as 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, under the 2016 Agreement, it is possible for Celgene to elect not to progress into preclinical development a product candidate that we have nominated and the joint research committee confirmed, without triggering a termination of the collaboration arrangement.
- Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing, which may result in a need for additional capital to pursue further development or commercialization of the applicable product candidate. For example, under the 2010 Agreement and the 2016 Agreement, it is possible for Celgene to terminate the agreement, upon 90 days prior written notice, with respect to any product candidate at any point in the research, development and clinical trial process, without triggering a termination of the remainder of the collaboration arrangement.
- Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our medicines or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.
- Collaborators with marketing and distribution rights to one or more medicines may not commit sufficient resources to the marketing and distribution of such medicine or medicines.
- Collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation. For example, under specified circumstances Celgene has the first right to maintain or defend our intellectual property rights with respect to 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 or any program under the 2016 Agreement, upon 90 days' notice and can terminate each entire agreement with us in connection with a material breach of the agreement by us that remains uncured for a period ranging from 60 to 90 days. CStone has the right, under certain circumstances, to terminate the CStone Agreement upon advance notice to us, and may, subject to specified cure periods, terminate the CStone Agreement in the event of our uncured material breach or under specified circumstances relating to our insolvency.
- Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all.

- If 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, the planned acquisition of Celgene by BMS could divert the attention of Celgene's management and adversely affect Celgene's ability to retain and motivate key personnel who are important to the continued development of the programs under our agreements with Celgene. In addition, if the transaction is completed as planned, thereafter 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.

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

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

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

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. For example, during the discovery phase of the 2016 Agreement, we may not directly or indirectly develop, manufacture or commercialize, except pursuant to the agreement, any medicine or product candidate with specified activity against certain metabolic targets except in connection with certain third-party collaborations or with respect to certain targets the rights to which have reverted back to us pursuant to the terms of the 2016 Agreement. Following the discovery phase until termination or expiration of the 2010 Agreement, either in its entirety or with respect to the relevant program, we may not directly or indirectly develop, manufacture or commercialize, outside of the collaboration, any medicine or product candidate with specified activity against any collaboration target that is within a licensed program or against any former collaboration target against which Celgene is conducting an independent program under the agreement. Following the discovery phase of the 2016 Agreement until termination or expiration of the applicable co-development and co-commercialization agreement or license agreement under the 2016 Agreement, we may not directly or indirectly develop, manufacture or commercialize, outside of the collaboration, any medicine or product candidate with specified activity against the collaboration target that is the subject of such co-development and co-commercialization agreement or license agreement, except in connection with certain third-party collaborations or with respect to certain targets the rights to which have reverted back to us pursuant to the terms of the 2016 Agreement. During the term of the CStone Agreement, we are prohibited from developing or commercializing, in the CStone Territory and in specified indications, other compounds or products that inhibit IDH1 mutations at specified levels of binding.

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

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

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

We do not independently conduct clinical trials of any of our product candidates. We rely and expect to continue to rely on third parties, such as CROs, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. In addition, we currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical testing. Any of these third parties may terminate their engagements with us, some in the event of an

uncured material breach and some at any time. If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third-parties or to do so on commercially reasonable terms. Switching or adding additional third parties involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays may occur in our product development activities. Although we seek to carefully manage our relationships with our CROs, we could encounter similar challenges or delays in the future and these challenges or delays could have a material adverse impact on our business, financial condition and prospects.

Our reliance on third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, and legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our responsibility to comply with any such standards. We and these third parties are required to comply with current good clinical practices, or cGCP, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area and comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce these cGCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of these third parties fail to comply with applicable cGCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, the EMA, or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with cGCP regulations. In addition, our clinical trials must be conducted with product produced under current good manufacturing practices, or cGMP, regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a U.S. government-sponsored database, clinicaltrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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

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

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

We do not have any manufacturing facilities. We currently rely, and expect to continue to rely, on third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing and for commercial supply of any of these product candidates for which we or our collaborators obtain marketing approval. To date, we have obtained materials for our product candidates for our ongoing preclinical and clinical testing from third-party manufacturers.

Although we have long-term supply agreements in place for commercial supply of TIBSOVO® with third-party manufacturers, we may be unable to establish any further long-term supply agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

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

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

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

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

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

Risks Related to Our Intellectual Property

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

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary medicines and technology. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and medicines that are important to our business. We do not yet have issued patents for all our most advanced product candidates in all markets we intend to commercialize.

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

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

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology or medicines or that effectively prevent others from commercializing competitive technologies and medicines. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore we cannot be certain that we were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, prior to March 2013, in the United States, the first to make the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to

the patent. Beginning in March 2013, the United States transitioned to a first inventor to file system in which, assuming the other requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent. We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or PTO, or become involved in opposition, derivation, revocation, reexamination, post-grant and inter partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize medicines without infringing third-party patent rights.

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

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

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

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

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

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. We have in the past and may in the future become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our medicines and technology, including interference proceedings before the PTO. For example, in 2011, The Leonard and Madlyn Abramson Family Cancer Research Institute at the Abramson Cancer Center of the University of Pennsylvania initiated a lawsuit against us, one of our founders, Craig B. Thompson, M.D., and Celgene, alleging misappropriation of intellectual property and, in 2012, the Trustees of the University of Pennsylvania initiated a similar lawsuit against us and Dr. Thompson. Each of these lawsuits was settled in 2012. We are not aware of any other legal proceedings having been filed against us to date. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we or one of our collaborators are found to infringe a third party's intellectual property rights, we or they could be required to obtain a license from such third party to continue developing and marketing our medicines and technology. However, we or our collaborators may not be able to obtain any required license on commercially reasonable terms or at all. Even if we or our collaborators were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us. We or our collaborators could be forced, including by court order, to cease developing and commercializing the infringing technology or medicine. In addition, we or our collaborators could be found liable for monetary damages. A finding of infringement could prevent us or our collaborators from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we or our collaborators have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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

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

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

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

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

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

We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position would be harmed.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

Even if we complete necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our product candidates. If we or our collaborators are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we or they will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and comparable regulatory authorities in other countries. With the exception of IDHIFA® and TIBSOVO®, we and our collaborators have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. Celgene has submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive AML and we submitted an

MAA to the EMA for TIBSOVO® for the treatment of adult patients with IDH1 mutant-positive R/R AML. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party contract research organizations to assist us in this process.

Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to the various regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the relevant regulatory authority. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use.

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

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

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

In order to market and sell our medicines in the 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. In particular, although Celgene has submitted an MAA to the EMA for IDHIFA® for IDH2 mutant-positive AML, and we submitted an MAA to 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. On March 29, 2017, the country formally notified the EU of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The United Kingdom had a period of a maximum of two years from the date of its formal notification to negotiate the terms of its withdrawal from, and future relationship with, the EU. If no formal withdrawal agreement can be reached between the United Kingdom and the EU, then it is expected that the United Kingdom's membership of the EU would automatically terminate on the deadline, which was initially March 29, 2019. That deadline has been extended to October 31, 2019 to allow the parties to negotiate a withdrawal agreement, which has proven to be extremely difficult to date. Discussions between the United Kingdom and the EU will continue to focus on withdrawal issues and transition agreements. However, limited progress to date in these negotiations and ongoing uncertainty within the UK Government and Parliament sustains the possibility of the United Kingdom leaving the EU without a withdrawal agreement and associated transition period in place, which is likely to cause significant market and economic disruption.

Since a significant proportion of the regulatory framework in the United Kingdom is derived from EU directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the EU. 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 candidate for which we or our collaborators obtain marketing approval could be subject to restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our medicines, when and if any of them are approved.

Any product candidate for which we or our collaborators obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such medicine, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to quality control and manufacturing, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and record keeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine, including the requirement to implement a risk evaluation and mitigation strategy.

The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our medicines for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws, 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 untitled letters;
- withdrawal of the medicine from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of medicines;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our medicines;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; and
- litigation involving patients using our medicines.

Non-compliance with 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, currently set at $10,781.40 to $21,562.80 per false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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

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.

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the EU General Data Protection Regulation (GDPR), which became effective on May 25, 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 the individuals to whom the personal 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 also imposes strict rules on the transfer of personal data to countries outside the EU, including the U.S., and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR 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 the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities.

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, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise.

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. It is unclear how this decision and any subsequent appeals and other efforts to repeal and replace the ACA will impact the ACA and our business. 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. More recently, on January 31, 2019, the HHS Office of Inspector General proposed modifications to the federal anti-kickback statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations.

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 and fires.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on the principal members of our management and scientific teams, each of whom is employed "at will," meaning we or they may terminate the employment relationship at any time. We do not maintain "key person" insurance for any of our executives or other employees. The loss of the services of any of these persons could impede the achievement of our research, development and commercialization objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors, including our scientific co-founders, may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

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

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

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

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

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

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

increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to Our Common Stock and Other Matters

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

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

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

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

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

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price and trading volume to decline.

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

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

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

The trading price of our common stock has been, and may continue to be, volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. For example, since January 1, 2014 the price of our common stock on the Nasdaq Global Select Market has ranged from $21.70 per share to $138.85 per share. The stock market in general and the market for biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated

to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- the timing and results of clinical trials of product candidates;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our development programs;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results, including fluctuations in levels of sales of TIBSOVO® or royalties on sales of IDHIFA®, or results of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover our stock;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this "Risk Factors" section.

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

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

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

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

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

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

As of June 30, 2019, our executive officers, directors and a small group of stockholders, in the aggregate, beneficially owned shares representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

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

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

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

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a company undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income or taxes may be limited. Our prior equity offerings and other changes in our stock ownership, some of which are outside of our control, may have resulted or could in the future result in an ownership change. We completed a review of our changes in ownership through December 31, 2018, and determined that we did not have a qualified ownership change since our last review as of December 31, 2017. We do not expect that this or any previous changes of ownership will result in our net operating loss carryforwards or certain other tax attributes expiring unutilized. Future ownership changes under Section 382 may limit the amount of net operating loss and tax credit carryforwards that we could potentially utilize to reduce future tax liabilities.

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

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

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

We are subject to taxation in numerous U.S. states and territories. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including as a result of applying the provisions the TCJA (as such provisions may be elaborated on or further developed in guidance, regulations and technical corrections pertaining to the TCJA) 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 6. Exhibits

Exhibit Number	Description of Exhibit	Incorporated by Reference				Filed Herewith
		Form	File Number	Date of Filing	Exhibit Number	
3.1	Restated Certificate of Incorporation	8-K	001-36014	July 30, 2013	3.1	
3.2	Amended and Restated By-Laws	8-K	001-36014	July 30, 2013	3.2	
10.1	Lease, dated as of April 11, 2019, by and between the Registrant and Thirty-Eight Sidney Street Limited LLC					X
10.2	Fourth Amendment to Lease, dated as of April 11, 2019, by and between the Registrant and Forest City 88 Sidney Street, LLC					X
10.3	Third Amendment of Lease, dated as of April 11, 2019, by and between the Registrant and UP 64 Sidney Street, LLC					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

SIGNATURES

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

AGIOS PHARMACEUTICALS, INC.

August 1, 2019 By: /s/ Jacqualyn A. Fouse

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

August 1, 2019 By: /s/ Andrew Hirsch

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

LANDLORD

THIRTY-EIGHT SIDNEY STREET LLC

TENANT

AGIOS PHARMACEUTICALS, INC.

38 SIDNEY BUILDING

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LEASE

RECITALS AND DEFINITIONS

Section 1.1 - Recitals.

This Lease (this "**Lease**") is entered into as of April 11, 2019, by and between THIRTY-EIGHT SIDNEY STREET LIMITED LLC, a Delaware limited liability company (the "**Landlord**") and AGIOS PHARMACEUTICALS, INC., a Delaware corporation ("**Tenant**").

In consideration of the mutual covenants herein set forth, the Landlord and the Tenant do hereby agree to the terms and conditions set forth in this Lease.

Section 1.2 - Definitions.

The following terms shall have the meanings indicated or referred to below:

"**Additional Rent**" means all charges payable by the Tenant pursuant to this Lease other than Annual Fixed Rent, including without implied limitation the Tenant's parking charges as provided in Section 2.4; the Tenant's Tax Expense Allocable to the Premises as provided in Section 3.2; the Tenant's Operating Expenses Allocable to the Premises in accordance with Section 3.3; amounts payable to Landlord for separately submetered utilities and services pursuant to Section 3.4; amounts payable for special services pursuant to Section 3.5; and the Landlord's share of any sublease or assignment proceeds pursuant to Section 6.8.

"**Annual Fixed Rent**" - See **Exhibit A**, and Section 3.1.

"**Building**" means the building located at 38 Sidney Street, Cambridge, Massachusetts in which the Premises are located.

"**Commencement Date**" - See **Exhibit A** and Section 2.5.

"**Common Areas**" means those portions of the Building which are not part of the Premises and to which the Tenant has appurtenant rights pursuant to Section 2.2.

"**Default Interest Rate**" - see Section 9.6.

"**External Causes**" means collectively, (i) Acts of God, war, civil commotion, fire, flood or other casualty, strikes or other extraordinary labor difficulties, shortages of labor or materials or equipment in the ordinary course of trade, government order or regulations or other cause not reasonably within the Landlord's or Tenant's control and not due to the fault or neglect of the Landlord or Tenant. In no event shall financial inability be deemed to be an External Cause.

"**Landlord's Address for Notices**"

Thirty-Eight Sidney Street LLC
c/o Brookfield Properties (USA II) LLC
350 Massachusetts Avenue
Cambridge, Massachusetts 02139
Attention: Asset Manager

with copies to:

Thirty-Eight Sidney Street LLC
c/o Brookfield Properties (USA II) LLC
250 Vesey Street
New York, NY 10281-1023
Attention: General Counsel

"**Lease Year**" means each one year period commencing on the Rent Commencement Date (provided, however, that if the Rent Commencement Date does not occur on the first day of a month, the first Lease Year shall end on the last day of the month in which the anniversary of the Rent Commencement Date occurs); and each subsequent Lease Year shall consist of one calendar year beginning on the day immediately following the expiration of the prior Lease Year.

"**Park**" means buildings and associated land located from time to time within University Park at MIT, as such area is depicted on **Exhibit B-2**.

"**Parking Passes**" – See **Exhibit A**,
"**Permitted Uses**" - See **Exhibit A**.

"**Premises**" means approximately 12,995 rentable square feet on the third (3rd) floor of the Building as defined in **Exhibit A**. See **Exhibit A**, **Exhibit B-1** and Section 2.1.

"**Property**" means, collectively, the Building and the parcel of land on which the Building sits.

"**Rules and Regulations**" - See Section 6.3 and **Exhibit D**.

"**Tenant's Initial Work**" – See Section 4.5.

"**Tenant's Notice Address**" – See **Exhibit A**.

"**Tenant's Work**" – See Section 4.3.

"**Term**" - See **Exhibit A**.

ARTICLE II

PREMISES AND TERM

Section 2.1 - Premises.

The Landlord hereby leases to the Tenant, and the Tenant hereby leases from the Landlord, for the Term, the Premises. The Premises shall exclude the entry and main lobby of the Building, first floor elevator lobby, first floor mail room, the common stairways and stairwells, elevators and elevator wells, boiler room, sprinklers, sprinkler rooms, elevator rooms, mechanical rooms, loading and receiving areas, electric and telephone closets, janitor closets, loading docks and bays, rooftop mechanical penthouses to the extent they house Building equipment, and pipes, ducts, conduits, wires and appurtenant fixtures and equipment serving exclusively or in common other parts of the Building. If the Premises at any time includes less than the entire rentable floor area of any floor of the Building, the Premises shall also exclude the common corridors, vestibules, elevator lobby and toilets located on such floor. Tenant acknowledges that, except as expressly set forth in this Lease, there have been no representations or warranties made by or on behalf of the Landlord with respect to the Premises, the Building or the Property or with respect to the suitability of any of them for the conduct of the Tenant's business. Tenant acknowledges that, except as expressly set forth in this Lease and subject to the Tenant Improvements Allowance described in **Exhibit A** hereto, it is accepting the Premises in its "as-is" condition as of the date of this Lease. Notwithstanding the foregoing, Landlord shall deliver possession of the Premises to Tenant vacant and free of all occupants and Landlord shall provide Tenant with a copy of a decommissioning closure report from a certified industrial hygienist certifying that the Premises has been decommissioned in accordance with applicable ordinances of the City of Cambridge.

Section 2.2 - Appurtenant Rights.

(a) The Tenant shall have, as appurtenant to the Premises, the nonexclusive right to use in common with others, subject to reasonable rules of general applicability to occupants of the Building from time to time made by the Landlord of which the Tenant is given notice: (i) the entry, vestibules and main lobby of the Building, first floor mailroom, the common stairways, elevators, elevator wells, boiler room, elevator rooms, sprinkler rooms, mechanical rooms, electric and telephone closets, janitor closets, loading docks and bays, rooftop mechanical penthouses and shafts to the extent they house Building equipment, and the pipes, sprinklers, ducts, conduits, wires and appurtenant fixtures and equipment serving the Premises in common with others, (ii) common walkways and driveways necessary or reasonably convenient for access to the Building, (iii) access to, and use of in common with other tenants of, loading and receiving areas and freight elevator, and electrical and telephone closets, all subject to Rules and Regulations then in effect, and (iv) if the Premises at any time includes less than the entire rentable floor area of any floor, the common corridors, vestibules, elevator lobby, lavatories, and freight elevator vestibule located on such floor (collectively, the "**Common Areas**"). Tenant shall have 24 hour, seven day per week access to the Premises, freight loading docks and freight elevator, subject to the provisions of this Lease and interruption for External Causes, casualty and condemnation. After-hours

Building access shall be provided via a card reader access system. Landlord shall provide Tenant with all equipment necessary for such after-hours access.

(b) The Tenant shall have, as appurtenant to the Premises, the parking rights set forth in Section 2.4.

(c) Subject to Section 4.1 with respect to installation requirements, Tenant shall have, as appurtenant to the Premises (and exclusively for use in connection with the occupancy of the Premises), the nonexclusive right, at no additional rental cost, to install heating, ventilation and air conditioning equipment, antennae and dishes on the roof of the Building in areas that in aggregate do not exceed Tenant's proportionate share of roof area of the Building, in each case in locations designated by Landlord, subject however, to reasonable rules of general applicability to occupants of the Building from time to time made by the Landlord of which the Tenant is given notice. Any such equipment installed by Tenant shall be for Tenant's own use and shall be subject to (i) Landlord's approval regarding location and installation specification, and any specifications arising from the roof warranty, including the requirement to use such contractor(s) as Landlord may specify for such work, such approval not to be unreasonably withheld, conditioned or delayed, and (ii) applicable City of Cambridge and other legal requirements. Tenant shall be responsible for all costs relating to the installation, maintenance and removal of such equipment installed by Tenant on the Building roof. Any installations by Tenant on the roof of the Building shall constitute Removable Equipment to be removed by Tenant at the expiration of the Term in accordance with Section 4.2 of this Lease.

Section 2.3 - Landlord' s Reservations.

(a) The Landlord reserves the right from time to time, without unreasonable interference with the Tenant's use, to alter or modify the Common Areas, provided that (i) the Landlord gives the Tenant reasonable advance written notice of any contemplated alterations or modifications which are reasonably likely to affect Tenant's rights hereunder in any material way, (ii) any such actions are effected in a good and workmanlike manner, and (iii) such alterations or modifications do not impair Tenant's access to the Premises or its practical use and enjoyment thereof or of the Appurtenant Rights.

(b) In addition to other rights reserved herein or by law, Landlord reserves the right from time to time, without unreasonable interruption of Tenant's use and access to the Premises (and in any event during the existence of an emergency) (i) to make additions to or reconstructions of the Building and to install, use, maintain, repair, replace and relocate for service to the Premises and other parts of the Building, the pipes, ducts, conduits, wires and appurtenant fixtures, wherever located in the Premises, the Building, or elsewhere in the Property, provided that, to the extent practicable such installations, replacements or relocations in the Premises shall be placed above ceiling surfaces, below floor surfaces, or to the outside of the interior face of perimeter walls and provided that substitutions are substantially equivalent or better for Tenant's use of the Premises

consistent with the Permitted Use; (ii) to name or change the name of the Building, and (iii) to grant easements and other rights with respect to the Property.

(c) Tenant acknowledges that the Park is comprised of several buildings, including the Building and both life science/office buildings ("**Commercial Buildings**") and residential buildings ("**Residential Buildings**"), together with common and publicly accessible landscaped areas, service drives, and sidewalks. Landlord has established a common scheme for the operation and maintenance of the Park to which this Lease and the other leases of space in the Park are subject pursuant to a legal instrument entitled the "**Declaration of Covenants**," provided, however, that the terms and conditions-of the Declaration of Covenants shall not diminish in any material and adverse manner any of Tenant's rights and benefits with respect to the Premises, or materially and adversely increase any of Tenant's obligations. Each Commercial Building, and certain of the Residential Buildings, are subject to the Declaration of Covenants, and contribute to the costs and expenses to be shared thereunder. However, Landlord and Tenant recognize that Residential Buildings may not contribute to such costs and expenses, and therefore, it is agreed that allocation of costs and expenses payable under the Declaration of Covenants among the building owners, the Building's allocable share of which are Operating Expenses under this Lease, shall be based on an aggregation of all such costs and expenses, less whatever contributions can be collected from the Residential Buildings, and allocated to the Building based on a numerator comprised of the total rentable area of the Building, and the denominator of which is the total rentable area of all of the Commercial Buildings in existence from time to time, or by such other method as Landlord may reasonably determine.

Section 2.4 - Parking.

From and after the Commencement Date, Landlord shall provide and the Tenant shall pay for the Parking Passes (as defined on **Exhibit A**) for use by the Tenant's employees, business invitees and visitors in accordance with **Exhibit A**. The Landlord shall operate, or cause to be operated, a parking garage known as the 80 Lansdowne Street Garage (the "**Garage**") to serve the Building and other buildings in University Park. The Tenant's parking privileges shall be initially located in the Garage and shall be on a nonexclusive basis (i.e., no reserved spaces); provided, however, Landlord agrees that the Garage shall be operated so as to maintain therein sufficient spaces to accommodate Tenant's Parking Passes described in **Exhibit A**. However, Tenant's parking privileges may be relocated by Landlord to Landlord's other parking facilities located at 55 Franklin Street, Cambridge, Massachusetts and/or 30 Pilgrim Street, Cambridge, Massachusetts as Landlord shall designate upon reasonable prior notice to Tenant from Landlord. In the event that Tenant's parking privileges are so relocated, Tenant's parking privileges at such new location shall be consistent with the terms set forth in this Section 2.4. All monthly users will have unlimited access to the Garage twenty-four (24) hours per day, seven days per week. Tenant acknowledges that the parking facilities within the Park may be owned by an entity other than Landlord. In no event are Parking Passes transferable other than to the holder, from time to time, of the tenant's interest under this Lease or a subtenant that has been demised all or a portion of the Premises in conformity with the requirements of this Lease. Parking Passes are

limited to use by employees of either of the foregoing. Tenant agrees that it and all persons claiming by, through and under it, shall at all times abide by the Rules and Regulations with respect to the use of the Garage provided by the Landlord pursuant to this Lease.

Charges for Tenant's parking privileges hereunder shall be at current monthly parking rates (which rates shall be consistent with market parking rates in parking facilities of comparable quality at mixed use office/research parks in East Cambridge/Kendall Square/Cambridgeport), and shall constitute Additional Rent and shall be payable monthly to Landlord at the time and in the fashion in which Annual Fixed Rent under this Lease is payable.

Upon written request from time to time, and subject to availability (as determined by Landlord in its sole discretion), Tenant may obtain additional Parking Passes on a month-to-month basis (i.e. terminable by either party on 30 days' prior written notice), which additional Parking Passes shall be provided to Tenant on all of the terms and conditions of this Article 2 except as expressly set forth in this sentence.

At any time during the Term Landlord shall have the right to assign Landlord's obligations to provide parking, as herein set forth, together with Landlord's right to receive Additional Rent for such parking spaces as herein provided, to a separate entity created for the purpose of providing the parking privileges set forth herein. In such event, Landlord and Tenant agree to execute and deliver appropriate documentation, including documentation with the new entity, reasonably necessary to provide for the new entity to assume Landlord's obligations to provide the parking privileges to Tenant as specified herein and for the Tenant to pay the Additional Rent attributable to the parking privileges directly to the new entity. Landlord shall, however, remain primarily liable for the provision of Tenant's parking privileges.

Section 2.5 - Commencement Date.

"**Commencement Date**" as defined in **Exhibit A**.

Section 2.6 - Extension Option.

Provided that there has been no Event of Default which is uncured and continuing on the part of the Tenant, and that Tenant (or a successor entity resulting from one or more Permitted Transfers pursuant to Section 6.8) is, as of the date of exercise of its rights under this Section 2.6, in occupancy of at least 75% of the Premises for its own business purposes, the Tenant shall have the right to extend the Term hereof for two (2) consecutive periods of five (5) years (the first such period being the "**First Extension Term**" the second such period being the "**Second Extension Term**" and, together with the First Extension Term, the "**Full Extension Term**") on the following terms and conditions:

(a) Such right to extend the Term shall be exercised by the giving of notice by Tenant to Landlord at least nine (9) months prior to the expiration of the Initial Term or First Extension Term, as applicable (the "**Extension Notice Deadline Date**"). Upon the giving of such notice on or before the Extension Notice Deadline Date, this Lease and the Term hereof shall be extended for an additional term, as specified above, without the

necessity for the execution of any additional documents except a document memorializing the Annual Fixed Rent for the applicable Extension Term to be determined as set forth below. Time shall be of the essence with respect to the Tenant's giving notice to extend the Term on or before the Extension Notice Deadline Date. In no event may the Tenant extend the Term under this Section 2.6 for more than ten (10) years after the expiration of the Initial Term, unless Landlord and Tenant shall mutually agree to such an extension.

(b) The First Extension Term and the Second Extension Term shall be upon all the terms, conditions and provisions of this Lease, except the Annual Fixed Rent during each such Extension Term shall be the then Fair Market Rent of the Premises for such Extension Term, to be determined under this Section 2.6.

(c) For purposes of the First Extension Term and Second Extension Term described in this Section 2.6, the Fair Market Rent of the Premises shall mean the then current fair market annual rent for leases of comparable space of a comparable nature and quality similarly improved located in the commercial markets that surround the MIT campus (East Cambridge/Kendall Square/Cambridgeport), so as to provide Landlord, on a net basis, the same as it would receive upon a re-letting at fair market value, taking into account all relevant factors including comparable building age, quality, level of finish, proximity to amenities and public transit, the condition to which such premises have been improved and the economic terms and conditions specified in this Lease that will be applicable thereto, including the savings, if any, due to the absence or reduction of brokerage commissions. The Landlord and Tenant shall endeavor to agree upon the Fair Market Rent of the Premises within thirty (30) days after the Tenant has exercised an option for an Extension Term. If the Fair Market Rent of the Premises is not agreed upon by the Landlord and the Tenant within this time frame, each of the Landlord and the Tenant shall retain a real estate professional with at least ten (10) years continuous experience in the business of appraising or marketing similar commercial real estate in the Cambridge, Massachusetts area who shall, within thirty (30) days of his or her selection, prepare a written report summarizing his or her conclusion as to the Fair Market Rent of the Premises. The Landlord and the Tenant shall simultaneously exchange such reports; provided, however, if either party has not obtained such a report within forty-five (45) days after the last day of the thirty (30) day period referred to above in this Section 2.6 and such party fails to deliver the required report within an additional fifteen (15) days of notice of such failure, then the determination set forth in the other party's report shall be final and binding upon the parties. If both parties receive reports within such time and the lower determination is within ten percent (10%) of the higher determination, then the average of these determinations shall be deemed to be the Fair Market Rent of the Premises. If these determinations differ by more than ten percent (10%), then the Landlord and the Tenant shall mutually select a person with the qualifications stated above (the "Final Professional") to resolve the dispute as to the Fair Market Rent of the Premises. If the Landlord and the Tenant cannot agree upon the designation of the Final Professional within ten (10) days of the exchange of the first valuation reports, either party may apply to the American Arbitration Association, the

Greater Boston Real Estate Board, or any successor thereto, for the designation of a Final Professional. Within ten (10) days of the selection of the Final Professional, the Landlord and the Tenant shall each submit to the Final Professional a copy of their respective real estate professional's determination of the Fair Market Rent of the Premises. The Final Professional shall then, within thirty (30) days of his or her selection, prepare a written report summarizing his or her conclusion as to the Fair Market Rent of the Premises (the "**Final Professional's Valuation**"). The Final Professional shall give notice of the Final Professional's Valuation to the Landlord and the Tenant and such decision shall be final and binding upon the Landlord and the Tenant. In the event that the commencement of either of the First Extension Term or Second Extension Term occurs prior to a final determination of the Fair Market Rent of the Premises therefor (the "**Extension Rent Determination Date**"), then the Tenant shall pay the Annual Fixed Rental at the then applicable Fixed Rental Rate (such amount being referred to as the "**Interim Rent**"). If the Annual Fixed Rent as finally determined for such Extension Term is determined to be greater than the Interim Rent, then the Tenant shall pay to the Landlord the amount of the underpayment for the period from the end of the Initial Term of this Lease until the Extension Rent Determination Date within thirty (30) days of the Extension Rent Determination Date. If the Annual Fixed Rent as finally determined for the Extension Term is determined to be less than the Interim Rent, then the Landlord shall credit the amount of such overpayment against the monthly installments of Annual Fixed Rent coming due after the Extension Rent Determination Date.

Section 2.7 - One-Time Right of First Offer.

Subject to the provisions of this Section 2.7 as well as the pre-existing rights of existing tenants of the Park, Tenant shall have a one-time right of first offer for all or any portion of the first (1st), second (2nd), third (3rd), fourth (4th) and fifth (5th) floors of the Building which may hereafter become vacant and available (the "**First Offer Space**") during the Term following the expiration or termination of the lease or occupancy agreement with the then tenant of such First Offer Space and subject to Landlord's right to grant any tenant of the First Offer Space the right to renew or continue its term of occupancy whether or not such rights are expressly granted by a lease or other written instrument. Landlord shall notify Tenant of the terms on which Landlord intends to offer to lease the First Offer Space ("**Landlord's ROFO Notice**") and the Annual Fixed Rent shall be at the then current Fair Market Rent for the First Offer Space taking into account all relevant factors. Within ten (10) business days after receipt of Landlord's ROFO Notice, Tenant may, by written notice delivered to Landlord, (i) reject Landlord's ROFO Notice, or (ii) unconditionally and irrevocably accept Landlord's offer to lease all but not less than all of such space for Tenant's own use on the terms set forth in Landlord's Notice. If Tenant fails to timely respond as aforesaid, such failure shall be deemed Tenant's rejection of Landlord's ROFO Notice. In the event Tenant exercises its right to the First Offer Space, Landlord and Tenant hereby agree to amend those provisions of this Lease which are necessarily affected by the increase in the rentable area and leaving all other provisions of this Lease in full force and effect without modification. After Tenant takes possession of the First Offer Space, the term "Premises" as used in this Lease, shall be deemed to refer to and include the First Offer Space.

If Landlord's ROFO Notice is rejected under clause (i) above (or deemed rejected through the Tenant's failure to timely respond), then Landlord may enter into a lease for the First Offer Space providing for an effective Annual Fixed Rent equal to or less than seven and one-half percent (7.5%) less than that specified in Landlord's ROFO Notice. For clarity, in the event that the Landlord proposes to enter into a lease for the First Offer Space providing for an effective Annual Fixed Rent greater than seven and one-half percent (7.5%) less than that specified in Landlord's ROFO Notice, Landlord shall notify Tenant of such terms by sending an additional Landlord's ROFO Notice that will be subject to the terms of the preceding paragraph.

Except as may be set forth in Landlord' s Notice, Landlord's failure to deliver, or delay in delivering, all or any part of the First Offer Space, for any reason, shall not constitute a default of Landlord, and shall not affect the validity of the Lease.

ARTICLE III

RENT AND OTHER PAYMENTS

Section 3.1 - Annual Fixed Rent.

From and after the Rent Commencement Date (as defined in **Exhibit A**), the Tenant shall pay, without notice or demand, monthly installments of one-twelfth ($1/12^{th}$) of the Annual Fixed Rent in effect and applicable to the Premises in advance for each full calendar month of the Term following the Rent Commencement Date and of the corresponding fraction of said one-twelfth ($1/12^{th}$) for any fraction of a calendar month at the Rent Commencement Date or end of the Term. The Annual Fixed Rent applicable to the Premises during the Term shall be as set forth in **Exhibit A**.

Section 3.2 - Real Estate Taxes.

From and after the Commencement Date, during the Term, the Tenant shall pay to the Landlord, as Additional Rent, the Tenant's Tax Expenses Allocable to the Premises (as such term is hereinafter defined) in accordance with this Section 3.2. The terms used in this Section 3.2 are defined as follows:

(a) "**Tax Year**" means the 12-month period beginning July 1 each year or if the appropriate governmental tax fiscal period shall begin on any date other than July 1, such other date.

(b) "**The Tenant's Tax Expense Allocable to the Premises**" means (i) that portion of the Landlord's Tax Expenses for a Tax Year which bears the same proportion thereto as the rentable floor area of the Premises (from time to time) bears to the Total Rentable Floor Area of the Building and (ii) in the event that the Premises are improved to a standard which is higher than other portions of the Property and the Property is re-assessed at a higher value, such portion of the Real Estate Taxes on the Property with respect to any Tax Year as is appropriate so that the Tenant bears the portion of the Real Estate Taxes which are properly allocable to the Premises, as reasonably determined by Landlord using good faith commercially reasonable judgment based on assessment values

and other information with respect to the Premises and the Building made available by the assessing authorities (Landlord's determination of such allocation shall take into account the rate of appreciation, if any, of real property in the City of Cambridge from the date of the prior assessment to the date of the new assessment, and the portion of any increased assessment on the Property which is allocable to any such general increase in the value of the real property in the City of Cambridge shall not be allocated disproportionately to Tenant).

(c) "**The Landlord's Tax Expenses**" with respect to any Tax Year means the aggregate Real Estate Taxes on the Property with respect to that Tax Year, reduced by any abatement received with respect to that Tax Year.

(d) "**Real Estate Taxes**" means (i) all real property taxes and special assessments of every kind and nature assessed by any governmental authority on the applicable property, but excluding any income taxes payable by Landlord as a result of payments made to Landlord by Tenant or any other tenant at the Property; and (ii) reasonable expenses of any proceedings for abatement of such taxes or special assessments. Any special assessments to be included within the definition of "Real Estate Taxes" shall be limited to the amount of the installment (plus any interest thereon) of such special tax or special assessment (which shall be payable over the longest period permitted by law) required to be paid during the Tax Year in respect of which such taxes are being determined. There shall be excluded from such taxes all income, estate, succession, inheritance, excess profit, franchise and transfer taxes; provided, however, that if at any time during the Term the present system of ad valorem taxation of real property shall be changed so that in lieu of the whole or any part of the ad valorem tax on real property, there shall be assessed on the Landlord a capital levy or other tax on the gross rents received with respect to the Property, or a federal, state, county, municipal or other local income, franchise, excise or similar tax, assessment, levy or charge (distinct from any now in effect) based, in whole or in part, upon any such gross rents, then any and all of such taxes, assessments, levies or charges, to the extent so based, shall be deemed to be included within the term "Real Estate Taxes."

Payments by the Tenant on account of the Tenant's Tax Expenses Allocable to the Premises shall be made monthly at the time and in the fashion herein provided for the payment of Annual Fixed Rent and shall be in an amount equal to the greater of (i) one-twelfth ($1/12^{th}$) of the Tenant's Tax Expenses Allocable to the Premises for the current Tax Year as reasonably estimated by the Landlord, or (ii) an amount reasonably estimated by any ground lessor of the Land or holder of a first mortgage on the Property, to be sufficient, if paid monthly, to pay the Landlord's Tax Expenses on the dates due to the taxing authority.

Not later than ninety (90) days after the Landlord's Tax Expenses are determinable for the first Tax Year of the Term or fraction thereof and for each succeeding Tax Year or fraction thereof during the Term, the Landlord shall render the Tenant a statement in reasonable detail showing for the preceding year or fraction thereof, as the case may be, real estate taxes on the Property, and any abatements or refunds of such taxes. Expenses incurred in obtaining any tax

abatement or refund may be charged against such tax abatement or refund before the adjustments are made for the Tax Year. If at the time such statement is rendered it is determined with respect to any Tax Year, that the Tenant has paid (i) less than the Tenant's Tax Expenses Allocable to the Premises or (ii) more than the Tenant's Tax Expenses Allocable to the Premises, then, in the case of (i) the Tenant shall pay to the Landlord, as Additional Rent, within thirty (30) days of such statement the amount of such underpayment and, in the case of clause (ii) the Landlord shall credit the amount of such overpayment against the monthly installments of the Tenant's Tax Expenses Allocable to the Premises next thereafter coming due (or refund such overpayment within thirty (30) days if the Term has expired and the Tenant has no further obligation to the Landlord).

To the extent that real estate taxes shall be payable to the taxing authority in installments with respect to periods less than a Tax Year, the statement to be furnished by the Landlord shall be rendered and payments made on account of such installments. Notwithstanding the foregoing provisions, no decrease in Landlord's Tax Expenses with respect to any Tax Year shall result in a reduction of the amount otherwise payable by Tenant if and to the extent said decrease is attributable to vacancies in the Building, rather than to a reduction in the assessed value of the Property as a whole or a reduction in the tax rate. Landlord shall, upon Tenant's request therefor, provide Tenant with copies of all applicable tax bills, statements, records and the like, as well as copies of Landlord's calculations and all other relevant information.

Section 3.3 - Operating Expenses.

From and after the Commencement Date, during the Term the Tenant shall pay to the Landlord, as Additional Rent, the Tenant's Operating Expenses Allocable to the Premises, as hereinafter defined, in accordance with this Section 3.3. The terms used in this Section 3.3 are defined as follows:

(a) "**The Tenant's Operating Expenses Allocable to the Premises**" means that portion of the Operating Expenses for the Property which bears the same proportion thereto as the Rentable Floor Area of the Premises bears to the Total Rentable Floor Area of the Building.

(b) "**Operating Expenses for the Property**" means Landlord's cost of operating, cleaning, maintaining and repairing the Property, and shall include without limitation, the cost of services on **Exhibit C**; premiums for insurance carried pursuant to Section 7.4; the amount deductible from any insurance claim actually made by Landlord during the time period in question (which amount is currently $50,000.00, and which amount may be increased during the Term and any Extension Term provided such increase is reasonable and customary); reasonable compensation and all fringe benefits, worker's compensation insurance premiums and payroll taxes paid to, for or with respect to all persons (Park/Building general manager and below, provided that such charges shall be prorated to reflect the percentage of rentable square feet of the Building as compared to all of the commercial rentable square feet at the Park) directly engaged in the operating, maintaining or cleaning of the Property; interior landscaping and maintenance; steam, water, sewer, gas, oil, electricity, telephone and other utility charges

(excluding such utility charges either separately metered or separately chargeable to tenants for additional or special services and those charges related to the cost of operating base Building equipment not used by Tenant, and costs of providing conditioned water for HVAC services); cost of building and cleaning supplies; the costs of routine environmental management programs operated by Landlord; market rental costs for equipment used in the operating, cleaning, maintaining or repairing of the Property, or the applicable fair market rental charges in the case of equipment owned by the Landlord; cost of cleaning; cost of maintenance, repairs and replacements; cost of snow removal; cost of landscape maintenance; security services; payments under service contracts with independent contractors; management fees at market rates; the cost of any capital improvement either required by law or regulation or which reduces the Operating Expenses for the Property or which improves the management and operation of the Property in a manner acceptable to Tenant, which cost shall be amortized in accordance with generally accepted accounting principles together with interest on the unamortized balance calculated at the rate from time to time announced by Bank of America, N.A. as its prime rate; charges reasonably allocated to the Building for the operating, cleaning, maintaining and repairing of the Park common areas and amenities; and all other reasonable and necessary expenses paid in connection with the operation, cleaning, maintenance, administration and repair of the Property. If for any reason portions of the Rentable Area of the Building not included in the Premises were not occupied by tenants or the Landlord was not supplying all tenants with the services being supplied under the Lease or any tenants in the Building were supplied with a lesser level of standard services than those supplied to the Tenant under this Lease, Landlord's Operating Expenses for the Property shall include the amounts reasonably determined by Landlord which would have been incurred if ninety-five percent (95%) of the rentable area in the Building were occupied and were applied with the same level of standard services as supplied to the Tenant under this Lease.

Operating Expenses for the Property shall not include the following: the Landlord's Tax Expense; cost of repairs or replacements (i) resulting from eminent domain takings, (ii) to the extent reimbursed by insurance, or (iii) required, above and beyond ordinary periodic maintenance, to maintain in serviceable condition the major structural elements of the Building, including the roof, exterior walls and floor slabs; replacement or contingency reserves; ground lease rents or payment of debt obligations; costs incurred due to negligent acts or omissions of Landlord, Landlord's agents, contractors or employees, or any other tenant of the Building; legal and other professional fees for matters not relating to the normal administration and operation of the Property; promotional, advertising, public relations or brokerage fees and commissions paid in connection with services rendered for securing or renewing leases; lease up and tenant improvement costs for space other than the Premises in the Building; costs of capital improvements not permitted hereinabove; and separately metered or sub metered utilities for other tenants in the Building. The Landlord's Operating Expenses shall be reduced by the amount of any proceeds, payments, credits or reimbursements which the Landlord receives from sources other than tenants and which are applicable to such Operating Expenses for the Property.

Payments by the Tenant for its share of the Operating Expenses for the Property shall be made in monthly installments of one-twelfth (1/12th) of Tenant's share of Operating Expenses. The amount so to be paid to the Landlord shall be an amount from time to time reasonably estimated by the Landlord to be sufficient to aggregate a sum equal to the Tenant's share of the Operating Expenses for the Property for each calendar year.

Not later than ninety (90) days after the end of each calendar year or fraction thereof during the Term or fraction thereof at the end of the Term, the Landlord shall render the Tenant a statement in reasonable detail and according to usual accounting practices certified by a representative of the Landlord, showing for the preceding calendar year or fraction thereof, as the case may be, the Operating Expenses for the Property and the Tenant's Operating Expenses Allocable to the Premises. Said statement to be rendered to the Tenant also shall show for the preceding calendar year or fraction thereof, as the case may be, the amounts of Operating Expenses already paid by the Tenant. If at the time such statement is rendered it is determined with respect to any calendar year, that the Tenant has paid (i) less than the Tenant's Operating Expenses Allocable to the Premises or (ii) more than the Tenant's Operating Expenses Allocable to the Premises, then, in the case of (i) Tenant shall pay to the Landlord, as Additional Rent, within thirty (30) days of such statement the amounts of such underpayment and, in the case of (ii) Landlord shall credit the amount of such overpayment against the monthly installments of the Tenant's Operating Expenses Allocable to the Premises next thereafter coming due (or refund such overpayment within thirty (30) days if the Term has expired and Tenant has no further obligation to the Landlord).

Tenant may, after ten (10) days' prior written notice to Landlord given within one hundred twenty (120) days of Landlord's delivery to Tenant of a statement of Operating Expenses for the Property, during Landlord's regular business hours and at Tenant's sole cost and expense, inspect Landlord's books and records relating to Operating Expenses and Real Estate Taxes for the Property. Such books and records shall be made available at the Property, unless such books and records are regularly kept in Cleveland, Ohio , in which case they will be made available for Tenant's inspection in Cleveland, Ohio. Tenant shall keep all information relating to Operating Expenses for the Property strictly confidential and shall in no event, whatsoever, disclose such information to any third party other than to Tenant's attorneys and accountants in connection with proceedings concerning this Lease. If it is mutually agreed for finally determined by a proceeding that Landlord's statement has overstated the Operating Expenses for the Property for any calendar year by more than four percent (4%) then Landlord shall reimburse Tenant for its reasonable audit costs incurred in connection with such audit. In the event that Tenant uses a third party to assist with the audit, such third party shall be a certified public accounting firm that is not engaged on a contingency basis.

Section 3.4 - Other Utility Charges.During the Term, the Tenant shall pay directly to the provider of the service all separately metered charges for steam, heat, gas, electricity, fuel and other services and utilities furnished to the Premises, and shall pay to Landlord as Additional Rent its pro rata share of water, sewer and other services and utilities which shall be prorated to reflect Tenant's proportional usage based upon Tenant's proportional occupancy of the Building. The costs of utilities supplied to the common areas and base building systems are included in

Operating Expenses and all major utilities other than water and sewer supplied to the Premises and other tenant spaces in the Building are separately metered. Tenant shall pay, as Additional Rent, for Tenant's pro rata share of water and sewer service to the Premises monthly within thirty (30) days following receipt of an invoice from Landlord.

Section 3.5 - Above-standard Services.

If the Tenant requests and the Landlord elects to provide any services to the Tenant in addition to those described in **Exhibit C**, the Tenant shall pay to the Landlord, as Additional Rent, the amount billed by Landlord for such services at Landlord's standard rates as from time to time in effect. The cost of such services shall not be deemed to be Operating Expenses for the Property as described in Section 3.3. If the Tenant has requested that such services be provided on a regular basis, the Tenant shall, if requested by the Landlord, pay for such services at the time and in the fashion in which Annual Fixed Rent under this Lease is payable. Otherwise, the Tenant shall pay for such additional services within thirty (30) days after receipt of an invoice from the Landlord. Landlord shall have the right from time to time to inspect Tenant's utility meters and to install timers thereon at Tenant's expense for purposes of monitoring above-standard service usage. Tenant shall pay for such work within thirty (30) days after receipt of an invoice from Landlord.

Section 3.6 - No Offsets.

Annual Fixed Rent and Additional Rent shall be paid by the Tenant without offset, abatement or deduction except as provided herein.

Section 3.7 - Net Lease.

It is understood and agreed that this Lease is a net lease and that the Annual Fixed Rent is absolutely net to the Landlord excepting only the Landlord's obligations to pay any debt service or ground rent on the Property, to provide the Landlord's services, and to pay the real estate taxes and operating expenses which the Tenant is not required to pay under this Lease.

ARTICLE IV

ALTERATIONS

Section 4.1 - Consent Required for Tenant's Alterations.

The Tenant shall not make alterations or additions to the Premises (including any Tenant's Work) except in accordance with complete, coordinated construction plans and specifications therefor first approved by the Landlord, which approval shall not be unreasonably withheld, conditioned or delayed. Except as otherwise provided in Section 4.2, Landlord agrees to state in writing simultaneously with its granting of any approval concerning any alteration or addition to the Premises the extent to which Tenant will need to remove the alteration or addition at issue upon the expiration or earlier termination of the Term. There will be no charge for Landlord's review of Tenant's plans, specifications and construction, except for Landlord's reasonable, third party, out-of-pocket expenses, which, as provided in Section 4.5 herein, with respect to the

Tenant's Initial Work, shall not exceed Five Thousand and 00/100 Dollars ($5,000.00). Notwithstanding the foregoing, the Tenant may, from time to time without the Landlord's prior consent and at the Tenant's own expense, make interior non-structural alterations affecting only the interior of the Premises, and not affecting Building systems, costing less than $50,000.00 in any one instance (or in the aggregate with respect to related alterations) without Landlord's prior written consent, but subject to the other terms of this Lease, and provided that Tenant provides notice of such alterations within a reasonable time after the completion of the same. The Landlord shall not be deemed unreasonable for withholding approval of any alterations or additions which (i) would adversely affect any structural or exterior element of the Building, (ii) would materially and adversely affect the general utility of the Building for use by existing tenants or prospective future tenants thereof, (iii) would affect the exterior appearance of the Building in a manner which is not acceptable to the Landlord, in its sole discretion, (iv) will require unusual expense to readapt the Premises to normal office space use; or (v) would adversely affect existing mechanical or electrical, plumbing, HVAC or other systems in the Building, in each case, with respect to clauses (i)-(v), as reasonably determined by the Landlord. The Landlord shall not be deemed unreasonable in delaying the approval of any alterations or additions to the extent that Landlord reasonably requires consultation with third party architects or engineers to review the plans for such work. In any notice withholding approval the Landlord shall specify, in reasonable detail, the nature of the Landlord's objection. Neither the Landlord's failure to object to any proposed alterations or additions, nor the Landlord's approval of any plans and specifications furnished by Tenant to Landlord, shall be construed as superseding in any respect, or as a waiver of Landlord's right to enforce, the Tenant's obligation to fulfill all of the terms and conditions of this Lease applicable to any work contemplated thereby. All alterations and additions to the Premises shall be designed in reasonable accordance with the Building design standards promulgated by Landlord from time to time.

Promptly following the performance of any alterations or additions to the Premises requiring Landlord's reasonable approval, the Tenant shall furnish Landlord an "as built" set of plans and specifications for the Premises and a report evidencing the completion of air balancing (to the extent such alterations or additions affected air balancing), in a format reasonably requested by the Landlord.

Notwithstanding anything to the contrary contained in this Section 4.1, if any of the Tenant's proposed alterations and/or additions affect the roof of the Building, the following additional conditions shall apply:

(a) Such alterations and changes will not in any way interfere with the proper functioning of, and Landlord's access to, equipment located on the roof of the Building or exceed roof loading requirements; and

(b) Adequate measures are taken to reduce the visibility and noise of mechanical equipment, antennae and dishes consistent with the appearance and design scheme required by the Rules and Regulations and any applicable laws, ordinances or regulations of the City of Cambridge.

Section 4.2 - Ownership of Alterations.

All alterations and additions shall be part of the Building and owned by the Landlord; provided, however, that the Landlord may require removal by the Tenant of all or any portion of any specialized alterations and additions made to the Premises. For purposes of the foregoing, "specialized alterations and additions" shall mean any alterations or additions which, as reasonably determined by the Landlord, (i) would adversely affect the general utility of the Building for use by existing tenants or prospective future tenants thereof, or (ii) will require unusual expense to readapt the Premises to normal office use. Landlord shall specify such items at the time of its approval of their installation. All movable trade fixtures and furnishings not attached to the Premises shall remain the property of the Tenant and shall be removed by the Tenant upon termination or expiration of this Lease. The Tenant shall repair any damage caused by the removal of any alterations, additions or personal property from the Premises. All personal property and equipment installed by Tenant during the Term ("**Removable Equipment**") shall be removed from the Premises and the Building upon the expiration or earlier termination of the Term of this Lease.

Any alterations and additions, if required to be removed upon the termination or expiration of this Lease as hereinabove provided, and all Removable Equipment shall be removed by the Tenant with reasonable care and diligence, including the capping off of all utility connections behind the adjacent interior finish, and the restoration of such interior finish to the extent necessary so that the Premises are left with complete wall, ceiling and floor finishes.

Section 4.3 - Construction Requirements for Alterations.

All construction work performed by or on behalf of the Tenant, including the Tenant's Initial Work (as hereinafter defined) ("**Tenant's Work**") shall be done in a good and workmanlike manner employing only first class materials and in compliance with the Rules and Regulations (as defined in Section 6.3) that apply to construction, and with all applicable laws and all lawful ordinances, regulations and orders of governmental authority and insurers of the Building. The Landlord or Landlord's authorized agent may (but without any implied obligation to do so) inspect the work of the Tenant at reasonable times and shall give notice of observed defects. Tenant's Work and the installation of furnishings shall always be coordinated in such manner as to maintain harmonious labor relations on the Property and not to damage the Building or interfere with Building construction or operation. Tenant's Work shall be performed by contractors or workmen first approved by the Landlord, which approval the Landlord agrees not to unreasonably withhold, condition or delay (Landlord shall provide its written consent or written notice of its reason for withholding consent within ten (10) days of any request for consent from Tenant). The Tenant, before starting any work, shall receive and comply with the Construction Rules and Regulations attached hereto as **Exhibit G** and shall (i) cause the Tenant's contractors to comply therewith; (ii) obtain "builder's risk" coverage (in an amount that is reasonable given the quality and quantity of the work to be undertaken) to enhance the insurance coverage otherwise required to be carried by the Tenant hereunder; (iii) secure all licenses and permits necessary for such work; (iv) deliver to the Landlord a statement of the names of its general contractor (or construction manager) and subcontractors (x) who will be performing work with a value in excess of $50,000.00, (y) who are to perform electrical or plumbing work; or (z) are otherwise to perform work that will affect the structure or base building systems of the

Building, and the estimated cost to design and construct any Tenant's Work; (v) except with respect to the Tenant's Initial Work, provide security satisfactory to the Landlord in its reasonable discretion and consistent with the security requirements for comparable work in comparable buildings in the Cambridge market protecting the Landlord against liens arising out of the furnishing of such labor and material; and (vi) cause each contractor to carry worker's compensation insurance in statutory amounts covering all the contractors' and subcontractors' employees and commercial general liability insurance on an occurrence basis with limits of $1,000,000 (individual) and $3,000,000 (aggregate) covering personal injury and death and property damage (all such insurance to be written in companies approved reasonably by the Landlord and insuring the Landlord, such individuals and entities affiliated with the Landlord as the Landlord may designate, any ground lessor or mortgagee that the Landlord may designate, and the Tenant as well as the contractors and to contain a requirement for at least thirty (30) days' notice to the Landlord prior to cancellation, nonrenewal or material change), and deliver to the Landlord certificates of all such insurance prior to the commencement of the applicable Tenant's Work. Tenant shall reimburse Landlord within 30 days after invoice for any reasonable out-of-pocket third-party expenses, which, as provided in Section 4.5 herein, with respect to the Tenant's Initial Work, shall not exceed Five Thousand and 00/100 Dollars ($5,000.00), incurred by the Landlord in connection with any request by the Tenant for consent to any alterations or additions pursuant to this Article 4.

Section 4.4 - Payment for Tenant Alterations.

Except as otherwise set forth in **Exhibit E** attached hereto, Tenant agrees to pay promptly when due the entire cost of any work done on the Premises by the Tenant, its agents, employees or independent contractors, and not to cause or permit any liens or notice of intent to file a lien for labor or materials performed or furnished in connection therewith to attach to the Premises or the Property and promptly to discharge (or bond over in a manner reasonably satisfactory to Landlord) any such liens which may so attach. If any such lien or notice of intent to file a lien shall be filed against the Premises or the Property and the Tenant shall fail to cause such lien or notice to be discharged within fifteen (15) days after receipt by the Tenant of notice of the filing thereof, the Landlord may cause such lien or notice to be discharged by payment or otherwise without investigation as to the validity thereof or as to any offsets or defenses which the Tenant may have with respect to the amount claimed. The Tenant shall reimburse the Landlord, as additional rent, for any cost so incurred and shall indemnify and hold harmless the Landlord from and against any and all claims, costs, damages, liabilities and expenses (including reasonable attorneys' fees) which may be incurred or suffered by the Landlord by reason of any such lien or its discharge.

Section 4.5 - Tenant's Initial Work.

Tenant shall have the right to perform initial work to the Premises following the Commencement Date (the "**Tenant's Initial Work**") to prepare the Premises for the conduct of Tenant's business. The construction of the Tenant's Initial Work shall be done in accordance with the terms of this Article IV and **Exhibit E** attached hereto, and pursuant to plans prepared by Tenant which shall have been approved by Landlord, which approval will not unreasonably

be withheld. Additionally, and subject to the terms set forth herein, Tenant may hire its own contractor, architect and engineer for the construction of the Tenant's Initial Work, subject to the approval of the Landlord, which shall not be unreasonably withheld. There shall be no construction oversight fee paid to Landlord. However, Landlord shall be reimbursed up to Five Thousand and 00/100 Dollars ($5,000.00) for any third party out of pocket costs incurred by Landlord in the review and approval of Tenant's plans, specifications, improvements and construction for the Tenant's Initial Work.

ARTICLE V

RESPONSIBILITY FOR CONDITION OF BUILDING AND PREMISES

Section 5.1 - Maintenance of Building and Common Areas by Landlord.

Except as otherwise provided in Article 8, Landlord shall make such repairs to the foundation, roof, exterior walls (including exterior glass), floor slabs, elevators, base building mechanical, plumbing and electrical and life safety systems (to the extent serving more than one tenant), and any other base structural elements of the Building as may be necessary to keep them in good order, condition and repair, and make such repairs to the mechanical systems and equipment serving the Building, except for any mechanical, plumbing and electrical systems and equipment that serve the Premises exclusively ("Tenant's Dedicated Mechanical Systems and Equipment"), and other Common Areas as are necessary to keep them in good order, condition and repair. The Landlord shall further perform the services designated as Landlord's Services on **Exhibit C**. Costs and expenses incurred by the Landlord under this Section 5.1 shall be included in Operating Expenses of the Property as permitted under Section 3.3. Subject to Section 7.5, the Tenant shall be responsible for 100% of the cost of any repair to the Premises, the Building, or the Land caused by the negligence or misconduct of the Tenant, or any agent, employee, contractor or invitee of the Tenant, notwithstanding anything to the contrary provided in Section 3.3.

Section 5.2 - Maintenance of Premises by Tenant.

The Tenant shall keep and maintain in good order, condition and repair the Premises and every part thereof and all of Tenant's Dedicated Mechanical Systems and Equipment, reasonable wear and tear and damage by fire or other casualty excepted (provided that subject to Section 7.5, the Landlord shall be responsible for damage caused by the fault or neglect of the Landlord, or the Landlord's agents, employees or contractors), excluding those repairs for which the Landlord is responsible pursuant to Sections 5.1, 8.1 and 8.5. The Tenant shall not permit or commit any damage (waste), and the Tenant shall, subject to Section 7.5, be responsible for the cost of repairs which may be made necessary by reason of damage to the Property caused by the negligence or misconduct of the Tenant, or any of the contractors, employees, agents or invitees of the Tenant. Mechanical, HVAC, and all systems and equipment shall be maintained in good order, condition and repair consistent with prevailing standards at comparable first class leased laboratory buildings, reasonable wear and tear, damage by fire or other casualty, and subject to

Section 7.5, damage caused by the fault or neglect of the Landlord, or the Landlord's agents, employees, or contractors excepted.

Section 5.3 - Delays in Landlord's Services.

The Landlord shall not be liable to the Tenant for any compensation or reduction of rent by reason of inconvenience or annoyance or for loss of business arising from the necessity of the Landlord or its agents entering the Premises for any purposes authorized in this Lease, or for repairing the Premises or any portion of the Building. In case the Landlord is prevented or delayed from making any repairs, alterations or improvements, or furnishing any services or performing any other covenant or duty to be performed on the Landlord's part, by reason of any External Cause, the Landlord shall not be liable to the Tenant therefor, nor, except as expressly otherwise provided in this Lease, shall the Tenant be entitled to any abatement or reduction of rent by reason thereof, nor shall the same give rise to a claim in the Tenant's favor that such failure constitutes actual or constructive, total or partial, eviction from the Premises.

The Landlord reserves the right to stop any service or utility system the Landlord provides or causes to be provided under this Lease when necessary by reason of accident or emergency or exercise of Landlord's rights pursuant to Section 2.3 hereof, or until necessary repairs have been completed; provided, however, that in each instance of stoppage, the Landlord shall exercise reasonable diligence to eliminate the cause thereof. Except in case of emergency repairs, the Landlord will give the Tenant reasonable advance written notice of the contemplated stoppage and will use reasonable efforts to avoid unnecessary inconvenience to the Tenant by reason thereof. To the extent that the Landlord is providing or causing to be provided heat, light or any utility or service, in no event shall the Landlord have any liability to the Tenant for the unavailability of the same to the extent that such unavailability is caused by External Causes, provided, however, that the Landlord is obligated to exercise reasonable efforts to restore such services or utility systems' operation.

If (i) the unavailability of heat, light or any utility or service provided or required to be provided by the Landlord, or the presence of Hazardous Materials in the Premises that is required to be removed or remediated pursuant to Section 5.5 herein, renders all or any portion of the Premises untenantable for the Tenant's use as permitted under this Lease, (ii) such untenantability is not due in whole or in part to the acts or omissions of Tenant, its agents, employees, contractors or invitees or any other party claiming by, through or under Tenant, and (iii) Tenant is reasonably unable to use or conduct and does not conduct its operations in the affected part or all of the Premises for more than five (5) business days after receipt of written notice of such untenantability from Tenant, Tenant shall receive an equitable and proportionate abatement of rent (including but not limited to abatement of Tenant's Tax Expenses and Tenant's Operating Expenses), taking into account the extent of the Tenant's loss of use of the Premises, for the period of time following the expiration of such five (5) business day period that Tenant is reasonably unable to use or conduct its operations on part or all of the Premises, and Tenant shall be entitled to terminate this Lease if Landlord is unable to restore such services within six (6) months from the date of interruption. Tenant shall have the right to terminate this Lease as aforesaid by written notice to Landlord at any time after the expiration of such six (6) month

period for so long as such interruption in service continues and the Premises remains untenantable and/or Tenant is reasonably unable to use or conduct its operations therein as a result, and such termination shall be effective as of the date that is thirty (30) days following Landlord's receipt of Tenant's termination notice unless such interruption is restored prior to the effective termination date. For all purposes of this Lease, if Tenant has responsibility for maintenance and repair of any aspect of the Building or any equipment or system therein, the functioning and performance of the same shall be the responsibility of the Tenant under this Lease, and shall in no event constitute a service or utility system that the Landlord provides or causes to be provided under this Lease.

Section 5.4 Tenant's Responsibilities Regarding Hazardous Materials.

Tenant covenants and agrees that Tenant shall not use, generate, store or dispose, nor shall the Tenant suffer or permit the use, generation, storing or disposal in the Premises or otherwise by any of Tenant's contractors, licensees, invitees, agents or employees, of any oil, toxic substances, hazardous wastes or hazardous materials (collectively, "Hazardous Materials") in, on or about the Premises, the Building or the Land, except for reasonable amounts of chemicals such as adhesives, lubricants, ink, solvents and cleaning fluids of the kind and in amounts and in the manner customarily found and used in business offices in order to conduct its business at the Premises for the Permitted Use (which Permitted Use is set forth on **Exhibit A**) and to maintain and operate the business machines located in the Premises provided that the same are stored and maintained strictly in accordance with all applicable laws. Tenant covenants and agrees that the Tenant shall comply with all applicable laws and regulations in handling and disposing of materials used in its research and other uses of the Premises, whether or not considered Hazardous Materials, and no dumping, flushing or other introduction of Hazardous Materials or such other inappropriate materials into the septic, sewage or other waste disposal systems serving the Premises shall occur, except as specifically permitted by law or regulation and subject to the conditions and qualifications imposed by any governmental license or permit. Tenant covenants and agrees that the Tenant shall, at its sole cost, promptly remove or remediate all Hazardous Materials that are found upon the Premises, the Building or the Land by virtue of the failure of the foregoing covenants and agreements to have been fulfilled, or otherwise as the result of the act or omission of Tenant, its agents, employees, contractors or invitees or any other party claiming by, through or under Tenant, in a manner complying with all applicable laws and regulations and the provisions of this Lease. If the Tenant should have any responsibility under this Section 5.4 to remove or remediate Hazardous Materials, the Tenant shall keep the Landlord reasonably informed as to the status of the environmental condition at issue, promptly furnish to the Landlord copies of all regulatory filings with any governmental regulatory agencies in connection therewith, and substantiate the performance of its obligations under this Section 5.4. At the expiration or earlier termination of the Term, the Tenant shall promptly remove or remediate any Hazardous Materials from the Premises in a manner consistent with accepted "best practices" and in compliance with all legal requirements relating to the closure of laboratory facilities and disposal of equipment and supplies therein.

If Tenant's transportation, storage or use of Hazardous Materials on the Premises results in the release onto or other contamination of any portion of the Property or adjacent areas,

including building or parking areas, soil or surface or ground water, or loss or damage to person(s) or property, without limitation, Tenant agrees to: (a) notify Landlord immediately of any release, threat of release, contamination, claim of contamination, loss or damage and (b) after consultation with Landlord, clean up the release, threat of release, or contamination as required by all applicable statutes, regulations and standards. In the event of such contamination, Tenant agrees to cooperate with Landlord, as Landlord may reasonably request, and provide such documents, affidavits and information as may be reasonably requested by Landlord (1) to comply with any applicable laws, and/or (2) for any other reason deemed necessary by Landlord in its reasonable discretion. Tenant shall notify Landlord promptly in the event of any spill or other release of any Hazardous Materials at, in, on, under or about the Premises that is required to be reported to a governmental authority under any applicable laws, shall promptly forward to Landlord copies of any notices received by Tenant relating to alleged violations of any applicable laws and shall promptly pay when due any fine or assessment against Landlord, Tenant, or the Premises relating to any violation during the Term of any applicable laws by Tenant, its employees, agents, or independent contractors, or with respect to the Premises or the remainder of the Property. If any governmental authority files a lien against the Premises or the remainder of the Property due to any act or omission, intentional or unintentional, of Tenant, its agents, or employees, or for which Tenant is responsible, resulting in the releasing, spilling, leaking, leaching, pumping, emitting, pouring, emptying or dumping of any Hazardous Materials, Tenant shall, within fifteen (15) days from the date that Tenant is first given notice of such lien (or within such shorter period of time as may be specified by Landlord if such governmental authority takes steps to cause the Premises to be sold pursuant to such lien) either (A) pay the claim and remove the lien or (B) furnish a cash deposit, bond or such other security as is reasonably satisfactory in all respects to Landlord and sufficient to discharge the lien completely. Tenant shall defend, indemnify and hold Landlord and the Landlord Parties harmless from and against any damages, liability or expense associated with claims by governmental or other third parties arising out of the presence, removal or remediation of Hazardous Materials for which Tenant is responsible for removal or remediation under this Section 5.4.

Section 5.5 Landlord's Responsibilities Regarding Hazardous Materials.

During the Term of this Lease, if the removal or remediation of Hazardous Materials from the Premises, Building or Land is required to be undertaken by applicable laws, then except to the extent such obligation is the responsibility of the Tenant under Section 5.4 hereof, Landlord covenants and agrees to undertake the same without charge to the Tenant or, if another tenant in the Building is responsible for such removal or remediation, to use all commercially reasonable efforts to enforce such tenant's obligations. Without limitation of the foregoing, if necessary to comply with any applicable legal requirements, should any existing environmental condition of the Land require the removal or remediation of Hazardous Materials, Landlord shall perform such removal or remediation, without charge to the Tenant, when and if required by applicable legal requirements. The Landlord shall keep the Tenant reasonably informed as to the status of the environmental condition at issue, promptly furnish to the Tenant copies of all regulatory filings with any governmental regulatory agencies in connection therewith, and substantiate the performance of its obligations under this Section 5.5. Tenant shall have no

liability for any environmental condition or violation of law that exists in the Premises as of the date of this Lease.

ARTICLE VI

TENANT COVENANTS

The Tenant covenants during the Term and for such further time as the Tenant occupies any part of the Premises:

Section 6.1 - Permitted Uses.

The Tenant shall occupy the Premises only for the Permitted Uses, and shall not injure or deface the Premises or the Property, nor permit in the Premises any auction sale. The Tenant shall not permit in the Premises any nuisance, or the emission from the Premises of any reasonably objectionable noise, odor or vibration, nor use or devote the Premises or any part thereof for any purpose which is contrary to law or ordinance or liable to invalidate or increase premiums (above those normally incurred for the Permitted Uses) for any insurance on the Building or its contents (unless the Tenant pays for any such increase in premiums and provided such actions do not interfere with the use and enjoyment of the Land by the Landlord, other tenants, visitors or invitees of the Building) or liable to render necessary any alteration or addition to the Building, nor commit or permit any waste in or with respect to the Premises, nor shall Tenant overload existing electrical or other Building systems.

Section 6.2 - Laws and Regulations.

The Tenant shall comply with all federal, state and local laws, regulations, ordinances, executive orders, federal guidelines, and similar requirements in effect from time to time, including, without limitation, City of Cambridge ordinances and all such requirements relating to Tenant's occupancy and use of the Premises and Hazardous Materials. Tenant shall also conform to recognized "best practices" standards with respect to the physical aspects of its operations carried on within the Premises. Tenant shall have the right to contest any notice of violation for any of the foregoing by appropriate proceedings diligently conducted in good faith.

Section 6.3 - Rules and Regulations.

The Tenant agrees to comply with the Rules and Regulations set forth in Exhibit F and such other reasonable and non-discriminatorily enforced rules and regulations of general applicability ("Rules and Regulations") as (i) may from time to time be made by the Landlord of which the Tenant is given written advance notice, so far as the same relate to the use of the Building, the Land and the Tenant's appurtenant parking privileges and (ii) may from time to time be promulgated with respect to all or any portion of the Building (including without limitation pursuant to the Declaration of Covenants). The Tenant shall not obstruct in any manner any portion of the Property not hereby leased; and, except as set forth in this Lease, shall not permit the placing of any signs, awnings or flagpoles, or the like, visible from outside the Building. Tenant shall not place or permit to be placed curtains, blinds or shades or similar window treatments visible from outside the Building in the Premises, except as may be otherwise

approved by Landlord. Landlord shall provide, at the Landlord's expense, a Building standard listing of Tenant's name in all multi-tenant Building directories. Subject to Tenant's compliance with Article IV, Tenant shall have the right to install, at Tenant's sole cost and expense, one (1) sign with its corporate logo at the entrance to the Premises, subject to the prior approval of such sign by Landlord, which approval shall not be unreasonably withheld or delayed.

Section 6.4 - Safety Compliance.

The Tenant shall keep the Premises equipped with all safety appliances required by law or ordinance or any other regulations of any public authority because of the manner of use made by the Tenant and to procure all licenses and permits so required because of such manner of use and, if requested by the Landlord, do any work so required because of such use, it being understood that the foregoing provisions shall not be construed to broaden in any way the Tenant's Permitted Uses.

Section 6.5 - Landlord's Entry.

The Tenant shall permit the Landlord and its agents (which agents shall be identified to Tenant and reasonably approved by Tenant for entry), after at least forty-eight (48) hours' prior notice except in the case of emergencies, and at times reasonably acceptable to Tenant, to enter the Premises at all reasonable hours for the purpose of inspecting or making repairs to the same, monitoring Tenant's compliance with the requirements and restrictions set forth in this Lease, and for the purpose of showing the Premises to prospective purchasers and mortgagees at all reasonable times and to prospective tenants within nine (9) months of the end of the Term provided that in connection with such entry, Tenant may provide procedures reasonably designed so as not to jeopardize Tenant's trade secrets, proprietary technology or critical business operations, including accompaniment of all such persons by an employee of the Tenant. In case of an emergency, the Landlord shall make good faith efforts to notify the Tenant in person or by telephone prior to such entry, and in any event, the Landlord shall notify Tenant promptly after such entry.

Section 6.6 - Floor Load.

The Tenant shall not place a load upon any floor in the Premises exceeding the floor load per square foot of area which such floor was designed to carry, and which is allowed by law. The Tenant's machines and mechanical equipment shall be placed and maintained by the Tenant at the Tenant's expense in settings sufficient to absorb or prevent vibration or noise that may be transmitted to the Building structure.

Section 6.7 - Personal Property Tax.

The Tenant shall pay promptly when due all taxes which may be imposed upon personal property (including, without limitation, fixtures and equipment) in the Premises to whomever assessed. Tenant shall have the right to contest the validity or amount of any such taxes by appropriate proceedings diligently conducted in good faith.

Section 6.8 - Assignment and Subleases.

The Tenant shall not assign, mortgage, pledge, hypothecate or otherwise transfer this Lease, or sublet (which term, without limitation, shall include granting of concessions, licenses and the like) the whole or any part of the Premises without, in each instance, having first received the consent of the Landlord which consent shall not be unreasonably withheld, conditioned or delayed. Except as specifically permitted herein, any assignment or sublease made without such consent shall be void. The Landlord shall not be deemed to be unreasonable in withholding its consent to any proposed assignment or subletting by the Tenant based on any of the following factors:

(a) The business of the proposed occupant is not consistent with the image and character which the Landlord desires to promote for the Building.

(b) The proposed assignment, mortgage or pledge would in any way materially diminish Landlord's rights with respect to the Premises.

(c) The proposed occupant is not sufficiently creditworthy in the reasonable opinion of Landlord based on a comparison of the creditworthiness of other similarly-situated companies in the same industry as the proposed occupant.

Notwithstanding anything to the contrary contained in this Section, Tenant shall have the right to assign or otherwise transfer this Lease or the Premises, or part of the Premises, without obtaining the prior consent of Landlord, (y) to its parent corporation, to a wholly owned subsidiary, to a corporation which is wholly owned by the same corporation which wholly owns Tenant, to an entity directly or indirectly controlling, controlled by or under common control with Tenant, any entity owning or controlling fifty percent (50%) or more of the outstanding voting interest of Tenant, or any entity of which Tenant owns or controls fifty percent (50%) or more of the voting interests, provided that (i) the transferee shall, prior to the effective date of the transfer, deliver to Landlord instruments evidencing such transfer and its agreement to assume and be bound by all the terms, conditions and covenants of this Lease to be performed by Tenant, all in form reasonably acceptable to Landlord, and (ii) at the time of such transfer there shall not be an uncured Event of Default under this Lease; or (z) to the purchaser of all or substantially all of its assets, any entity resulting from the merger or consolidation of Tenant, any successor entity resulting from a bona fide reorganization or Tenant, or to any entity into which the Tenant may be merged or consolidated (along with all or substantially all of its assets) (the "**Acquiring Company**"), provided that (i) the net assets of the Acquiring Company at the time of the transfer or merger shall not be less than Two Hundred Fifty Million Dollars ($250,000,000.00), (ii) the Acquiring Company continues to operate the business conducted in the Premises consistent with the Permitted Uses described in **Exhibit A** hereto, (iii) the Acquiring Company shall assume in writing, in form reasonably acceptable to Landlord, all of Tenant's obligations under this Lease, (iv) Tenant shall provide to Landlord such additional information regarding the Acquiring Company as Landlord shall reasonably request, and (v) Tenant shall pay Landlord's reasonable expenses incurred in connection therewith (up to a maximum amount of $5,000.00). The transfers described in this paragraph are referred to hereinafter as "**Permitted Transfers**." Notwithstanding any other provision of this Lease, any public offering of shares or other

ownership interest in Tenant or any private equity financing of Tenant by one or more investors who regularly invest in private companies shall not be deemed an assignment and shall not be subject to Landlord approval.

Whether or not the Landlord consents, or is required to consent, to any assignment or subletting, the Tenant named herein (to the extent that the Tenant continues to exist as a distinct entity separate and apart from the entity to which the Lease is assigned) shall remain fully and primarily liable for the obligations of the tenant hereunder, including, without limitation, the obligation to pay Annual Fixed Rent and Additional Rent provided under this Lease.

Landlord shall consent, or set forth in reasonable detail any reason for disapproval, within ten (10) business days of request and receipt of the information or items described in (z)(i) and (iii) above. In the event that Landlord fails to respond with ten (10) business days, Tenant shall send a second written notice requesting consent to Landlord, which states that Landlord's failure to respond within five (5) business days after receipt of the second notice shall be deemed approval.

The Tenant shall give the Landlord notice of any proposed sublease or assignment, whether or not the Landlord's consent is required hereunder, specifying the provisions of the proposed subletting or assignment, including (i) the name and address of the proposed subtenant or assignee, (ii) a copy of the proposed subtenant's or assignee's most recent annual financial statement, (iii) all of the material terms and provisions upon which the proposed subletting or assignment is to be made, and (iv) such other information concerning the proposed subletting or assignment and/or the proposed subtenant or assignee as Landlord shall reasonably request provided Landlord requests such other information with five (5) business days after receipt of Tenant's request. The Tenant shall reimburse the Landlord promptly for reasonable legal and other expenses incurred by the Landlord in connection with any request by the Tenant for consent to any assignment or subletting, in the aggregate amount of up to $5,000.00. If this Lease is assigned, or if the Premises or any part thereof is sublet or occupied by anyone other than the Tenant, the Landlord may, at any time during the continuance of an Event of Default hereunder without cure, collect rent and other charges from the assignee, sublessee or occupant and apply the net amount collected to the rent and other charges herein reserved, but no such assignment, subletting, occupancy or collection shall be deemed a waiver of the prohibitions contained in this Section 6.8 or the acceptance of the assignee, sublessee or occupant as a tenant, or a release of the Tenant from the further performance by the Tenant of covenants on the part of the Tenant herein contained. After deducting reasonable and ordinary sublease transaction expenses which shall be limited to any broker's commissions, architectural and engineering fees, alteration costs and allowances for the assignee or subtenant, and reasonable legal fees, the Tenant shall pay to the Landlord fifty percent (50%) of any amounts the Tenant receives from any subtenant or assignee as rent, additional rent or other forms of compensation or reimbursement other than those which are less than or equal to the then due and payable proportionate monthly share of Annual Fixed Rent, Additional Rent and all other monies due to Landlord pursuant to this Lease (allocable in the case of a sublease to that portion of the Premises being subleased). The consent by the Landlord to an assignment or subletting shall not be construed to relieve the Tenant from

obtaining or waive or release the covenant in the Lease that Tenant obtain the express consent in writing of the Landlord to any further assignment or subletting.

Landlord may elect, prior to approving or disapproving any proposed assignment or sublease of more than fifty percent (50%) of the entire Premises for all or substantially all of the remaining Term, to repossess the portion of the Premises that was proposed to be subleased or assigned, provided that such repossession shall not take effect earlier than thirty (30) days after the proposal by Tenant of a proposed assignment or sublease of more than fifty percent (50%) of the entire Premises for all or substantially all of the remaining Term. Landlord shall, within ten (10) business days after Tenant's request for consent, notify Tenant of Landlord's exercise of its right to recapture such portion of the Premises in accordance with the terms of this Section. Landlord may thereafter lease such portion of the Premises in such a manner as the Landlord may in its sole discretion determine. In the event Landlord elects to repossess the Premises as provided above, then all of the Tenant's rights and obligations hereunder with respect to such portion of the Premises shall cease and shall be of no further force and effect. The provisions of this paragraph shall not apply to Permitted Transfers. Notwithstanding anything herein to the contrary, Tenant shall be permitted to submit notice to Landlord of its intention to enter into an assignment or a sublease of more than fifty percent (50%) of the entire Premises for all or substantially all of the remaining Term, prior to naming a proposed assignee or subtenant, in which event Landlord shall, within forty-five (45) days thereafter, notify Tenant of Landlord's exercise of its right to recapture such portion of the Premises in accordance with the terms of this Section. If Landlord shall not exercise such right to recapture in the event of a proposed assignment of this Lease, or a sublet of more than fifty percent (50%) of the entire Premises for all or substantially all of the remaining Term, any recapture right shall be deemed waived with respect to such space in connection with a subsequent assignment or sublease of the same premises submitted to Landlord for consent within nine (9) months after the expiration of Landlord's 45-day recapture election period; provided that any assignment or subletting shall in all events remain subject to Landlord's reasonable approval as provided in this Section 6.8. For avoidance of doubt, if Landlord has waived its recapture right prior to Tenant naming a proposed assignee or subtenant, Landlord shall not have a right to recapture once the proposed assignee or subtenant has been identified and presented for Landlord's approval.

ARTICLE VII

INDEMNITY AND INSURANCE

Section 7.1 - Indemnity.

(a) To the maximum extent this agreement may be made effective according to law and subject to the waivers set forth in Section 7.5 below, Tenant agrees to indemnify and save harmless Landlord and Landlord's managing agent, beneficiaries, partners, subsidiaries, affiliates, officers, directors, agents, employees, and any Superior Lessor and Superior Mortgagee (the "Landlord Parties") from and against all claims, loss, cost, damage or expense of whatever nature arising: (i) from any accident, injury or damage whatsoever to any person, or to the property of any person, occurring in the Premises; (ii) from any accident, injury or damage occurring outside of the Premises but

on the Property or at the Park where such accident, damage or injury results or is claimed to have resulted from an act or omission on the part of Tenant or Tenant's agents, employees or contractors; or (iii) in connection with the conduct or management of the Premises or of any business therein, or any thing or work whatsoever done, or any condition created (other than by Landlord) in the Premises; and, in any case, occurring after the date of this Lease until the end of the Term of this Lease and thereafter so long as Tenant is in occupancy of any part of the Premises, provided that the foregoing indemnity shall not include any cost or damage arising from any act, omission or negligence of the Landlord, or the Landlord's agents, employees or contractors.

(b) To the maximum extent this agreement may be made effective according to law and subject to the waivers set forth in Section 7.5 below, Landlord agrees to defend, indemnify and save harmless Tenant from and against all claims, loss, cost, damage or expense (including but not limited to reasonable attorneys' fees) of whatever nature arising out of all acts, failures, omissions or negligence of Landlord, or its agents, employees, or contractors, except to the extent that such claims, loss, cost, damage or expense is due to the willful misconduct or act, omission or neglect of Tenant, its agents, contractors, employees, licensees, invitees or servants.

(c) The foregoing indemnities and hold harmless agreements shall include indemnity against reasonable attorneys' fees and all other costs, expenses and liabilities incurred in connection with any such claim or proceeding brought thereon, and the defense thereof.

Section 7.2 - Liability Insurance.

Tenant agrees to maintain in full force from the date upon which the Tenant first enters the Premises for any reason, throughout the Term, and thereafter, so long as the Tenant is in occupancy of any part of the Premises, a policy of commercial general liability insurance under which the Landlord (and any individuals or entities affiliated with the Landlord, any ground lessor and any holder of a mortgage on the Property of whom the Tenant is notified by the Landlord) and the Tenant are named as additional insureds, and under which the insurer provides a contractual liability endorsement insuring against all cost, expense and liability arising out of or based upon any and all claims, accidents, injuries and damages described in Section 7.1, in the broadest form of such coverage from time to time available. Each such policy shall be noncancellable and nonamendable (to the extent that any proposed amendment reduces the limits or the scope of the insurance required in this Lease) with respect to the Landlord and such ground lessors and mortgagees without thirty (30) days' prior notice to the Landlord and such ground lessors and mortgagees and at the election of the Landlord either a certificate of insurance or a duplicate original policy shall be delivered to the Landlord. The minimum limits of liability of such insurance as of the Commencement Date shall be Five Million Dollars ($5,000,000.00) in the aggregate for combined bodily injury (or death) and damage to property ($3,000,000.00 per occurrence), and from time to time during the Term such limits of liability shall be increased to reflect such higher limits as are customarily required pursuant to new leases of space in the Boston-Cambridge area with respect to similar properties and uses.

Section 7.3 - Personal Property at Risk.

The Tenant agrees to maintain in full force at all times throughout the Term, policy(s) of all risk property damage insurance naming Landlord (and the Additional Named Insureds) and the Tenant as insureds as their interests may appear, covering all of Tenant's leasehold improvements and alterations to the extent of their full replacement costs as updated from time to time during the Term.

The Tenant agrees that all of the furnishings, fixtures, equipment, effects and property of every kind, nature and description of the Tenant and of all persons claiming by, through or under the Tenant may be on the Premises or elsewhere in the Building or on the Property or parking facilities provided hereby, shall be at the sole risk and hazard of the Tenant, and if the whole or any part thereof shall be destroyed or damaged by fire, water or otherwise, or by the leakage or bursting of water pipes, steam pipes, or other pipes, by theft or from any other cause, no part of said loss or damage is to be charged to or be borne by the Landlord, except that, subject to the waivers set forth in Section 7.5 below, the Landlord shall in no event be exonerated from any liability to the Tenant or to any person, for any injury, loss, damage or liability to the extent caused by the gross negligence or willful misconduct of Landlord or Landlord's agents, employees, or contractors.

Section 7.4 - Landlord's Insurance.

The Landlord shall carry such casualty and liability insurance upon and with respect to operations at the Building, as may from time to time be deemed reasonably prudent by the Landlord or required by any mortgagee holding a mortgage thereon or any ground lessor of the Land, and in any event, insurance against loss by fire and the risks now covered by extended coverage endorsement No. 4 in an amount equal to the replacement value of the Building, exclusive of foundations, site preparation and other nonrecurring construction costs.

Section 7.5 - Waiver of Subrogation.

Any property insurance carried by either party with respect to the Building, Land, Premises, parking facilities or any property therein or occurrences thereon shall, without further request by either party, include a clause or endorsement denying to the insurer rights of subrogation against the other party to the extent rights have been waived by the insured prior to occurrence of injury or loss. Each party, notwithstanding any provisions of this Lease to the contrary, hereby waives any rights of recovery against the other for injury or loss to property, including, without limitation, injury or loss to property caused by negligence of such other party, the loss from which is covered by insurance then being carried by them or which loss would have been covered had the party carried the insurance coverages and amounts required of them under this Lease to the extent of the limits of insurance carried with respect thereto, less the amount of any deductible. Any deductibles and such self-insured retentions shall be deemed to be "insurance" for purposes of this waiver.

ARTICLE VIII

CASUALTY AND EMINENT DOMAIN

Section 8.1 - Restoration Following Casualties.

If, during the Term, the Building or the Premises shall be damaged by fire or casualty, subject to termination rights of the Landlord and the Tenant provided below in this Article 8, the Landlord shall proceed promptly to exercise diligent efforts to restore, or cause to be restored, the Building to substantially the condition thereof just prior to time of such damage (exclusive of improvements, alterations and property required to be insured by Tenant under this Lease), but the Landlord shall not be responsible for delay in such restoration which may result from External Causes or due to any acts or omissions of Tenant or any of Tenant's agents, employees or contractors. Provided that the Landlord complies with its obligations to carry casualty insurance in accordance with Section 7.4, the Landlord shall have no obligation to expend in the reconstruction of the Building more than the sum of the amount of any deductible and the actual amount of insurance proceeds made available to the Landlord by its insurer, and any additional costs associated with changes to the Premises desired by the Tenant and permitted by Article 4 shall be paid by the Tenant in the manner reasonably required by the Landlord. Any restoration of the Building or the Premises shall be altered to the extent necessary to comply with then current and applicable laws and codes. The Landlord shall, as soon as possible after any casualty, but in any event no later than sixty (60) days after such casualty, provide to the Tenant a reasonable written estimate ("Contractor's Estimate") from a reputable construction or design professional as to the time frame within which the Landlord will be able to repair the casualty damage and the cost of repairing such damage.

Section 8.2 - Landlord's Termination Election.

If the Landlord reasonably determines, based upon the Contractor's Estimate, that (a) the amount of insurance proceeds available to the Landlord is insufficient to cover the cost of restoring the Building by more than the amount of any deductible, or (b) the Landlord will be unable to restore the Building within nine (9) months from the date of such casualty, then the Landlord may terminate this Lease by giving notice to the Tenant. Any such termination shall be effective on the date designated in such notice from the Landlord, but in any event not later than sixty (60) days after such notice, and if no date is specified, effective upon the delivery of such notice. Failure by the Landlord to give the Tenant notice of termination within sixty (60) days following the occurrence of the casualty shall constitute the Landlord's agreement to restore the Building as contemplated in Section 8.1.

Section 8.3 - Tenant's Termination Election.

If, based upon the Contractor's Estimate, the time period for repairing any casualty damage will exceed nine (9) months after the date of any casualty, then the Tenant shall have the right, exercisable by written notice given on or before the date thirty (30) days after the Landlord gives to the Tenant the Contractor's Estimate, to terminate this Lease.

If neither the Landlord nor the Tenant exercise their termination rights, but the Landlord has failed to restore the Building within the sixty (60) days following the expiration of the period of restoration set forth in the Contractor's Estimate, such period to be subject, however, to

extension where the delay in completion of such work is due to External Causes or delays caused by Tenant but in no event beyond an additional two (2) months of extension for External Causes), the Tenant shall have the right to terminate this Lease at any time after the expiration of such period (in either case, as extended by delay due to External Causes or Tenant caused delays as aforesaid) until the restoration is substantially completed, such termination to take effect thirty (30) days following Landlord's receipt of Tenant's notice unless such restoration is completed prior to such termination date. However, if the Landlord has been diligently prosecuting the repair of all casualty and damage, and if the Landlord reasonably determines at any time, and from time to time, during the restoration, based upon certification by its architect or other design professional, that such restoration will not be able to be completed before the deadline date after which the Tenant may terminate this Lease under this Section 8.3, and the Landlord specifies in a notice to Tenant to such effect a later date that the Landlord estimates will be the date upon which such restoration will be completed, then the Tenant may terminate this Lease within thirty (30) days of the Landlord's notice as aforesaid, failing which the deadline date shall be extended to the date set forth in Landlord's notice (as extended by delay due to External Causes as aforesaid). The Landlord shall exercise reasonable efforts to keep the Tenant advised of the status of restoration work from time to time, and promptly following any request for information during the course of the performance of the restoration work.

Section 8.4 - Casualty at Expiration of Lease.

If the Premises shall be damaged by fire or casualty in such a manner that the Premises cannot, in the ordinary course, reasonably be expected to be repaired within one hundred twenty (120) days from the commencement of repair work and such casualty or damage occurs within the last eighteen (18) months of the Term (as the same may have been extended prior to such casualty or damage), either party shall have the right, by giving notice to the other not later than sixty (60) days after such casualty or damage, to terminate this Lease, whereupon this Lease shall terminate as of the date of such casualty.

Section 8.5 - Eminent Domain.

Except as hereinafter provided, if the Premises, or such portion thereof as to render the balance (if reconstructed to the maximum extent practicable in the circumstances) unsuitable for continued occupancy for the purposes contemplated under this Lease, shall be taken by condemnation or right of eminent domain, the Landlord and the Tenant shall each have the right to terminate this Lease by notice to the other of its desire to do so, provided that such notice is given not later than thirty (30) days after receipt by the Tenant of notice of the effective date of such taking. If so much of the Building shall be so taken that the Landlord reasonably determines, in good faith, that it would be necessary to substantially alter the Building so that a rebuilt Building will not be substantially similar to the Building before such taking, the Landlord shall have the right to terminate this Lease by giving notice to the Tenant of the Landlord's desire to do so not later than thirty (30) days after the effective date of such taking.

Should any part of the Premises be so taken or condemned during the Term, and should this Lease be not terminated in accordance with the foregoing provisions, the Landlord agrees to use reasonable efforts to put what may remain of the Premises into proper condition for use and

occupation as nearly like the condition of the Premises prior to such taking as shall be practicable, subject, however, to applicable laws and codes then in existence. The Landlord shall have no obligation to expend in the aforesaid restoration more than the proceeds of any award received in any condemnation or eminent domain proceeding, or any sum paid in lieu thereof.

Section 8.6 - Rent After Casualty or Taking.

If the Premises shall be damaged by fire or other casualty, until the Lease is terminated or the Premises is restored, the Annual Fixed Rent and Additional Rent shall be justly and equitably abated and reduced according to the nature and extent of the loss of use thereof suffered by the Tenant. In the event of a taking which permanently reduces the area of the Premises, a just proportion of the Annual Fixed Rent and applicable Additional Rent shall be abated for the remainder of the Term.

Section 8.7 Temporary Taking.

In the event of any taking of the Premises or any part thereof for a temporary use not in excess of twelve (12) months, (i) this Lease shall be and remain unaffected thereby and Annual Fixed Rent and Additional Rent shall not abate, and (ii) the Tenant shall be entitled to receive for itself such portion or portions of any award made for such use with respect to the period of the taking which is within the Term.

Section 8.8 Taking Award.

Except as otherwise provided in Section 8.7, the Landlord shall have and hereby reserves and accepts, and the Tenant hereby grants and assigns to the Landlord, all rights to recover for damages to the Building and the Land, and the leasehold interest hereby created, and to compensation accrued or hereafter to accrue by reason of such taking, damage or destruction, as aforesaid, and by way of confirming the foregoing, the Tenant hereby grants and assigns to the Landlord, all rights to such damages or compensation. Nothing contained herein shall be construed to prevent the Tenant from prosecuting in any condemnation proceedings a separate claim for relocation expenses and Tenant's personal property.

ARTICLE IX

DEFAULT

Section 9.1 - Tenant's Default.

Each of the following shall constitute an "Event of Default":

(a) Failure on the part of the Tenant to pay the Annual Fixed Rent, Additional Rent or other charges for which provision is made herein on or before the date on which the same become due and payable, if such condition continues for five (5) business days after written notice that the same are due; provided, however if Tenant shall fail to pay any of the foregoing (after receipt by Tenant of written notice from Landlord) when due

two (2) times in any period of twelve (12) consecutive months, then Landlord shall not be required to give notice to Tenant of any future failure to pay during the remainder of the Term and any extension thereof, and such failure shall thereafter constitute an Event of Default if not cured within five (5) business days after the same are due.

(b) Failure on the part of the Tenant to perform or observe any other term or condition contained in this Lease if the Tenant shall not cure such failure within thirty (30) days after written notice from the Landlord to the Tenant thereof, provided that in the case of breaches that are not reasonably susceptible to cure within thirty (30) days through the exercise of due diligence, then so long as the Tenant commences such cure within thirty (30) days, and the Tenant diligently pursues such cure to completion, such breach shall not be deemed to create an Event of Default.

(c) The taking of the estate hereby created on execution or by other process of law; or a judicial declaration that the Tenant, or any guarantor of this Lease, is bankrupt or insolvent according to law; or any assignment of the property of the Tenant, or any guarantor of this Lease, for the benefit of creditors; or the appointment of a receiver, guardian, conservator, trustee in bankruptcy or other similar officer to take charge of all or any substantial part of the property of Tenant, or any guarantor of this Lease, by a court of competent jurisdiction, which officer is not dismissed or removed within ninety (90) days; or the filing of an involuntary petition against the Tenant, or any guarantor of this Lease, under any provisions of the bankruptcy act now or hereafter enacted if the same is not dismissed within ninety (90) days; the filing by the Tenant, or any guarantor of this Lease, of any voluntary petition for relief under provisions of any bankruptcy law now or hereafter enacted.

If an Event of Default shall occur, then, in any such case, whether or not the Term shall have begun, Landlord and its agents lawfully may, in addition to any remedies for any preceding Event of Default and any remedies otherwise available at law or equity, immediately or at any time thereafter without further demand or notice in accordance with process of law, enter upon any part of the Premises in the name of the whole or mail or deliver a notice of termination of the Term of this Lease addressed to Tenant at the Premises or any other address herein, and thereby terminate the Term and repossess the Premises as of Landlord's former estate. At Landlord's election such notice of termination may be included in any notice of default. Upon such entry or mailing the Term shall terminate, all executory rights of Tenant and all obligations of Landlord will immediately cease, and Landlord may expel Tenant and all persons claiming under Tenant and remove their effects without any trespass and without prejudice to any remedies for arrears of rent or prior breach; and Tenant waives all statutory and equitable rights to its leasehold (including rights in the nature of further cure or redemption, if any to the extent such rights may be waived). If Landlord engages attorneys in connection with any failure to perform by Tenant hereunder, Tenant shall reimburse Landlord for the reasonable fees of such attorneys on demand as Additional Rent. Without implying that other provisions do not survive, the provisions of this Article shall survive the Term or earlier termination of this Lease.

Section 9.2 - Damages.

In the event that this Lease is terminated, the Tenant covenants to pay to the Landlord punctually all the sums ("**Periodic Payments**") and perform all the obligations which the Tenant covenants in this Lease to pay and to perform in the same manner and to the same extent and at the same time as if this Lease had not been terminated, and all of the Landlord's expenses in connection with reletting the Premises including, without limitation, all repossession costs, brokerage commissions, fees for legal services and expenses of preparing the Premises for such reletting. However, the Landlord may elect, at any time, to demand that Tenant pay to Landlord in lieu of any further obligations to make Periodic Payments, and payments on account of the Landlord's reletting costs thereafter accruing, as compensation, an amount (the "Lump Sum Payment") equal to the excess, if any, of the discounted present value of the total rent reserved for the then remainder of the Term over the then discounted present fair rental value of the Premises for the then remainder of the Term. The discount rate for calculating such sum under the preceding clause (x) shall be the then current rate of United States Treasury securities having a maturity date as close as possible to the end of the Term (had the Lease not been terminated). In calculating the rent reserved, there shall be included, in addition to the Annual Fixed Rent and all Additional Rent, the value of all other considerations agreed to be paid or performed by the Tenant over the remainder of the Term. Should the parties be unable to agree on a fair rental value for the purposes of determining the Lump Sum Payment under clause (x), above, the matter shall be submitted, upon the demand of either party, to the Boston office of the American Arbitration Association, with a request for arbitration in accordance with the rules of the Association by a single arbitrator who shall be real estate broker with at least ten years' experience marketing major office and laboratory projects in the Boston, Massachusetts area. The parties agree that a decision of the arbitrator shall be conclusive and binding upon them.

In calculating the Periodic Payments to be made by the Tenant under the foregoing covenant, the Tenant shall be credited with the net proceeds of any rent obtained by reletting the Premises, after deducting all the Landlord's expenses in connection with such reletting, including, without limitation, all repossession costs, brokerage commissions, fees for legal services and expenses of preparing the Premises for such reletting, provided that Tenant shall never be entitled to receive any portion of the re-letting proceeds, even if the same exceed the rent originally due hereunder but Tenant shall be credited with such excess amount to offset its obligation to Landlord. The Landlord may (i) relet the Premises, or any part or parts thereof, for a term or terms which may, at the Landlord's option, exceed or be equal to or less than the period which would otherwise have constituted the balance of the Term, and may grant such concessions and free rent as the Landlord in its reasonable commercial judgment considers advisable or necessary to relet the same, (ii) make such alterations, repairs and improvements in the Premises as the Landlord in its reasonable commercial judgment considers advisable or necessary to relet the same, and (iii) any obligation to relet imposed by law shall be subject to the reasonable requirements of Landlord to lease to high quality tenants on such terms (based on then-market standards) as Landlord may from time to time deem appropriate and to develop the Building and Park in a harmonious manner with an appropriate mix of uses, tenants, floor areas and terms of tenancies, and the like, and Landlord shall not be obligated to relet the Premises to any party to whom Landlord or its affiliate may desire to lease other available space in the Park. No action of the Landlord in accordance with foregoing or failure to relet or to collect rent under reletting shall operate to release or reduce the Tenant's liability. The Landlord shall be entitled

to seek to rent other properties of the Landlord prior to reletting the Premises without being in breach of any obligation to the Tenant.

Section 9.3 - Cumulative Rights.

The specific remedies to which either party may resort under the terms of this Lease are cumulative and, except as expressly set forth herein, are not intended to be exclusive of any other remedies or means of redress to which it may be lawfully entitled in case of any breach or threatened breach by the other party of any provisions of this Lease. In addition to the other remedies provided in this Lease, each party shall be entitled to seek the restraint by injunction of the violation or attempted or threatened violation of any of the covenants, conditions or provisions of this Lease or to a decree compelling specific performance of any such covenants, conditions or provisions. Nothing contained in this Lease shall limit or prejudice the right of the Landlord to prove for and obtain in proceedings for bankruptcy, insolvency or like proceedings by reason of the termination of this Lease, an amount equal to the maximum allowed by any statute or rule of law in effect at the time when, and governing the proceedings in which, the damages are to be proved, whether or not the amount be greater, equal to, or less than the amount of the loss or damages referred to above.

Section 9.4 - Landlord's Self-help.

If there shall be an Event of Default, or if emergency circumstances should exist where, upon the giving of notice or passage of time, such circumstances would constitute an Event of Default, then the Landlord shall have the right, but not the obligation, after the giving by the Landlord of notice thereof to the Tenant (except in case of emergency circumstances in which case no prior notice need be given), to perform such obligation. In the event the Landlord exercises its rights under this Section 9.4 in case of emergency, the Landlord shall notify the Tenant as soon as reasonably possible after the taking of such action. The Landlord may exercise its rights under this Section without waiving any other of its rights or releasing the Tenant from any of its obligations under this Lease. The Tenant shall be liable to the Landlord for all of the Landlord's reasonable costs associated with effecting such cure.

Section 9.5 - Enforcement Expenses; Litigation.

Each party hereto shall promptly reimburse the other for all costs and expenses, including without limitation reasonable legal fees, incurred by such party in exercising and enforcing its rights under this Lease following the other party's failure to comply with its obligations hereunder, whether or not such failure constitutes an Event of Default pursuant to Sections 9.1 or 9.7 hereof.

If either party hereto, without fault, is made or becomes a party to any litigation commenced by or against the other party by or against a third party, or incurs costs or expenses related to such litigation, involving any part of the Property and the enforcement of any of the rights, obligations or remedies of such party without fault, then the party becoming involved in any such litigation because of a claim against such other party hereto shall receive from such other party hereto all costs and reasonable attorneys' fees incurred by such party in such

litigation. Landlord shall pay all reasonable attorney's fees incurred by Tenant in connection with any legal action concerning an alleged breach of this Lease by Landlord to the extent that Tenant is the prevailing party. Tenant shall pay all reasonable attorney's fees incurred by Landlord in connection with any legal action concerning an alleged breach of this Lease by Tenant to the extent that Landlord is the prevailing party.

LANDLORD AND TENANT WAIVE TRIAL BY JURY IN ANY ACTION TO WHICH THEY ARE PARTIES UNDER THIS LEASE.

Section 9.6 - Interest on Overdue Payments.

Any Annual Fixed Rent and Additional Rent not paid within any applicable grace period shall bear interest from the date due to the Landlord until paid at the variable rate (the "**Default Interest Rate**") equal to the higher of (i) the rate at which interest accrues on amounts not paid when due under the terms of the Landlord's financing for the Building, as from time to time in effect, and (ii) one and one-half percent (1.5%) per month.

Section 9.7 - Landlord's Right to Notice and Cure.

The Landlord shall in no event be in default in the performance of any of the Landlord's obligations hereunder unless and until the Landlord shall have failed to perform such obligations within thirty (30) days after notice by the Tenant to the Landlord expressly specifying wherein the Landlord has failed to perform any such obligation, provided that in the case of breaches of obligations under this Lease which are susceptible to cure but cannot be cured within thirty (30) days through the exercise of due diligence, so long as the Landlord commences such cure within thirty (30) days, such breach remains susceptible to cure, and the Landlord diligently pursues such cure, such breach shall not be deemed an event of default under this Agreement. In the event of a breach or default of this Agreement by the Landlord, Tenant shall be afforded any and all rights and remedies afforded at law or inequity.

ARTICLE X

MORTGAGEES' AND GROUND LESSORS' RIGHTS

Section 10.1 - Subordination.

At the election of the holder of any mortgage (which term for the purpose of this Article shall include a "deed of trust," "ground lease," or similar financing encumbrance) encumbering the Landlord's interest in the Property, this Lease shall be subject and subordinate to the lien of any mortgages thereon, so that the rights of any such mortgagee shall be superior to all rights hereby or hereafter vested in the Tenant, subject however to Section 10.5 hereof, provided, that with respect to any future mortgage or ground lease, such future mortgagee or ground lessor shall have entered into a commercially reasonable subordination non-disturbance and attornment agreement with Tenant. Landlord represents and warrants that as of the Commencement Date, the sole holder of any mortgage on the Property is Citi Real Estate Funding, Inc., Barclays Capital Real Estate, Inc., Bank of America, N.A., and Great American Capital Corporation, and the sole holder of any ground lease on the Property is The Massachusetts Institute of

Technology. The forms of subordination, non-disturbance and attornment agreement attached hereto as **Exhibit G** and **Exhibit H**, are acceptable to Tenant in connection with any mortgage or ground lease, as applicable, to which this Lease shall be subordinated. Landlord shall use commercially reasonable efforts to provide Tenant with the subordination, non-disturbance and attornment agreements from the current mortgagee and current ground lessor, respectively, in the forms attached to this Lease as **Exhibit G** and **Exhibit H**.

Section 10.2 - Attornment; Prepayment of Rent not to Bind Mortgagee.

In the event any holder shall succeed to the interest of Landlord, the Tenant shall, and does hereby agree to attorn to such holder and to recognize such holder as its Landlord and Tenant shall promptly execute and deliver any instrument that such holder may reasonably request to evidence such attornment. Upon such attornment, the holder shall not be: (i) liable in any way to the Tenant for any act or omission, neglect or default on the part of Landlord under this Lease; (ii) subject to any counterclaim or setoff which theretofore accrued to Tenant against Landlord; (iii) bound by any modification of this Lease subsequent to such mortgage entered into without such holder's consent or by any previous prepayment of regularly scheduled monthly installments of Annual Fixed Rent or more than (1) month, which was not approved in writing by the holder; (iv) liable to the Tenant beyond the holder's interest in the Property; or (v) liable for any portion of a security deposit not actually received by the holder. The covenant and agreement contained in this Lease with respect to the rights, powers and benefits of any such holder constitute a continuing offer to any person, corporation or other entity, which by accepting or requiring an assignment of this Lease or by entry of foreclosure assumes the obligations herein set forth with respect to such holder; every such holder is hereby constituted a party to this Lease and an obligee hereunder to the same extent as though its name was written hereon as such; and such holder shall at its written election be entitled to enforce such provisions in its own name. No Annual Fixed Rent, Additional Rent (other than estimated monthly payments on account of Additional Rent which the Tenant is required to pay pursuant to the provisions of this Lease), or any other charge payable to the Landlord shall be paid more than thirty (30) days prior to the due date thereof under the terms of this Lease and payments made in violation of this provision shall, except to the extent that such payments are actually received by a mortgagee (which term shall for the purpose of this Lease include a "trustee," "ground lessor" or similar holder of a financing encumbrance) be a nullity as against any of Landlord's mortgagees and the Tenant shall be liable for the amount of such payments to such mortgagee.

Section 10.3 - Tenant's Duty to Notify Mortgagee: Mortgagee's Ability to Cure.

The Tenant hereby agrees that, if the Tenant provides the Landlord with any notice of default or claimed default on the part of the Landlord under the Lease, the Tenant shall concurrently therewith send a copy of such notice to the holder of any mortgage of whom the Tenant has been given prior written notice together with its address. In such event, the mortgagee shall be permitted (but not obligated) to cure any such default within the cure period provided to Landlord and any additional period to which such mortgagee shall be entitled pursuant to this Section 10.3. No act or failure to act on the part of the Landlord which would entitle the Tenant under the terms of this Lease, or by law, to be relieved of the Tenant's

obligations to pay Annual Fixed Rent or Additional Rent hereunder or to terminate this Lease, shall result in a release or termination of such obligations of the Tenant or a termination of this Lease unless (i) the Tenant shall have first given written notice of the Landlord's act or failure to act to any mortgagee of whom Tenant has been given prior notice, specifying the act or failure to act on the part of the Landlord which would give basis to the Tenant's rights; and (ii) no such mortgagee, after receipt of such notice, shall have corrected or cured the condition complained of within the period provided for Landlord's cure, plus a reasonable period thereafter not to exceed thirty (30) days.

Section 10.4 - Estoppel Certificates.

The Tenant shall from time to time, upon not less than fifteen (15) days' prior written request by the Landlord, execute, acknowledge and deliver to the Landlord a statement in writing certifying to the Landlord or an independent third party, with a true and correct copy of this Lease attached thereto, together with all amendments thereto, to the extent such statements continue to be true and accurate, (i) that this Lease is unmodified and in full force and effect (or, if there have been any modifications, that the same is in full force and effect as modified and stating the modifications); (ii) that the Tenant has no knowledge of any defenses, offsets or counterclaims against its obligations to pay the Annual Fixed Rent and Additional Rent and to perform its other covenants under this Lease (or if there are any defenses, offsets, or counterclaims, setting them forth in reasonable detail); (iii) that there are no known uncured defaults of the Landlord or the Tenant under this Lease (or if there are known defaults, setting them forth in reasonable detail); (iv) the dates to which the Annual Fixed Rent, Additional Rent and other charges have been paid; (v) the Commencement Date and that the Tenant has accepted, and is in full possession of the Premises, including all improvements, additions and alterations thereto required to be made by Landlord under the Lease (except to the extent stated); (vi) that the Landlord has satisfactorily complied with all of the requirements and conditions precedent to the occurrence of the Commencement Date (except to the extent stated); (vii) that the Tenant has been in occupancy since the Commencement Date and paying rent since the specified dates (except to the extent stated); (viii) that no monetary or other considerations, including, but not limited to, rental concessions for Landlord, special tenant improvements or Landlord's assumption of prior lease obligations of Tenant have been granted to Tenant by Landlord for entering into Lease (except as set forth in this Lease or as otherwise specified in such estoppel); (ix) that the Tenant has no notice of a prior assignment, hypothecation, or pledge of rents or of the Lease (except to the extent stated); (x) that the Lease represents the entire agreement between Landlord and Tenant; (xi) that any notice to Tenant may be given it by certified or registered mail, return receipt requested, or delivered, at the Premises, or at another address specified; and (xii) such factual other matters with respect to the Tenant and this Lease as the Landlord may reasonably request. Any statement delivered pursuant to this Section may be relied upon by any prospective purchaser, mortgagee, trustee or ground lessor of the Premises or any interest therein, and shall be binding on the Tenant.

Landlord shall from time to time, upon not less than fifteen (15) days' prior written request by the Tenant, execute, acknowledge and deliver to the Tenant a statement in writing certifying to the Tenant or an independent third party, with a true and correct copy of this Lease

attached thereto, to the extent such statements continue to be true and accurate (i) that this Lease is unmodified and in full force and effect (or, if there have been any modifications, that the same is in full force and effect as modified and stating the modifications); (ii) that the Landlord has no knowledge of any defenses, offsets or counterclaims against its obligations to perform its covenants under this Lease (or if there are any defenses, offsets, or counterclaims, setting them forth in reasonable detail); (iii) that there are no known uncured defaults of the Tenant or the Landlord under this Lease (or if there are known defaults, setting them forth in reasonable detail); (iv) the dates to which the Annual Fixed Rent, Additional Rent and other charges have been paid; (v) the Commencement Date and that the Tenant is in full possession of the Premises; (vi) that Landlord has no notice of a prior assignment of the Lease or sublease of space therein; (vii) that the Lease represents the entire agreement between Landlord and Tenant; (viii) that any notice to Landlord may be given if by certified or registered mail, return receipt requested, or delivered to the Landlord's address set forth in Section 1.2 of this Lease, or at another address specified; and (xii) such other factual matters with respect to the Tenant and this Lease as the Tenant may reasonably request. Any statement delivered pursuant to this Section may be relied upon by any prospective lender of Tenant, any prospective assignee or subtenant of Tenant or any prospective purchaser of Tenant or Tenant's assets, and shall be binding on the Landlord.

Section 10.5 Assignment of Rents.

With reference to any assignment by the Landlord of the Landlord's interest in this Lease, or the rents payable hereunder, conditional in nature or otherwise, which assignment is made to the holder of a mortgage or a ground lessor on property which includes the Premises, the Tenant agrees;

(a) That the execution thereof by the Landlord, and the acceptance thereof by the holder of such mortgage or ground lessor, shall never be treated as an assumption by such holder or ground lessor of any of the obligations of the Landlord hereunder, unless such holder or ground lessor shall, by notice sent to the Tenant, specifically make such election; and

(b) That, except as aforesaid, such holder or ground lessor shall be treated as having assumed the Landlord's obligations hereunder only upon foreclosure of such holder's mortgage or the taking of possession of the Property, or, in the case of a ground lessor, the termination of the ground lease

ARTICLE XI

MISCELLANEOUS

Section 11.1 - Notice of Lease.The Tenant agrees not to record this Lease, but upon request of either party, both parties shall execute and deliver a memorandum of this Lease in form appropriate for recording or registration, an instrument acknowledging the Commencement Date of the Term, and if this Lease is terminated before the Term expires, an instrument in such form acknowledging the date of termination.

Section 11.2 - Notices.

Whenever any notice, approval, consent, request, election, offer or acceptance is given or made pursuant to this Lease, it shall be in writing. Communications and payments shall be addressed, if to the Landlord, at the Landlord's Address for Notices as set forth in Section 1.2 or at such other address as may have been specified by prior notice to the Tenant; and if to the Tenant, at the Tenant's Notice Address with a copy to Attn: Stuart A. Offner, Esq., Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., One Financial Center, Boston, MA 02111, or at such other place as may have been specified by prior notice to the Landlord. Any communication so addressed shall be deemed duly given on the earlier of (i) the date received, or (ii) on the next business day if sent by a nationally recognized overnight courier service. If the Landlord by notice to the Tenant at any time designates some other person to receive payments or notices, all payments or notices thereafter by the Tenant shall be paid or given to the agent designated until notice to the contrary is received by the Tenant from the Landlord. Notices to either party under this Lease may be given by legal counsel to such party.

Section 11.3 - Successors and Limitation on Liability on the Landlord.

The obligations of this Lease shall run with the land, and this Lease shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns, except that the original Landlord named herein and each successor Landlord shall be liable only for obligations accruing during the period of its ownership. Neither the Tenant, nor anyone claiming by, under or through the Tenant, shall be entitled to obtain any judgment in enforcing the terms and conditions of this Lease creating personal liability on the part of the Landlord or enforcing any obligations of the Landlord against any assets of the Landlord other than its interest in the Property, and proceeds therefrom and, without limitation of the foregoing, in no event shall any personal liability arise on the part of any of the Landlord's officers, employees, directors or shareholders. Likewise, no personal liability shall arise on the part of the Tenant's officers, employees, directors or shareholders, as this Lease shall create liability on the part of the Tenant and not personal liability on the part of such officers, employees, directors or shareholders.

Section 11.4 - Waivers by the Landlord.

The failure of the Landlord or the Tenant to seek redress for violation of, or to insist upon strict performance of, any covenant or condition of this Lease, shall not be deemed a waiver of such violation nor prevent a subsequent act, which would have originally constituted a violation, from having all the force and effect of an original violation. The receipt by the Landlord of Annual Fixed Rent or Additional Rent with knowledge of the breach of any covenant of this Lease shall not be deemed a waiver of such breach. No provision of this Lease shall be deemed to have been waived by the Landlord or the Tenant, as the case may be, unless such waiver be in writing signed by the Landlord or the Tenant, as the case may be. No consent or waiver, express or implied, by the Landlord or Tenant to or of any breach of any agreement or duty shall be construed as a waiver or consent to or of any other breach of the same or any other agreement or duty.

Section 11.5 - Acceptance of Partial Payments of Rent.

No acceptance by either party of a lesser sum than the amount then due to such party shall be deemed to be other than a partial installment of such rent due, nor shall any endorsement or statement on any check or any letter accompanying any check or payment as rent be deemed an accord and satisfaction, and either party may accept such check or payment without prejudice to the other party's right to recover the balance of such installment or pursue any other remedy in this Lease provided. The delivery of keys to any employee of the Landlord or to the Landlord's agent or any employee thereof shall not operate as a termination of this Lease or a surrender of the Premises.

Section 11.6 - Interpretation and Partial Invalidity.

If any term of this Lease, or the application thereof to any person or circumstances, shall to any extent be invalid or unenforceable, the remainder of this Lease, or the application of such term to persons or circumstances other than those as to which it is invalid or unenforceable, shall not be affected thereby, and each term of this Lease shall be valid and enforceable to the fullest extent permitted by law. The titles of the Articles are for convenience only and not to be considered in construing this Lease. This Lease contains all of the agreements of the parties with respect to the subject matter thereof and supersedes all prior dealings between them with respect to such subject matter.

Section 11.7 - Quiet Enjoyment.

So long as the Tenant pays Annual Fixed Rent and Additional Rent, performs all other Tenant covenants of this Lease and observes all conditions hereof, the Tenant shall peaceably and quietly have, hold and enjoy the Premises free of any claims by, through or under, or superior to, the Landlord including, without limitation, any ground lessor, mortgagee, or manager of the Property.

Section 11.8 - Brokerage.

Jones Lang LaSalle New England LLC and CBRE (the "Brokers") shall be the only brokerage firms recognized in connection with this Lease transaction, and Landlord shall pay Brokers a brokerage fee under the terms of a separate agreement. Each party represents and warrants to the other that it has had no dealings with any broker or agent other than the Brokers in connection with this Lease and shall indemnify and hold harmless the other from claims for any brokerage commission by any other broker or agent claiming same by, through or under the indemnifying party.

Section 11.9 - Surrender of Premises and Holding Over.

The Tenant shall surrender possession of the Premises on the last day of the Term and the Tenant waives the right to any notice of termination or notice to quit at the end of the Term. The Tenant covenants that upon the expiration or sooner termination of this Lease, it shall, without notice, deliver up and surrender possession of the Premises broom clean and in the same condition in which the Tenant has agreed to keep the same during the continuance of this Lease and in accordance with the terms hereof, normal wear and tear and damage by fire or other casualty

excepted, first removing therefrom all personal property of the Tenant (including the Removable Equipment) and any alterations or additions required to be removed pursuant to Section 4.2 of this Lease, and repairing all damage caused by such removal. Upon the expiration of this Lease or if the Premises should be abandoned by the Tenant, or this Lease should terminate for any cause, and at the time of such expiration, vacation, abandonment or termination, the Tenant or Tenant's agents, subtenants or any other person should leave any property of any kind or character on or in the Premises after having vacated the Premises, the fact of such leaving of property on or in the Premises shall be conclusive evidence of intent by the Tenant, and individuals and entities deriving their rights through the Tenant, to abandon such property so left in or upon the Premises, and such leaving shall constitute abandonment of the property. Landlord shall have the right and authority without notice to the Tenant or anyone else, to remove and destroy, or to sell or authorize disposal of such property, or any part thereof, without being in any way liable to the Tenant therefor and the proceeds thereof shall belong to the Landlord as compensation for the removal and disposition of such property.

If the Tenant fails to surrender possession of the Premises upon the expiration or sooner termination of this Lease, then Tenant shall be deemed a tenant at sufferance only and Tenant shall pay to Landlord, as rent for any period after the expiration or sooner termination of this Lease, an amount equal to 150% of the Annual Fixed Rent and all Additional Rent payable under this Lease immediately prior to such holding over for each month or partial month of such holding over. Acceptance by the Landlord of such payments shall not constitute a consent to a holdover hereunder or result in a renewal or extension of the Tenant's rights of occupancy. Such payments shall be in addition to and shall not affect or limit the Landlord's right of re-entry, Landlord's right to collect such damages as may be available at law, or any other rights of the Landlord under this Lease or as provided by law.

Section 11.10 Financial Reporting.

Tenant shall from time to time (but at least annually) on the anniversary of the Lease provide Landlord with financial statements of Tenant, together with related statements of Tenant's or its parent's operations for the most recent fiscal year then ended, certified to Landlord by an independent certified public accounting firm. If Tenant or its parent is a public company, in lieu of such certification, Landlord may refer to Tenant's or its parent's website for such information.

Section 11.11 - Ground Lease.

This Lease shall in all respects be subject to the ground lease between the Landlord as lessee and the Massachusetts Institute of Technology ("MIT") as lessor dated as of June 28, 1988, as the same may be amended from time to time (as so amended, the "Ground Lease"), provided that, simultaneously with the execution hereof, MIT and Tenant shall execute a recognition, non-disturbance and attornment agreement in the form attached hereto as Exhibit G (the "NDA'').

Section 11.12 - Protection of REIT Status.

In the event that Landlord determines that any of the financial obligations of Tenant to Landlord as set forth in this Lease might (a) fail to qualify as "rents from real property" within the meaning of Section 856(d) of the Internal Revenue Code of 1986, as amended (the "**Code**") or "Impermissible Tenant Services" under REIT rules, or (b) otherwise jeopardize the status of any of Landlord's affiliates, including Forest City Realty Trust, Inc. or Brookfield Properties, Inc., as a "real estate investment trust" ("**REIT**") within the meaning of Section 856 of the Code, then, at Landlord's option, Landlord may, in its sole discretion, assign any of its rights and obligations under this Lease to a designee chosen by Landlord for such purpose (which, in each case, shall be an affiliate of Landlord), or cause one or more such designees (which, in each case, shall be an affiliate of Landlord) to perform such activities to the extent required to maintain such status as a REIT, provided, however, that any assignment permitted pursuant to this Section shall not increase Tenant's obligations nor decrease Tenant's rights in this Lease, and shall not result in the imposition of any additional charge or expense upon Tenant.

Section 11.13 - OFAC.

Tenant represents, warrants and covenants to Landlord that (1) neither Tenant nor any of its partners, members, principal stockholders or any other constituent entity either in control of the operation or management of Tenant or having a controlling financial interest in Tenant has been or will be designated or named as a terrorist, "Specifically Designated and Blocked Person," or other banned or blocked person, entity, nation or transaction pursuant to any law, order, rule or regulation that is enforced or administered by the Office of Foreign Assets Control or on the most current list published by the U.S. Treasury Department Office of Foreign Assets Control at its official website, http://www.treas.gov/ofac/t11 sdn.pdf or at any replacement website or other replacement official publication of such list (such list, or any such replacement official publication of such list, the "**OFAC List**")), or by any Executive Order or the United States Treasury Department; and (1)Tenant has not engaged, and will not engage, in this transaction, directly or indirectly, on behalf of, or instigating or facilitating, and will not instigate or facilitate, this transaction, directly or indirectly, on behalf of, any such person, group, entity or nation. A breach of any Tenant representation, warranty and covenant contained in this Section shall be an immediate and material Event of Default of Tenant under this Lease without notice or cure rights. Tenant hereby agrees to defend, indemnify and hold harmless Landlord from and against any and all claims, damages, losses, risks, liabilities and expenses (including reasonable attorneys' fees and costs) arising from or related to Tenant's breach of any of the foregoing representations, warranties and/or covenants.

Section 11.14 - Cambridge Employment Plan.

The Tenant agrees to sign an agreement with the Employment and Training Agency designated by the City Manager of the City of Cambridge as provided in subsections (a) - (g) of Section 24-4 of Ordinance Number 1005 of the City of Cambridge, adopted April 23, 1984.

Section 11.15 - Parking and Transportation Demand Management.

Tenant covenants and agrees to work cooperatively with Landlord to develop a parking and transportation demand management ("PTDM") program that comprises part of a comprehensive PTDM for the Park. In connection therewith, the use of single occupant vehicle commuting will be discouraged and the use of alternative modes of transportation and/or

alternative work hours will be promoted. Without limitation of the foregoing, Tenant agrees that its PTDM program (and Tenant will require in any sublease or occupancy agreement permitting occupancy in the Premises that such occupant's PTDM program) will include offering a subsidized MBTA transit pass, either constituting a full subsidy or a subsidy in an amount equal to the maximum deductible amount therefore allowed under the federal tax code, to any employee working in the Premises requesting one. Tenant agrees to comply with the traffic mitigation measures required by the City of Cambridge, and Tenant shall otherwise comply with all legal requirements of the City of Cambridge pertaining thereto.

IN WITNESS WHEREOF, this Lease has been executed and delivered as of the date first above written as a sealed instrument.

LANDLORD:

THIRTY-EIGHT SIDNEY STREET LLC

By: /s/ Michael Farley

Name: Michael Farley

Title: Senior Vice President

TENANT:

AGIOS PHARMACEUTICALS, INC., a Delaware corporation

By: /s/ Andrew Hirsch

Name: Andrew Hirsch

Title: Chief Financial Officer

EXHIBIT A
Basic Lease Terms

Premises:	The area depicted on Exhibit B-1, comprising 12,995 rentable square feet on a portion of the third (3rd) floor of the Building.
Building:	The building located at 38 Sidney Street (the "Building") in Cambridge, Massachusetts
Commencement Date:	The date that Landlord delivers possession of the Premises to Tenant vacant and free of all occupants and Landlord provides Tenant with a decommissioning closure report from a certified industrial hygienist that the Premises has been decommissioned in accordance with applicable ordinances of the City of Cambridge. Landlord estimates that the Commencement Date will occur on May 1, 2019.
Rent Commencement Date:	The Rent Commencement Date shall be the date which is the earlier of (i) the date which is one hundred twenty (120) days following the Commencement Date, or (ii) the date on which Tenant actually occupies any portion of the Premises for the conduct of its business therein.
Term:	The period commencing on the Commencement Date and expiring on February 29, 2028.
Annual Fixed Rent for the Term:	$70.00 per rentable square foot, as adjusted in accordance with the terms of Section 3.1 of the Lease. Beginning with the second Lease Year, and on each subsequent anniversary thereafter, Annual Fixed Rent for the Premises shall increase to an amount equal to one hundred three percent (103%) of the Annual Fixed Rent immediately preceding such anniversary.
Tenant's Address for Notices:	88 Sidney Street, Cambridge, Massachusetts 02139 *With copy to*:
Parking Privileges:	Commencing on the Rent Commencement Date and continuing through the Term, Tenant shall be entitled to use and shall pay for 1.5 parking passes per 1,000 rsf (which shall initially be equal to twenty (20) parking passes) in accordance with Section 2.4 of the Lease. Subject to availability, Tenant shall have the right to subscribe for additional parking spaces from Landlord; such lease for additional parking spaces shall be on a month-to-month basis at the then-prevailing fair market value for such parking passes.
Permitted Uses:	General business and administrative offices and customary accessory uses supporting the foregoing, as set forth in Section 6.1 of the Lease.
Tenant Improvements Allowance:	$974,625.00
Total Rentable Floor Area of Building:	122,554 rsf

EXHIBIT B-1

DEPICTION OF THE PREMISES

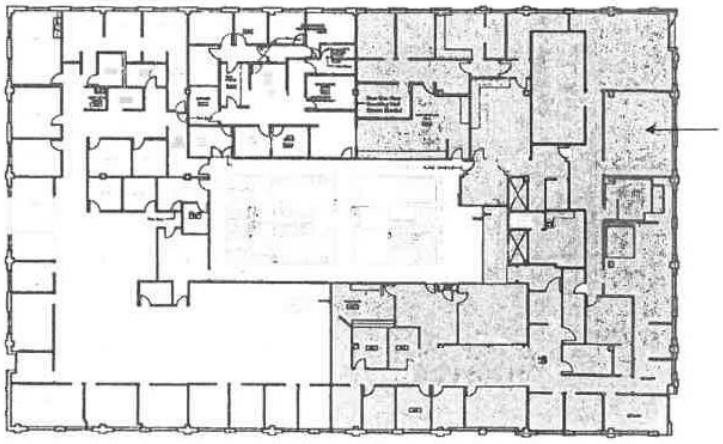

EXHIBIT B-2

MAP OF THE PARK

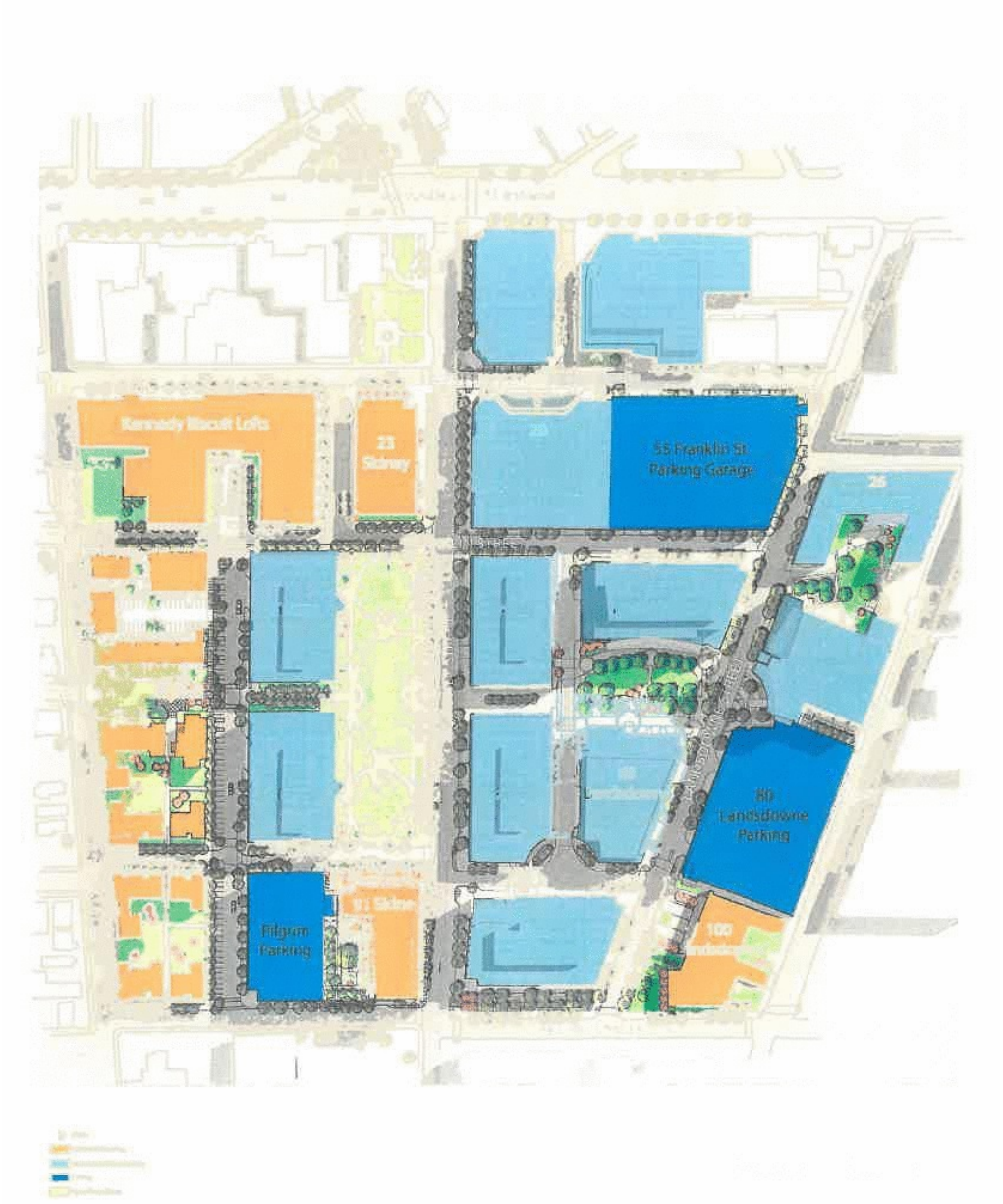

EXHIBIT C

STANDARD SERVICES

Landlord shall provide, or cause to be provided, the following standard services throughout the Term, which services may be modified from time to time by Landlord:

A. Regular maintenance of interior plants and exterior landscaping of the Building and all University Park common areas.

B. Regular maintenance, sweeping and snow removal of exterior areas around the Building, parking areas and throughout University Park.

C. Complete interior and exterior cleaning of all windows two times per year.

D. Daily, weekday maintenance of hallways, passenger elevators, common area bathrooms, lobby areas and vestibules.

E. Periodic cleaning of stairwells, freight elevators, and back of house areas.

F. Daily, weekday rubbish removal of all common area trash receptacles.

G. Daily, weekday cleaning of tenant space in a manner comparable to similar first-class office space in the Cambridge area.

H. Maintenance and repair of all base Building mechanical, electrical, plumbing and life safety systems and all other building systems serving the common areas.

I. Operation and maintenance of Building surveillance and alarm systems, links to the University Park command center, and security officer services in the Building and throughout University Park as appropriate in Landlord's reasonable determination.

J. Conditioned air for HVAC purposes shall be provided to the Premises from central mechanical equipment and shall be available 24 hours per day, 7 days per week; provided, however, Landlord reserves the right, pursuant to Section 3.5 of this Lease, to charge for conditioned air provided after normal business hours (8am – 6pm) if Landlord reasonably determines that demand for such conditioned air is not consistently needed throughout the Building during such non-business hours. Any charges for conditioned air shall include Landlord's reasonable estimate of the cost of energy, additional equipment maintenance and wear and tear associated with such after hours use, but shall not include a surcharge or profit to Landlord.

K. All utilities for all interior common areas and exterior building lighting.

L. Regular maintenance of banners, building directories and other building standard directional signage and amenities.

M. Reasonably adequate water and sewer service to the Premises.

EXHIBIT D

RULES AND REGULATIONS

DEFINITIONS

Wherever in these Rules and Regulations the word "Tenant" is used, it shall be taken to apply to and include the Tenant and its agents, employees, invitees, licensees, contractors, any subtenants and is to be deemed of such number and gender as the circumstances require. The word "Premises" is to be taken to include the space covered by the Lease. The word "Landlord" shall be taken to include the employees and agents of Landlord. Other capitalized terms used but not defined herein shall have the meanings set forth in the Lease. Any consents or approvals required of Landlord herein shall not be unreasonably withheld or delayed.

GENERAL USE OF BUILDING

A. Space for admitting natural light into any public area or tenanted space of the Building shall not be covered or obstructed by Tenant except in a manner reasonably approved by Landlord.

B. Toilets, showers and other like apparatus shall be used only for the purpose for which they were constructed.

C. Intentionally Omitted.

D. No sign, advertisement, notice or the like, shall be used in the Building by Tenant (other than at its office or as permitted in the Lease). If Tenant violates the foregoing, Landlord may remove the violation without liability and may charge all costs and expenses incurred in so doing to Tenant.

E. Tenant shall not throw or permit to be thrown anything out of windows or doors or down passages or elsewhere in the Building, or bring or keep any pets therein, or commit or make any indecent or improper acts or noises. In addition, Tenant shall not do or permit anything which will obstruct, injure, annoy or interfere with other tenants or those having business with them, or affect any insurance rate on the Building or violate any provision of any insurance policy on the Building.

F. Unless expressly permitted by the Landlord in writing:

(1) No additional locks or similar devices shall be attached to any door or window and no keys other than those provided by the Landlord shall be made for any door. If more than two keys for one lock are desired by the Tenant, the Landlord may provide the same upon payment by the Tenant. Upon termination of this lease or of the Tenant's possession, the Tenant

shall surrender all keys to the Premises and shall explain to the Landlord all combination locks on safes, cabinets and vaults.

(2) In order to insure proper use and care of the Premises Tenant shall not install any shades, blinds, or awnings or any interior window treatment without consent of Landlord. Blinds must be building standard.

(3) All doors to the Premises are to be kept closed at all times except when in actual use for entrance to or exit from such Premises. The Tenant shall be responsible for the locking of doors and the closing of any transoms and windows in and to the Premises. Any damage or loss resulting from violation of this rule shall be paid for by the Tenant.

(4) The Tenant shall not install or operate any steam or internal combustion engine, boiler, machinery in or about the Premises, or carry on any mechanical business therein. All equipment of any electrical or mechanical nature shall be placed in settings which absorb and prevent any vibration, noise or annoyance.

G. Landlord shall designate the time when and the method whereby freight, small office equipment, furniture, safes and other like articles may be brought into, moved or removed from the Building or Premises, and to designate the location for temporary disposition of such items.

H. The Premises shall not be defaced in any way. No changes in the HVAC, electrical fixtures or other appurtenances of said Premises shall be made without the prior approval of Landlord and in accordance with Landlord's construction rules and regulations.

I. For the general welfare of all tenants and the security of the Building, Landlord may require all persons entering and/or leaving the Building on weekends and holidays and between the hours of 7:30 am to 6:00 pm to register with the Building attendant or custodian by signing his name and writing his destination in the Building, and the time of entry and actual or anticipated departure, or other procedures deemed necessary by Landlord.

J. No animals, birds, pets, and no bicycles or vehicles of any kind shall be brought into or kept in or about said Premises or the lobby or halls of the Building. Tenant shall not cause or permit any unusual or objectionable odors, noises or vibrations to be produced upon or emanate from said Premises.

K. Unless specifically authorized by Landlord, employees or agents of Landlord shall not perform for nor be asked by Tenant to perform work other than their regularly assigned duties.

L. Landlord shall have the right to prohibit any advertising by Tenant which, in Landlord's reasonable opinion tends to impair the reputation of the Building or its desirability as an office building and, upon written notice from Landlord, Tenant shall promptly discontinue such advertising.

M. Canvassing, soliciting and peddling in the Building is prohibited and Tenant shall cooperate to prevent the same from occurring.

N. All parking, Building operation, or construction rules and regulations which may be reasonably established from time to time by Landlord on a uniform basis shall be obeyed.

O. Tenant shall not place a load on any floor of said Premises exceeding the floor load limits as set forth on Exhibit A. Landlord reserves the right to prescribe the weight and position of all safes and heavy equipment.

P. Tenant shall not install or use any air conditioning or heating device or system other than those approved by Landlord.

Q. Landlord shall have the right to make such other and further reasonable rules and regulations as in the judgment of Landlord may from time to time be needful for the safety, appearance, care and cleanliness of the Building and for the preservation of good order therein, and Tenant shall be given reasonable notice of same.

R. The access road and loading areas, parking areas, sidewalks, entrances, lobbies, halls, walkways, elevators, stairways and other common area provided by Landlord shall not be obstructed by Tenant, or used for any purpose other than for ingress and egress.

S. In order to insure proper use and care of the Premises Tenant shall not install any call boxes or communications systems or wiring of any kind without Landlord's permission and direction.

T. In order to insure proper use and care of the Premises Tenant shall not manufacture any commodity, or prepare or dispense for sale, except through vending machines for the benefit of employees and invitees of Tenant, any foods or beverages, tobacco, flowers, or other commodities or articles without the written consent of Landlord.

U. In order to insure use and care of the Premises Tenant shall not enter any janitors' closets, mechanical or electrical areas, telephone closets, loading areas, roof or Building storage areas without the prior written consent of Landlord.

V. In order to insure proper use and care of the Premises Tenant shall not place door mats in public corridors without consent of Landlord.

EXHIBIT E

WORK LETTER

1. Landlord shall provide to Tenant the Tenant Improvements Allowance set forth on **Exhibit A** attached to this Lease, for application to the costs and expenses, more particularly set forth below, incurred by or on behalf of Tenant to construct the Tenant's Initial Work. If Tenant incurs costs to perform the Tenant's Initial Work in excess of the Tenant Improvements Allowance, then all such excess costs shall be born solely by Tenant. The Tenant must apply to Landlord for reimbursement from the Tenant Improvements Allowance within eighteen (18) months following the Commencement Date. Any portion of such Tenant Improvements Allowance for which application for reimbursement has not been made within such 18-month period shall be cancelled and no longer available.

2. The application of the Tenant Improvements Allowance by Landlord shall be limited to payment of the following costs and expenses incurred by or on behalf of Tenant in connection with the construction of the Tenant's Initial Work: the actual documented and verified hard costs pursuant to Tenant's design and construction contracts, including without limitation the associated contractor's overhead and profit and general conditions, incurred in the construction of the Tenant's Initial Work, and including capital equipment installed within the Premises. Tenant may apply up to 20% of the Tenant Improvements Allowance to the following soft costs incurred by Tenant: architectural, engineering and project management fees, data/telecom cabling and other move-related expenses (excluding the purchase of furniture, fixtures or equipment). During the construction of the Tenant's Initial Work with respect to which Tenant desires to have the Tenant Improvements Allowance applied, and in accordance with the commercially reasonable terms and conditions typically imposed upon a landlord pursuant to a construction loan agreement, such as, without limitation, retainage, lien waiver, and other requisition conditions, Tenant shall, on a monthly basis (as the Tenant's contractor submits to Tenant its application for payment), deliver to Landlord a requisition for payment showing the costs of the Tenant's Initial Work in question and the amount of the current payment requested from Landlord for disbursement from the Tenant Improvements Allowance within thirty (30) days after receipt of Tenant's requisition. Payments made on account of Tenant's requisitions shall be made from the Tenant Improvements Allowance. Following the completion of the Tenant's Initial Work, Tenant shall deliver to the Landlord, within ninety (90) days of completion, a statement showing the final costs of such Tenant's Initial Work, the amounts paid to date, or on behalf of the Tenant, and any amounts available for release of retainage along with as-built plans for the Tenant's Initial Work.

EXHIBIT F

CONSTRUCTION RULES AND REGULATIONS

These Landlord's construction rules, regulations and work procedures ("Construction Rules and Regulations") are designed to provide efficient scheduling of work while protecting the buildings tenants from unnecessary noise and inconvenience. Prepared in accordance with standard lease provisions, this document contains detailed information to assist you in planning construction projects undertaken throughout your term of occupancy. Please review it carefully before design begins. It is intended that these Construction Rules and Regulations be shared with tenant architects, engineers and contractors as appropriate.

These Landlord's Construction Rules and Regulations are intended to supplement the terms and conditions established in Article IV of the Lease Agreement. In some cases, certain guidelines or requirements set forth within these standard Construction Rules and Regulations may conflict with specific terms negotiated and set forth within a specific lease agreement, particularly with regard to notification and approval requirements for smaller projects or projects of limited scope. In all such cases, the provisions of the lease agreement shall govern and shall supersede specific conflicting requirements set forth herein. In all cases, however, including those where specific Landlord approval may not be required, the provisions of these Construction Rules and Regulations governing activities of tenant contractors shall be respected and adhered to.

For convenience, the key requirements are collected in the "Summary" section on the balance of this page; the remainder of the document sets forth these Construction Rules and Regulations in more detail.

SUMMARY

1. Contact the Property Manager (PM), who will assist you in completing your project efficiently and with minimum impact on other tenants in the Building.

1. Incorporate the provisions of these Rules and Regulations and any applicable "Indoor Air Quality Guidelines for Tenant Improvement Work" into all of your construction agreements and contracts. Except to the extent otherwise provided in your specific lease, you will need written approval from the PM prior to commencing work. A signed building permit shall suffice.

3. At least two weeks before construction commencement, provide two sets of drawings and specifications to the PM for approval to the extent required by your Lease. The Property Manager must also approve your list of contractors and subcontractors.

4. At least one week before commencement of construction, submit to the PM your construction schedule; addresses and telephone numbers of supervisors, contractors and subcontractors; copies of permits; and proof of current insurance.

5. All unusually noisy, disruptive, or odor and dust producing work, as well as the delivery of construction materials, must occur outside of regular business hours unless otherwise permitted by the PM.

6. We expect all contractors to maintain safe and orderly conditions and labor harmony.

7. Before occupying the completed space (to the extent not previously occupied), submit the final certificate of occupancy and any other final sign-offs to the Property Manager. We also require an air balancing report signed by a professional engineer if the work affects base building HVAC. A complete set of "as built" drawings as well as electronic "as-built" drawings in format compatible with AutoCAD (as updated from time to time) must be supplied to the Property Manager.

1. DEFINITIONS

1.1 Buildings: 38 Sidney Street

Cambridge, MA 02139

1.2 Property Manager: Jay Kiely, or such other individual as Landlord may designate, from time to time.

1.3 Building Standards Book: Tenant Interior Standards at 38 Sidney Street, if existing, as amended by Landlord, from time to time.

1.4 Consultants: Any architectural, engineering, or design consultant engaged by a Tenant in connection with Tenant Work.

1.5 Contractor: Any contractor engaged by a Tenant of the Building for the performance of any Tenant Work, and any subcontractor, employed by any such Contractor.

1.6 Plans: All drawings and specifications including but not limited to architectural, electrical, mechanical, plumbing and fire protection construction drawings and specifications required for the proper construction of the Tenant Work.

1.7 Regular Business Hours: Monday through Friday, 7:30 A.M. through 6:00 P.M., excluding holidays.

1.8 Tenant: Any occupant of the Building.

1.9 Tenant Interior Standards: A manual that may be established and provided by Landlord which set forth design guidelines, typical details, standard finishes and other information to be utilized by Tenant in the design of improvements and modifications to its Premises.

1.10 Tenant Work: Any alternations, improvements, additions, repairs or installations in the Building performed by or on behalf of any Tenant.

1.11 Tradesperson: Any employee (including, without limitation, any mechanic, laborer, or tradesperson) employed by a Contractor performing Tenant Work.

2.0 GENERAL

2.1 All Tenant Work shall be performed in accordance with these Construction Rules and Regulations, subject to any exclusions or applicable provisions set forth within your Lease Agreement.

2.2 The provisions of these rules and regulations governing the actions or activities of Contractors and Tradespersons shall be incorporated in all agreements governing the performance of all Tenant Work, including, without limitation, any agreements governing services to be rendered by each Contractor and Consultant.

2.3 Except as otherwise provided in these Rules and Regulations or the lease, all inquiries, submissions and approvals in connection with any Tenant Work shall be processed through the PM on behalf of the Landlord.

3.0 PLANS

3.1 Review and Approval: Any Tenant wishing to perform Tenant Work must first obtain the Landlord's written approval of its plans for such Tenant Work except to the extent otherwise provided in the Lease. Tenant may select its own space planner(s) and/or architect(s) for the design of the tenant work. To ensure operating consistency of the Premises with the Building and minimize any impacts to base building or tenant systems Tenant shall either (a) retain Landlord's designated mechanical, electrical, plumbing and structural engineers (s) for design and construction oversight of its Tenant Work or (b) obtain Landlord's prior approval for the selection of other mechanical, electrical, plumbing and structural engineers with respect to such Tenant Work, such approval not to be unreasonably withheld. In case of (b) above, Landlord may at its discretion require that Tenant engage and pay for the reasonable costs of a peer review by Landlord's designated engineer to ensure operating consistency.

3.2 Submission

Requirements: a. Any Tenant performing Tenant Work shall, at the earliest possible time, furnish to the PM two full sets of plans and specifications describing such Tenant Work.

b. All such Plans shall be drafted in accordance with the Construction Drawing Requirements set out in the Building Standards Book.

c. The design manifested in the Plans will be reviewed by the Landlord and shall comply with the Tenant Interior Standards and the requirements of the Lease.

4. PRECONSTRUCTION NOTIFICATION AND APPROVALS

4.1 Approval to Commence Work

a. Tenant shall submit to Property Manager for approval in accordance with the Lease, the names of all prospective Contractors prior to any such Contractors entering the Property for the purpose of commencing Work.

b. No Tenant Work shall be undertaken by any Contractor or Tradesperson unless and until all the matters set forth in Article 4.2 below have been received for the Tenant Work.

4.2 No Tenant Work shall be performed until each of the following has been provided to the Property Manager. In the event that Tenant proposes to change any of the following, the Property Manager shall be immediately notified of such change.

a. Schedule for the work, indicating start and completion dates, any phasing and special working hours, and also a list of anticipated shutdowns of building systems. The schedule of the Tenant Work is subject to Landlord's reasonable approval.

b. List of all Contractors and Subcontractors, including addresses, telephone numbers, trades employed, and the union affiliation, if any, of each Contractor and Subcontractor.

c. Names and telephone numbers of the supervisors of the work.

d. Copies of all necessary governmental permits, licenses and approvals.

e. Proof of current insurance, to the limits set out in Exhibit A to these Construction Rules and Regulations, naming Landlord and others so designated as an additional insured party.

f. Notice of the involvement of any Contractor in any ongoing or threatened labor dispute.

g. To the extent required pursuant to the Lease, Payment, Performance and Lien Bonds from sureties acceptable to Landlord, in form acceptable to Landlord, naming Landlord as an additional obligee. (This requirement may be waived at the discretion of the Property Manager).

h. Evidence that Tenant has made provision for written waivers of lien from all Contractors and suppliers of material to the extent such waivers are permitted pursuant to applicable law.

4.3 Reporting Incidents

All accidents, disturbances, labor disputes or threats thereof, and other noteworthy events pertaining to the Building or the Tenant's property shall be reported immediately to the Property Manager. A written report must follow within 24 hours.

5. CONSTRUCTION SCHEDULE

5.1 Coordination

a. All Tenant Work shall be carried out expeditiously and with minimum disturbance and disruption to the operation of the Building and without causing discomfort, inconvenience, or annoyance to any of the other tenants or occupants of the Building.

b. All schedules for the performance of construction, including materials deliveries, must be coordinated through the Property Manager. The Property Manager shall have the right, without incurring any liability to any Tenant, to stop activities and/or to require rescheduling of Tenant Work being conducted in violation of these Rules and Regulations and/or the Lease.

c. If any Tenant Work requires the shutdown of risers and mains for electrical, mechanical, sprinklers and plumbing work, such work shall be supervised by a representative of Landlord. No Tenant Work will be performed in the Building's mechanical or electrical equipment rooms without the supervision of a representative of Landlord, the cost of which shall be reimbursed by the Tenant.

5.2 Time Restrictions

a. Subject to Paragraph 5.1 of these rules and regulations, general construction work will generally be permitted at all times, including during Regular Business Hours.

b. Tenant shall provide the Property Manager with at least twenty-four (24) hours' notice before proceeding with Special Work, as hereinafter defined, and such Special Work will be permitted only at times agreed to by the Property Manager during periods outside of Regular Business Hours. "Special Work" shall be defined as the following operations:

(1) All utility disruptions, shutoffs and turnovers;

(2) Activities involving high levels of noise, including demolition, coring, drilling and ramsetting;

(3) Activities resulting in excessive dust or odors, including demolition and spray painting.

c. The delivery of construction materials to the Building, their distribution within the Building, and the removal of waste materials shall also be confined to periods outside Regular Business Hours, unless otherwise specifically permitted in writing by the Property Manager.

d. If coordination, labor disputes or other circumstances reasonably require, the Property Manager may change the hours during which regular construction work can be scheduled.

e. Security, when required by Landlord for Special Work, will be $45.00 per hour.

6. CONTRACTOR PERSONNEL

6.1 Work in Harmony

a. All Contractors shall be responsible for employing skilled and competent personnel and suppliers who shall abide by the rules and regulations herein set forth.

b. Should a work stoppage or other labor dispute occur anywhere in or about the Building as a result of the presence, anywhere in the Building, of a Contractor engaged directly or indirectly by a Tenant, Landlord may require any such Contractor to vacate the premises demised by such Tenant and the Building, and to cease all further construction work therein, until such time as the work stoppage or other labor dispute is resolved.

6.2 Conduct

a. While in or about the Building, all Tradespersons shall perform in a dignified, quiet, courteous, and professional manner at all times. Tradespersons shall wear clothing suitable for their work and shall remain fully attired at all times. All Contractors will be responsible for their Tradespersons' proper behavior and conduct.

a. The Property Manager reserves the right to remove anyone who, or any Contractor which; is causing a disturbance to any tenant or occupant of the Building or any other person using or servicing the Building; is interfering with the work of others; or is in any other way displaying conduct or performance not compatible with the Landlord's standards.

b. There will be no smoking allowed inside the Building or at or near the front entrances.

c. The use of radios and similar devices shall only be permitted at the discretion of the PM, and then only at volumes that are not audible outside the confines of the immediate construction site.

6.3 Access

a. All Contractors and Tradespersons shall contact the Property Manager prior to commencing work, to confirm work location and Building access, including elevator usage and times of operation.

b. No Contractor or Tradesperson will be permitted to enter any private or public space in the Building, other than the Premises or the common areas of the Building necessary to give direct access to the premises of Tenant for which he has been employed, without the prior approval of the Property Manager.

a. All Contractors and Tradespersons must obtain permission from the Property Manager prior to undertaking work in any space outside of the Tenant's premises. This requirement includes ceiling spaces below the premises where any work required must be undertaken at the convenience of the affected Tenant and outside of Regular Business Hours. Contractors undertaking such work shall take all appropriate measures to protect the affected premises, and shall ensure that all removable items are reinstalled and all cleaning be completed prior to opening of the next business day.

d. Contractors shall ensure that all furniture, equipment and accessories in areas potentially affected by any Tenant Work shall be adequately protected by means of drop cloths or other appropriate measures.

e. Temporary access doors for tenant construction areas connecting with a public corridor will be to building standards, i.e., door, frame, hardware and lockset. A copy of the key will be furnished to the Property Manager.

6.4 Safety

a. All Contractors shall police ongoing construction operations and activities at all times, keeping the premises orderly, maintaining cleanliness in and about the premises, and ensuring safety and protection of all areas, including truck docks, elevators, lobbies and all other public areas which are used for access to the premises.

b. All Contractors shall appoint a supervisor who shall be responsible for all safety measures, as well as for compliance with all applicable governmental laws, ordinances, rules and regulations such as, for example, "OSHA" and "Right-to-Know" legislation.

6.5 Parking

a. Parking is not allowed in or near truck docks, in handicapped or fire access lanes, or any private ways in or surrounding the property. Vehicles so parked will be towed at the expense of the Contractor for whom the owner of such vehicle is employed.

b. The availability of parking in any authorized parking areas of the Building is limited. Use of such parking for Contractors and their personnel is restricted and must be arranged with and approved by the Property Manager.

7. BUILDING MATERIALS

7.1 Delivery

All deliveries of construction materials shall be made at the predetermined times approved by the Property Manager and shall be effected safely and expeditiously only at designated loading areas.

7.2 Transportation in Building

a. Distribution of materials from delivery point to the work area in the Building shall be accomplished with the least amount of disruption to the operation of the Building as possible. Elevators will be assigned for material delivery and will be controlled by the Property Manager.

b. Contractors shall provide adequate protection to all carpets, wall surfaces, doors and trim in all public areas through which materials are transported. Contractors shall continuously clean all such areas. Protective measures shall include runners over carpet, padding in elevators and any other measures determined by the Property Manager.

c. Any damage caused to the Building through the movement of construction materials or otherwise shall be the responsibility of Tenant who has engaged the Contractor involved. Charges for such damage will be submitted by the Landlord directly to the Tenants Contractor.

7.3 Storage and Placement

a. All construction materials shall be stored only in the premises where they are to be installed. No storage of materials will be permitted in any public areas, loading docks or corridors leading to the premises.

b. No flammable, toxic, or otherwise hazardous materials may be brought in or about the Building by any Contractor unless: (i) authorized by the Property Manager (if not customarily used in construction of Tenant Improvements), (ii) all applicable laws, ordinances, rules and regulations are complied with, and (iii) all necessary permits have been obtained. All necessary precautions shall be taken by the Contractor handling such materials against damage or injury caused by such materials.

c. All materials required for the construction of the premises must comply with Building standards, must conform to the plans and specifications approved by Landlord, and must be installed in the locations shown on the drawings approved by the Landlord.

d. All construction activities and all Tenant Work shall be subject to reasonable inspection by PM or other Landlord Representative.

e. No material alterations to approved plans will be made without prior knowledge and approval of the Property Manager. Such changes shall be documented on the

as-built drawings required to be delivered to Landlord pursuant to Paragraph 10 of the rules and regulations.

f. All protective devices (e.g., temporary enclosures and partitions) and materials, as well as their placement, must be approved by the Property Manager.

g. It is the responsibility of the Contractor to ensure that the temporary placement of materials does not impose a hazard to the Building or its occupants, either through overloading, or interference with Building systems, access, and egress or in any other manner whatsoever.

h. All existing and/or new openings made through the floor slab for piping, cabling, etc. must be fire stopped with a UL listed product approved by the Property Manager. All holes in the floor slab at abandoned floor outlets, etc. will be filled with solid concrete.

7.4 Salvage and Waste Removal

a. All rubbish, waste and debris shall be neatly and cleanly removed from the Building by Contractors daily unless otherwise approved by the Property Manager. The Building's trash compactor shall not be used for construction or other debris. For any demolition waste and debris, each Contractor must make arrangements with the Property Manager for the scheduling and location of an additional dumpster to be supplied at the cost of the Tenant engaging such Contractor. Where, in the opinion of the Property Manager, such arrangements are not practical, such Contractors will make alternative arrangements for removal at the cost of the Tenant engaging such Contractors.

b. Contractors shall, prior to removing any item (including, without limitation, building standard doors, frames and hardware, light fixtures, ceiling diffusers, ceiling exhaust fans, sprinkler heads, fire horns, ceiling speakers and smoke detectors) from the Building, notify the Property Manager that it intends to remove such item. At the election of Property Manager, Contractors shall deliver any such items to the Property Manager. Such items will be delivered, without cost, to an area designated by the Property Manager which area shall be within the Building or the complex in which the Building is located.

8. CONTRACTORS INSURANCE

Prior to commencing any Tenant Work, and throughout the performance of the Tenant Work, each Contractor shall obtain and maintain insurance in accordance with Exhibit A attached hereto. Each Contractor shall, prior to making entry into the Building provide Landlord with certificates that such insurance is in full force and effect.

9. SUBMISSIONS UPON COMPLETION

a. Upon completion of any Tenant Work and prior to taking occupancy (if not previously occupied), Tenant shall submit to Landlord a permanent certificate of occupancy and final approval of any other governmental agencies having jurisdiction.

b. A properly executed air balancing report, signed by a professional engineer, shall be submitted to Landlord upon completion of all mechanical work. Such report shall be subject to Landlord's approval.

c. Tenant shall submit to Landlord's Representative a final "as-built" set of sepia drawings as well as electronic "as-built" drawings compatible with AutoCAD, as updated from time to time.

EXHIBIT A TO CONSTRUCTION RULES AND REGULATIONS

INSURANCE REQUIREMENTS FOR CONTRACTORS

When Tenant Work is to be done by Contractors in the Building, the Tenant authorizing such work shall be responsible for including tin the contract for such work the following insurance and indemnity requirements to the extent that they are applicable. Insurance certificates must be received prior to construction. Landlord shall be named as an additional insured party on all certificates.

INSURANCE

Each Contractor and each Subcontractor shall, until the completion of the Tenant Work in question, procure and maintain at its expense, the following insurance coverages with companies acceptable to Landlord in the following minimum limits:

Workers' Compensation

(Including coverage for Occupational Disease)

Limit of Liability

Workers' Compensation Statutory Benefits

Employer's Liability $500,000

Comprehensive General Liability

(Including Broad Form Comprehensive Liability Enhancement, Contractual Liability assumed by the Contractor and the Tenant under Article 15.3 of the Lease and Completed Operations coverage).

Limit of Liability

Bodily Injury & Property Damage $10,000,000 combined single limit

Comprehensive Automobile Liability

(including coverage for Hired and Non-owned Automobiles)

Limit of Liability

Bodily Injury & Property Damage $1,000,000 per occurrence

Forest City Management will provide you with a current list of additional insureds.

SUPPLEMENT TO RULES AND REGULATIONS FOR

DESIGN CONSTRUCTION OF TENANT WORK

FACT SHEET FOR INSERT

1. PROPERTY MANAGER'S OFFICE

CONTACT(S): Jay Kiely (or designee)

LOCATION: Brookfield Properties (USA (II) LLC

38 Sidney Street

Cambridge, MA 02139

TELEPHONE NUMBER: 617-914-2587

2. PERSONNEL, MATERIAL AND EQUIPMENT ACCESS

LOCATION OF LOADING DOCK: Rear of Building, Blanche Street

NORMAL HOURS OF ACCESS: 7:30AM – 6:00PM

ENTRANCES NOT AVAILABLE: All building lobbies.

3. USE OF ELEVATORS

LOCATION OF ELEVATORS: Specific locations of service elevators will be pointed out by the building staff.

NORMAL HOURS OF OPERATION: 7:30AM – 6:000PM

ELEVATORS NOT AVAILABLE: All passenger elevators.

4. SPECIAL CONDITIONS AND PRECAUTIONS

38 Sidney Street is a no smoking building. Therefore, smoking will not be allowed inside the building or at or near the front entrance.

Contractors, Sub Contractors, Design Personnel may be required to sign in and out of the property. This procedure will be at the Property Manager's discretion.

Delivery of Tenant specialty equipment that is unable to fit onto the freight elevators will need to be coordinated with the Property Manager.

EXHIBIT G

FORM OF SUBORDINATION, NON-DISTURBANCE AND ATTORNMENT AGREEMENT

RETURN TO:

SUBORDINATION, NON-DISTURBANCE AND ATTORNMENT AGREEMENT

THIS SUBORDINATION, NON-DISTURBANCE AND ATTORNMENT AGREEMENT (hereinafter referred to as "Agreement") made this _____ day of _____, among _____ (together with its successors, assigns, designees and/or nominees, collectively hereinafter referred to as "Lender"), _____ (hereinafter referred to as "Tenant"), and _____, a _____ (hereinafter referred to as "Landlord").

R E C I T A L S:

A. Tenant is the tenant and lessee under a certain _____, as amended by _____ (as the same may now or hereafter be amended, restated, replaced or otherwise modified, collectively, the "Lease") relating to the premises described in the Lease (hereinafter referred to as the "Premises"), located at the real property more particularly described on Exhibit A attached hereto (hereinafter referred to as the "Property").

B. Lender has made or will make a loan to Landlord (hereinafter referred to as the "Loan"), which such Loan is (i) secured by, among other things, a deed of trust, mortgage or security deed (as the same may be amended, restated, extended, or otherwise modified from time to time, the "Mortgage") from Landlord to Lender covering the Property including the Premises and (ii) evidenced by certain other documents and instruments by and among Lender and Landlord, among others (the same, together with the Mortgage, collectively, the "Loan Documents").

C. Tenant has agreed that the Lease shall be subject and subordinate to the Loan and Loan Documents, provided Tenant is assured of continued occupancy of the Premises under the terms of the Lease.

NOW, THEREFORE, for and in consideration of the mutual covenants herein contained, the sum of Ten Dollars ($10.00) and other good and valuable considerations, the receipt and

sufficiency of which are hereby acknowledged, and notwithstanding anything in the Lease to the contrary, it is hereby agreed as follows:

1. Subordination and Consent. Lender, Tenant and Landlord do hereby covenant and agree that the Lease with all rights, options, liens and charges created thereby (including, without limitation, any option or rights contained in the Lease, or otherwise existing, to acquire any or all of the Premises, or any superior leasehold interest therein), is and shall continue to be subject and subordinate in all respects to the lien and terms of the Loan Documents, and to any renewals, modifications, consolidations, replacements and extensions thereof and to all advances made thereunder. Tenant acknowledges that Landlord will, pursuant to the Mortgage, assign the Lease as security for the Loan, and Tenant hereby expressly consents to such assignment. Tenant agrees that if there is a default by Landlord in the performance and observance of any of the terms of such Loan, Lender may, at its option, demand all rents due under the Lease be paid by Tenant directly to Lender at the address specified below, or as otherwise specified by Lender. Tenant agrees that upon Lender's written request for payment of rent directly to Lender, Tenant will timely remit any and all payments due under the Lease directly to, and payable to, Lender. Such payments to Lender will constitute performance of Tenant's payment obligations under the Lease.

2. Non-Disturbance. Lender does hereby agree with Tenant that, in the event Lender succeeds to Landlord's interest in the Premises by foreclosure, conveyance in lieu of foreclosure or otherwise, so long as Tenant complies with and performs its obligations under the Lease, (a) the Lease shall continue in full force and effect as a direct Lease between Lender and Tenant, upon and subject to all of the terms, covenants and conditions of the Lease, for the balance of the term of the Lease, and Lender will not disturb the possession of Tenant, and (b) the Premises shall be subject to the Lease and Lender shall recognize Tenant as the tenant of the Premises for the remainder of the term of the Lease in accordance with the provisions thereof; provided, however, that Lender shall not be:

(i) subject to any claims, offsets or defenses which Tenant might have against any prior landlord (including Landlord);

(ii) liable for any act or omission of any prior landlord (including Landlord);

(iii) bound by any rent or additional rent which Tenant might have paid for more than the current month or any security deposit or other prepaid charge paid to any prior landlord (including Landlord);

(iv) bound by any amendment or modification of the Lease made not in accordance with the terms of the Loan Documents; or

(v) liable for any deposit that Tenant may have given to any previous landlord (including Landlord) which has not, as such, been transferred to Lender.

Nothing contained herein shall prevent Lender from naming Tenant in any foreclosure or other action or proceeding initiated by Lender pursuant to the Loan Documents to the extent necessary under applicable law in order for Lender to avail itself of and complete the foreclosure or other remedy. Tenant acknowledges and agrees that it has no right or option of any nature whatsoever, whether pursuant to the Lease or otherwise, to purchase the Premises or the Property, or any portion thereof or any interest therein, and to the extent that Tenant has had, or hereafter acquires, any such right or option, the same is hereby acknowledged to be subject and subordinate to the lien and terms of the Loan Documents and is hereby waived and released as against Lender.

3. Attornment. Tenant does hereby agree with Lender that, in the event Lender becomes the owner of the Property by foreclosure, conveyance in lieu of foreclosure or otherwise, then Tenant shall attorn to and recognize Lender as the landlord under the Lease for the remainder of the term thereof, and Tenant shall perform and observe its obligations thereunder, subject only to the terms and conditions of the Lease. Tenant further covenants and agrees to execute and deliver upon request of Lender an appropriate agreement of attornment to Lender and any subsequent titleholder of the Premises.

4. Lease Defaults. In the event Landlord shall fail to perform or observe any of the terms, conditions or agreements in the Lease, Tenant shall give written notice thereof to Lender and Lender shall have the right (but not the obligation) to cure such default. Tenant shall not take any action with respect to such default under the Lease, including without limitation any action in order to terminate, rescind or avoid the Lease or to withhold any rent or other monetary obligations thereunder, for a period of thirty (30) days following receipt of such written notice by Lender; provided, however, that in the case of any default which cannot with diligence be cured within said thirty (30) day period, if Lender shall proceed promptly to cure such default and thereafter prosecute the curing of such default with diligence and continuity, the time within which such default may be cured shall be extended for such period as may be necessary to complete the curing of such default with diligence and continuity.

5. Obligations and Liability of Lender. Lender shall have no obligations nor incur any liability with respect to any warranties of any nature whatsoever, whether pursuant to the Lease or otherwise, including, without limitation, any warranties respecting use, compliance with zoning, hazardous wastes or environmental laws, Landlord's title, Landlord's authority, habitability, fitness for purpose or possession. Furthermore, in the event that Lender shall acquire Landlord's interest in the Property, Lender shall have no obligation, nor incur any liability, beyond Lender's then equity interest, if any, in the Property, and Tenant shall look exclusively to such equity interest of Lender, if any, in the Property for the payment and discharge of any obligations or liability imposed upon Lender hereunder, under the Lease (or under any new lease with Tenant), and Lender is hereby released and relieved of any other obligations or liability hereunder, under the Lease or under any such new lease. Lender shall not, either by virtue of the Loan Documents or this Agreement, be or become a mortgagee in possession or be or become subject to any liability or obligation under the Lease or otherwise until Lender shall have acquired the Landlord's interest in the Property and then such liability or obligation of Lender under the Lease (as modified by the terms of this Agreement) shall extend only to those liability

or obligations accruing subsequent to the date that Lender has acquired Landlord's interest in the Property. Without limiting the generality of the foregoing, neither the Loan Documents nor this Agreement shall, prior to Lender's acquisition of Landlord's interest in the Property, operate to place responsibility for the control, care, management or repair of the Property upon Lender or impose upon Lender responsibility for the carrying out of any of the terms or conditions of the Lease, and Lender shall not be responsible or liable for any waste committed on either the Premises or the Property by any party whatsoever, for any dangerous or defective condition of the Property or for any negligence in the management, upkeep, repair or control of either the Premises or the Property.

6. Severability. If any portion or portions of this Agreement shall be held invalid or inoperative, then all of the remaining portions shall remain in full force and effect, and, so far as is reasonable and possible, effect shall be given to the intent manifested by the portion or portions held to be invalid or inoperative.

7. Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the State of _____.

8. Notices. So long as the Mortgage remains outstanding and unsatisfied, Tenant will mail or deliver to Lender, at the address and in the manner hereinbelow provided, a copy of all notices permitted or required to be given to the Landlord by Tenant under and pursuant to the terms and provisions of the Lease. All notices or other communications required or permitted to be given pursuant to the provisions hereof shall be in writing and shall be considered as properly given if (i) mailed to the addressee by first class United States mail, postage prepaid, registered or certified with return receipt requested, (ii) by delivering same in person to the addressee, or (iii) by delivery to a third party commercial delivery service for same day or next day delivery to the office of the addressee with proof of delivery. Notice so given shall be effective, as applicable, upon (i) the third (3rd) day following the day such notice is deposited with the U.S. Postal Service, (ii) delivery to the addressee, or (iii) upon delivery to such third party delivery service. Notice given in any other manner shall be effective only if and when received by the addressee. For purposes of notice, the addresses of the parties shall be:

Lender: _

Landlord: _

Tenant: _

Notwithstanding the foregoing, any party shall have the right to change its address for notice hereunder to any other location within the continental United States by the giving of thirty (30) days' notice to the other parties in the manner set forth herein.

9. Successors and Assigns. This Agreement shall be binding upon and inure to the benefit of the parties hereto and their respective heirs, legal representatives, successors, successors-in-title and assigns. Without limitation of any provision contained herein, as used herein, the term (i) "landlord" refers to Landlord and to any successor to the interest of Landlord under the Lease and (ii) "Lender" refers to Lender and to any assignee of the note secured by the Mortgage and Lender's servicer of the Loan, if any.

10. Tenant's Personal Property. In no event shall the Mortgage cover or encumber (and shall not be construed as subjecting in any manner to the lien thereof) any of Tenant's moveable trade fixtures, business equipment, furniture, signs or other personal property at any time placed on or about the Premises.

11. Counterparts. This Agreement may be executed in one or more counterparts, each of which when so executed shall be deemed to be an original, but all of which when taken together shall constitute one and the same instrument.

12. Headings. The headings, captions, and arrangements used in this Agreement are for convenience only and shall not affect the interpretation of this Agreement.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the parties hereto have executed this Agreement under seal as of the date first above written.

LENDER:

a _

By:_
its Authorized Signatory

TENANT:

a _

By:_
Name:_
Title:_

LANDLORD:

a _

By:_
Name:_
Title:_

_____, as guarantor of the obligations of Tenant under the Lease, has executed this Agreement under seal for the purpose of acknowledging and consenting to the same.

GUARANTOR:

a _

By:_
Name:_
Title:_

STATE OF §
§
COUNTY OF §

This instrument was acknowledged before me on the _____ day of _____, _____, by _____, of _____, a _____, on behalf of said _____.

[S E A L]

My Commission Expires: Notary Public – State of _

Printed Name of Notary Public

STATE OF §
§
COUNTY OF §

This instrument was acknowledged before me on the _____ day of _____, _____, by _____, of _____, a _____, on behalf of said _____.

[S E A L]

My Commission Expires: Notary Public – State of _

Printed Name of Notary Public

STATE OF §
§
COUNTY OF §

This instrument was acknowledged before me on the _____ day of _____, _____, by _____, of _____, a _____, on behalf of said _____.

[S E A L]

My Commission Expires: Notary Public – State of _

Printed Name of Notary Public

EXHIBIT H

FORM OF GROUND LEASE SNDA

Agreement dated as of _____ __, 2014 (this "**Agreement**"), by and between MASSACHUSETTS INSTITUTE OF TECHNOLOGY, a Massachusetts educational corporation chartered by Massachusetts law ("**Ground Lessor**"), THIRTY-EIGHT SIDNEY STREET LIMITED LLC, a Delaware limited liability company ("**Landlord**") and AGIOS PHARMACEUTICALS, INC., a Delaware corporation ("**Tenant**").

BACKGROUND

Ground Lessor and Landlord are parties, as landlord and tenant respectively, to a Construction and Lease Agreement (the "**Ground Lease**"), more particularly described on **Exhibit A** attached hereto, for certain real property located at 38 Sidney Street in Cambridge, Massachusetts, a legal description of which is set forth on **Exhibit B** attached hereto (the "**Land**"). Landlord has constructed a building (the "Building") on the Land. Tenant has entered into a lease dated as of _____ __, 2019 (the "**Lease**") with Landlord for certain premises in the Building and appurtenant rights, including parking rights, related thereto (the "**Premises**"), the Premises being more particularly described in the Lease.

AGREEMENTS

Non-Disturbance. If the Ground Lease is terminated, for any reason, Ground Lessor shall not disturb Tenant in Tenant's possession of the Premises and without any hindrance or interference from the Ground Lessor, shall permit Tenant peaceably to hold and enjoy the Premises for the remainder of the unexpired term of the Lease, together with any extension periods provided for therein, upon and subject to the same terms, covenants and conditions as are contained in the Lease, and shall recognize the Lease as modified hereby. The foregoing is on the condition that Tenant is not in default under the Lease beyond any applicable notice and grace periods contained in the Lease. Ground Lessor represents and warrants that there are no mortgages on Ground Lessor's interest in the Land and/or the Building as of the date of this Agreement.

Attornment. Tenant hereby agrees that if the Ground Lease is terminated for any reason, Tenant shall attorn to Ground Lessor and shall be liable to and recognize Ground Lessor as Landlord under the Lease for the balance of the term of the Lease upon and subject to all of the terms and conditions thereof. In such case, upon receipt of notice from Ground Lessor setting forth the effective date of the termination of the Ground Lease, Tenant shall pay to the Ground Lessor all obligations required to be paid and performed by Tenant under the Lease arising after the date of termination. The Lease shall continue in full force and effect as a direct lease between Ground Lessor and Tenant.

2. Additional Conditions. Tenant agrees that Ground Lessor shall not be: (i) liable for any act or omission of any person or party who may be landlord under the Lease prior to any termination of the Ground Lease ("Prior Landlord") except for a default by such Prior Landlord under the Lease that began prior to the termination of the Ground Lease, is ongoing and continuing following the termination of the Ground Lease, is susceptible of being cured and for which Tenant has provided Ground Lessor with notice as required hereunder (a "Continuing Default"); (ii) subject to any offsets or defenses which Tenant might have against Prior Landlord except for a Continuing Default; and (iii) bound by any prepayment of rent or additional rent, or any other charge which Tenant might have paid to Prior Landlord for more than the then current month (other than a bona fide security deposit paid by Tenant to Landlord under the Lease, estimated monthly payments made on account of additional rent as and when required to be made pursuant to the provisions of the Lease, or other rent, additional rent or charges which have been received by Ground Lessor). Nothing herein, however, shall constitute a waiver of Tenant's rights as against such individual or entity which is the landlord under the Lease as of the time of any event or circumstances which may give rise to a claim of the Tenant against such individual or entity. In addition, nothing herein shall relieve any successor landlord under the Lease from its obligation to comply with those obligations of a Landlord under the Lease during the period for which it is the owner of the Landlord's interest in the Lease.

3. Landlord's Defaults. Tenant hereby agrees that, if Tenant provides Landlord with any notice of default or claimed default on the part of Landlord under the Lease, Tenant shall concurrently therewith send a copy of such notice to Ground Lessor. In such event, Ground Lessor shall be permitted (but not obligated) to cure any such default within the period of time allotted thereto in the Lease.

4. Notices. Duplicates of all notices delivered by any party to another party and required by this Agreement shall be delivered concurrently to all other parties to this Agreement. All notices shall be written, delivered by certified or registered mail, and sent, if to Ground Lessor, to 238 Main Street, Suite 200, Cambridge, Massachusetts 02142, Attention: Managing Director, Real Estate, if to Tenant to Agios Pharmaceuticals, Inc., 88 Sidney Street, Cambridge, Massachusetts 02139, with a copy to Mintz, Levin, Cohn, Ferris, Glovsky, and Popeo, P.C., One Financial Center, Boston, Massachusetts 02111, Attention: Stuart A Offner, Esq., and if to Landlord to 38 Sidney Street, Cambridge, MA 02139-4234, Attention: Asset Manager, or such addresses as may, from time to time, be set forth in notices to the other parties hereunder.

5. Exculpation of Ground Lessor. Ground Lessor shall not be personally liable hereunder. Tenant agrees to look to Ground Lessor's interest in the Land and Building only for satisfaction of any claim against Ground Lessor hereunder.

6. Successors and Assigns. This Agreement shall bind Tenant, its successors and assigns, and shall benefit Tenant and only such successor and assigns of Tenant as are permitted by the Lease and shall bind and benefit Ground Lessor and its successors and assigns (provided that after transfer of Ground Lessor's entire interest in the Land to another party, Ground Lessor shall have no liability for any act or omission of such party) and shall bind and benefit Landlord and its successors and assigns.

[remainder of page intentionally left blank]

EXECUTED as an instrument under seal as of the date set forth above.

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
Ground Lessor

By: _
Name: _____
Title: _____

AGIOS PHARMACEUTICALS, INC.
Tenant

By:__
Name: _____
Title: _____

THIRTY-EIGHT SIDNEY STREET LIMITED LLC,
a Delaware limited liability company

By:_
Name:_
Its:_

COMMONWEALTH OF MASSACHUSETTS)
) ss:
COUNTY OF MIDDLESEX)

BEFORE ME, a Notary Public in and for said County and State, personally appeared the MASSACHUSETTS INSTITUTE OF TECHNOLOGY, by _____, its _____, who acknowledged that he did sign the foregoing instrument and that the same is his free act and deed and the free act and deed of said corporation.

IN TESTIMONY HEREOF, I set my hand and official seal at Cambridge, this _____ day of _____, 201_.

Notary Public
My Commission Expires:_

COMMONWEALTH OF MASSACHUSETTS)
) ss:
COUNTY OF_____)

BEFORE ME, a Notary Public in and for said County and State, personally appeared the above-named AGIOS PHARMACEUTICALS, INC., by _____ who acknowledged that he/she did sign the foregoing instrument and that the same is his/her free act and deed and the free act and deed of said corporation.

IN TESTIMONY HEREOF, I set my hand and official seal at _____, this _____ day of _____, 201_.

Notary Public
My Commission Expires:_

COMMONWEALTH OF MASSACHUSETTS)
) ss:
COUNTY OF MIDDLESEX)

BEFORE ME, a Notary Public in and for said County and State, personally appeared the above-named THIRTY-EIGHT SIDNEY STREET LIMITED LLC, by Michael Farley, Managing Member, who acknowledged that he did sign the foregoing instrument and that the same is his free act and deed and the free act and deed of said corporation on behalf of said limited liability company.

IN TESTIMONY HEREOF, I set my hand and official seal at Cambridge, this _____ day of _____, 201_.

Notary Public
My Commission Expires:_

EXHIBIT A

Description of Ground Lease

The ground lease (the "Ground Lease") between the Landlord as lessee and Massachusetts Institute of Technology ("MIT") as lessor dated as of August 20, 1986.

EXHIBIT B

Legal Description

PARCEL ONE:

A certain parcel of land in said Cambridge, bounded and described as follows:

Beginning at the intersection of the southeasterly line of Sidney Street and the southwesterly line of Franklin Street:

Thence running S 51 ° 35' 25" E, along said southwesterly line of Franklin Street, a distance of 39.15 feet to a point at a private way;

Thence running S 37° 18' 54" W, along the north westerly Line of said private way, a distance of 199.53 feet, to a private way, formerly known as Auburn Street;

Thence running N 51° 25' 00" W, along the northeasterly line of said private way, a distance of 143.00 feet, to a point on the aforesaid southeasterly line of Sidney Street;

Thence running N 38° 25' 13" E, along said southeasterly line of Sidney Street, a distance of 199.06 feet, to a point of beginning.

PARCEL TWO:

Together with the benefit of the rights set forth in the Parking Easement Agreement by and between University Park Phase II Limited Partnership, as Owner, and Thirty-Eight Sidney Street Limited Partnership, as Pass Holder, dated June 12, 2000 and recorded in Book 31552, Page 565 and filed as Document No. 1143014, as affected by a Recognition and Attornment Agreement by and between Massachusetts Institute of Technology, University Park Phase II Limited Partnership and Thirty Eight Sidney Street Limited Partnership dated as of June 12, 2000 and recorded in Book 31553, Page 1 and filed as Document No. 1143015, as further amended and affected by Parking Exchange Agreement dated as of April 16, 2002 by and among University Park Phase II Limited Partnership, FC 65/80 Landsdowne, Inc. and Thirty Eight Sidney Street Limited Partnership, as joined in and assented to by MIT recorded in Book 35498, Page 523 and filed as Document No. 1210856, as further affected by Assignment of FC 65180 Landsdowne, Inc.'s interest in said Parking Exchange Agreement to U P 65/80 Landsdowne, LLC as set forth in Assignment of Parking Easement Agreement dated as of February 22, 2010 and recorded in

Book 54324, Page 171, and as further affected by Subordination, Recognition and Attornment Agreement dated as of June 15, 2011 by and among Sun Life Assurance Company of Canada, Thirty Eight Sidney Street Limited Partnership and UP 65/80 Landsdowne, LLC and recorded in Book 56994, Page 182.

PARCEL THREE:

Together with the benefit of the easements and other rights in the nature of an interest in real estate as set forth in the Declaration of Covenants by Massachusetts Institute of Technology dated December 15, 1997 recorded in Book 28297, Page 479 and filed as Document No. 1058425.

PARCEL FOUR:

Together with the benefit of the easement to use Blanche Street as set forth in the Easement and Assumption Agreement by and between Massachusetts Institute of Technology and Forest City 38 Sidney Street, Inc. dated October 6, 1988 and recorded in Book 19411, Page 537, as assigned to Thirty-Eight Sidney Street Limited Partnership dated August 22, 2000 and recorded in Book 31771, Page 236.

FOURTH AMENDMENT TO LEASE

THIS FOURTH AMENDMENT TO LEASE (the "**Fourth Amendment**") made and entered into this 11th day of April, 2019 (the "**Effective Date**"), by and between **FOREST CITY 88 SIDNEY STREET, LLC,** a Delaware limited liability company ("**Landlord**"); and **AGIOS PHARMACEUTICALS, INC**., a Delaware corporation ("**Tenant**").

W I T N E S S E T H:

WHEREAS, Landlord and Tenant entered into a certain lease agreement dated September 15, 2014, as amended by that certain First Amendment to Lease dated November 21, 2014, that certain Second Amendment to Lease dated July 20, 2015, and that certain Third Amendment to Lease (the "**Third Amendment**") dated as of November 17, 2017 (as so amended, the "**Lease**") with respect to a certain premises containing146,034 rentable square feet ("**Premises**") in the building located at and commonly known as 88 Sidney Street, Cambridge, Massachusetts ("**Building**"), as more fully set forth in the Lease;

WHEREAS, the Term of the Lease is currently scheduled to expire by its terms on February 28, 2025 (such date, as defined in the Third Amendment, the "**Modified Expiration Date**");

WHEREAS, Tenant and Landlord's affiliate are simultaneously herewith entering into a lease of premises located at 38 Sidney Street Cambridge, Massachusetts (the "**38 Sidney Lease**"), and Landlord and Tenant would like to extend the Term so as to be coterminous with the term of the 38 Sidney Lease.

NOW, THEREFORE, for and in consideration of the mutual covenants and agreements hereinafter set forth and for other good and valuable consideration, the receipt and legal sufficiency of which are hereby mutually acknowledged, Landlord and Tenant hereby agree that the Lease shall be modified and amended as follows:

1. Defined Terms. Capitalized terms used in this Fourth Amendment which are not defined herein shall have the meanings ascribed thereto in the Lease. The meanings of capitalized terms defined herein which are also defined in the Lease shall supersede the meanings given thereto in the Lease.

2. Term. The Extended Term (as defined in the Third Amendment) is hereby amended and the Term of the Lease is hereby extended from and after the Original Expiration Date through February 29, 2028 (the "**Expiration Date**") (the extension of the Term set forth in the Third Amendment and as extended by this Section 2 of this Fourth Amendment is referred to herein collectively as the "**Extended Term**"). The Extended Term shall be upon all of the same terms, conditions and provisions of the Lease except as expressly set forth otherwise in this Fourth Amendment. Tenant shall continue to have the extension options set forth in Section 2.6 of the Lease following the expiration of the Extended Term, except that (i) references to the "Initial Term" in Section 2.6 shall be deemed references to the Extended Term, and (ii) for purposes of determining the Extension Fair Rental Value of the Premises under Section 2.6(c), the comparable transactions considered by the real estate professionals and the Final Professional shall be leases of comparable space in the commercial markets that surround the MIT campus (East Cambridge/Kendall Square/Cambridgeport) taking into account all relevant factors including comparable building age, quality, level of finish, and proximity to amenities and public transit.

3. Condition of Premises. Tenant is in possession of the Premises, and hereby accepts the Premises for the Extended Term in its AS IS condition, WITHOUT REPRESENTATION OR WARRANTY by Landlord, and Tenant agrees that Landlord has no obligation to perform any alterations or improvements to the Premises to prepare or improve the same for Tenant's use or occupancy for the Extended Term, except as otherwise expressly set forth in the Lease.

4. Rent. Section 3 of the Third Amendment is hereby deleted and of no further force or effect. During the Extended Term, Tenant shall pay Annual Fixed Rent for the Premises in the amounts set forth below:

Time Period:	Annual Rate	Annual Fixed Rent for Premises:	Monthly Installment:
April 15, 2022 – February 16, 2023	$90.04	$13,148,901.40	$1,095,741.78
February 17, 2023 – February 16, 2024	$92.74	$13,543,193.20	$1,128,599.43
February 17, 2024 – February 28, 2025	$95.52	$13,949,167.70	$1,162,430.64
March 1, 2025 – February 28, 2026	$100.00	$14,603,400.00	$1,216,950.00
March 1, 2026 – February 28, 2027	$103.00	$15,041,502.00	$1,253,458.50
March 1, 2027 – February 29, 2028	$106.09	$15,492,747.10	$1,291,062.26

5. Additional Rent. During the Extended Term, Tenant shall continue to pay The Tenant's Tax Expenses Allocable to the Premises, The Tenant's Operating Expenses Allocable to the Premises and all other Additional Rent in accordance with the terms and conditions of the Lease.

6. Bike Storage Area; Bike Storage Allowance. Landlord agrees that Tenant shall have the right to install and construct an enclosed bicycle storage facility on the exterior courtyard of the Property adjacent to the Building in a size and location reasonably approved by Landlord (the "**Bike Storage Area**"). Tenant shall submit construction plans and specifications to Landlord and the final design and ultimate construction of the Bike Storage Area shall be subject to Landlord's review and approval of such construction plans and specifications and to Tenant's first obtaining all necessary governmental and community permits and approvals. Landlord shall reimburse Tenant up to $100,000.00 (the "**Bike Storage Allowance**") toward the total hard costs incurred by Tenant in connection with the construction of the Bike Storage Area. If Tenant incurs costs in excess of the Bike Storage Allowance, then all such excess costs shall be born solely by Tenant. The Tenant must apply to Landlord for reimbursement from the Bike Storage Allowance within eighteen (18) months after the Effective Date. Any portion of such Bike Storage Allowance for which application for reimbursement has not been made within such eighteen (18) month period shall be cancelled and no longer available. The application of the Bike Storage Allowance by Landlord shall be limited to payment of the following costs and expenses incurred by or on behalf of Tenant in connection with the construction of the Bike Storage Area: the actual documented and verified cost pursuant to Tenant's design and construction contracts, including without limitation the associated contractor's overhead and profit and general conditions, incurred in the construction of the Bike Storage Area, and including capital equipment installed within the Bike Storage Area, architectural, engineering and project management fees, but excluding the making of improvements, installation of fixtures or incorporation of other items which are moveable rather than permanent improvements in the nature of trade fixtures, examples of which may include furniture, telephone communications and security equipment. During the construction of the Bike Storage Area with respect to which Tenant desires to have the Bike Storage Allowance applied, and in accordance with the commercially reasonable terms and conditions typically imposed upon a landlord pursuant to a construction loan agreement, such as, without limitation, retainage, lien waiver, and other requisition conditions, Tenant shall, on a monthly basis (as the Tenant's contractor submits to Tenant its application for payment), deliver to Landlord a requisition for payment showing the costs of the leasehold improvements in question and the amount of the current payment requested from Landlord for disbursement from the Bike Storage Allowance within thirty (30) days after receipt of Tenant's requisition. Payments made on account of Tenant's requisitions shall be made from the Bike Storage Allowance. Following the completion and commencement of use of the Bike Storage Area, Tenant shall deliver to the Landlord, within ninety (90) days of completion, a statement showing the final costs of such Bike Storage Area, the amounts paid to date, or on behalf of the Tenant, and any amounts available for release of retainage. The construction of all improvements to the Bike Storage Area (including fixtures therein such as bicycle racks and storage equipment, shall become the property of Landlord upon the expiration or earlier termination of the Term of the Lease without compensation to Tenant.

7. Amendment to Lease; Inapplicable Provisions. The Premises includes the entire rentable square footage of the Building and Tenant's rights of first offer set forth in Section 2.7 of the Lease and Tenant's modified right of first offer set forth in Section 2.9 of the Lease are no longer applicable and are of no further force or effect.

8. Notice Addresses. Landlord's Address for Notices set forth in Exhibit A to the Lease is hereby amended to provide that notices Landlord shall be as follows (and to MIT in the event of a notice of default to Landlord):

Forest City 88 Sidney Street, LLC
c/o Brookfield Properties (USA II) LLC
350 Massachusetts Avenue
Cambridge, Massachusetts 02139
Attention: Asset Manager

with a simultaneous copy to:

Forest City 88 Sidney Street, LLC
c/o Brookfield Properties (USA II) LLC
250 Vesey Street
New York, NY 10281-1023
Attention: General Counsel

9. Brokerage. Tenant represents and warrants that it has not dealt with any broker in connection with the consummation of this Fourth Amendment other than Jones Lang LaSalle New England LLC, and CBRE, New England (the "**Brokers**"), and in the event any claim is made against Landlord relative to dealings by Tenant with any brokers other than the Brokers, Tenant shall defend the claim against Landlord with counsel of Tenant's selection, first approved by Landlord (which approval shall not be unreasonably withheld), and shall save harmless and indemnify Landlord on account of loss, cost or damage which may arise by reason of such claim. Landlord represents and warrants that it has not dealt with any broker in connection with the consummation of this Fourth Amendment other than the Brokers, and in the event any claim is made against Tenant relative to dealings by Landlord with any brokers, Landlord shall defend the claim against Tenant with counsel of Landlord's selection, first approved by Tenant (which approval shall not be unreasonably withheld), and shall save harmless and indemnify Tenant on account of loss, cost or damage which may arise by reason of such claim. Landlord shall be responsible for the payment of a commission to the Brokers in connection with this Fourth Amendment pursuant to a separate agreement between Landlord and the Broker.

10. Counterparts. This Fourth Amendment may be executed in any number of multiple counterparts, each of which shall be deemed an original, but all of which shall constitute one and the same instrument.

11. Ratification of Lease. Except as expressly supplemented, amended or modified by this Fourth Amendment, the Lease is hereby ratified and confirmed in all respects, and shall continue in full force and effect. In the event of any inconsistency between the terms of this Fourth Amendment and the Lease, the terms of this Fourth Amendment shall control. From and after the date hereof, all references to the Lease shall mean the Lease as modified by this Fourth Amendment.

12. Successors and Assigns. This Fourth Amendment shall be binding upon and inure to the benefit of the parties hereto, their respective successors and assigns.

13. Authority. Landlord and Tenant each represent and warrant that the persons signing this Fourth Amendment have full right and authority to enter into this Fourth Amendment. This Fourth Amendment shall be subject to the consent of Landlord's mortgagee and Ground Lessor.

IN WITNESS WHEREOF, the parties hereto have executed this Fourth Amendment as of the day and year first written above.

LANDLORD:

FOREST CITY 88 SIDNEY STREET, LLC
a Delaware limited liability company

By: /s/ Michael Farley
Michael Farley, Senior Vice President

TENANT:

AGIOS PHARMACEUTICALS, INC.,
a Delaware corporation

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

THIRD AMENDMENT OF LEASE

THIS THIRD AMENDMENT OF LEASE (the "**Third Amendment**") made and entered into this 11th day of April, 2019 (the "**Effective Date**"), by and between UP 64 SIDNEY STREET, LLC, a Delaware limited liability company, ("**Landlord**"), and AGIOS PHARMACEUTICALS, INC., a Delaware corporation ("**Tenant**").

W I T N E S S E T H:

WHEREAS, Landlord and Tenant entered into a Lease dated November 17, 2017, as amended by a First Amendment of Lease (the "**First Amendment**") dated April 11, 2018 and that certain Second Amendment to Lease (the "**Second Amendment**") dated as of December 14, 2018 (as so amended, collectively, the "**Lease**") for space comprising a total area of 42,564 rentable square feet consisting of the entire fourth (4th) floor containing 27,083 rentable square feet (the "**Fourth Floor Premises**") and a portion of the first (1st) floor containing 15,481 rentable square feet (the "**First Floor Premises**" and collectively with the Fourth Floor Premises, the "**Premises**") in the building located at 64 Sidney Street in Cambridge, Massachusetts (the "**Building**"); and

WHEREAS, the Term of the Lease is currently scheduled to expire by its terms on February 28, 2025 (such date, as defined in the Third Amendment, the "**Expiration Date**");

WHEREAS, Tenant and Landlord's affiliate are simultaneously herewith entering into a lease of premises located at 38 Sidney Street Cambridge, Massachusetts (the "**38 Sidney Lease**"), and Landlord and Tenant would like to extend the Term so as to be coterminous with the term of the 38 Sidney Lease.

NOW, THEREFORE, for and in consideration of the mutual covenants and agreements hereinafter set forth and for other good and valuable consideration, the receipt and legal sufficiency of which are hereby mutually acknowledged, and intending to be legally bound, Landlord and Tenant hereby agree that the Lease shall be modified and amended as follows:

1. Defined Terms. Capitalized terms used in this Third Amendment which are not defined herein shall have the meanings ascribed thereto in the Lease. The meanings of capitalized terms defined herein which are also defined in the Lease shall supersede the meanings given thereto in the Lease.

2. Term. The Term of the Lease is hereby extended from and after the Expiration Date through February 29, 2028 (the "**Expiration Date**") (the extension of the Term set forth in this Third Amendment is referred to herein collectively as the "**Extended Term**"). The Extended Term shall be upon all of the same terms, conditions and provisions of the Lease except as expressly set forth otherwise in this Third Amendment. Tenant shall continue to have the extension options set forth in Section 2.6 of the Lease following the expiration of the Extended Term, except that (i) references to the "Initial Term" in Section 2.6 shall be deemed references to the Extended Term, and (ii) for purposes of determining the Extension Fair Rental Value of the Premises under Section 2.6(c), the comparable transactions considered by the real estate professionals and the Final Professional shall be leases of comparable space in the commercial markets that surround the MIT campus (East Cambridge/Kendall Square/Cambridgeport) taking into account all relevant factors including comparable building age, quality, level of finish, and proximity to amenities and public transit.

3. Condition of Premises. Tenant is in possession of the Premises, and hereby accepts the Premises for the Extended Term in its AS IS condition, WITHOUT REPRESENTATION OR WARRANTY by Landlord, and Tenant agrees that Landlord has no obligation to perform any alterations or improvements to the Premises to prepare or improve the same for Tenant's use or occupancy for the Extended Term, except as otherwise expressly set forth in the Lease.

4. Rent.

(a) Tenant shall continue to pay the Fixed Rent payable under the Lease for the Premises through the Expiration Date in accordance with the terms and conditions of the Lease.

(b) During the Extended Term, Tenant shall pay Annual Fixed Rent for the Fourth Floor Premises in the amounts set forth below:

Time Period:	Annual Rate	Annual Fixed Rent for Premises:	Monthly Installment:
March 1, 2025 – February 28, 2026	$100.00	$2,708,300.00	$225,691.67
March 1, 2026 – February 28, 2027	$103.00	$2,789,549.00	$232,462.42
March 1, 2027 – February 29, 2028	$106.09	$2,873,235.47	$239,436.29

(c) During the Extended Term, Tenant shall pay Annual Fixed Rent for the First Floor Premises in the amounts set forth below:

Time Period:	Annual Rate	Annual Fixed Rent for Premises:	Monthly Installment:
March 1, 2025 – February 28, 2026	$82.50	$1,277,182.50	$106,431.88
March 1, 2026 – February 28, 2027	$84.98	$1,315,575.30	$109,631.28
March 1, 2027 – February 29, 2028	$87.52	$1,354,897.12	$112,908.04

5. Additional Rent. During the Extended Term, Tenant shall continue to pay The Tenant's Tax Expenses Allocable to the Premises, The Tenant's Operating Expenses Allocable to the Premises and all other Additional Rent in accordance with the terms and conditions of the Lease. Notwithstanding anything to the contrary in the First Amendment and the Second Amendment, Tenant shall pay to Landlord, as Additional Rent, its pro rata share of water, sewer and other services and utilities which shall be prorated to reflect Tenant's proportional usage based upon Tenant's proportional occupancy of the Building.

6. Additional Right of First Offer. The additional right of first offer set forth in Section 9 of the First Amendment is hereby deleted and replaced with the following new text:

> "Tenant shall have a one-time right of first offer for all or any portion of second (2nd) and third (3rd) floors of the Building (the "**Additional First Offer Space**") in the event that

the Additional First Offer Space becomes vacant and available during the Term following the expiration or termination of the lease or occupancy agreement with the then tenant of such Additional First Offer Space and subject to Landlord's right to grant any tenant of the Additional First Offer Space the right to renew or continue its term of occupancy whether or not such rights are expressly granted by a lease or other written instrument. Landlord shall notify Tenant of the terms on which Landlord intends to offer to lease the Additional First Offer Space ("**Landlord's Additional ROFO Notice**"), and the Annual Fixed Rent shall be at the then current Fair Market Rent taking into account all relevant factors. Within ten (10) business days after receipt of Landlord's Additional ROFO Notice, Tenant may, by written notice delivered to Landlord, (i) reject Landlord's Additional ROFO Notice, or (ii) unconditionally and irrevocably accept Landlord's offer to lease all (but not less than all) of such space for Tenant's own use on the terms set forth in Landlord's Additional ROFO Notice. If Tenant fails to timely respond as aforesaid, such failure shall be deemed Tenant's rejection of Landlord's Additional ROFO Notice. In the event Tenant exercises its right to the Additional First Offer Space, Landlord and Tenant hereby agree to amend those provisions of this Lease which are necessarily affected by the increase in the rentable area and leaving all other provisions of this Lease in full force and effect without modification. After Tenant takes possession of the Additional First Offer Space, the term "Premises" as used in this Lease, shall be deemed to refer to and include the Additional First Offer Space.

If Landlord's Additional ROFO Notice is rejected under clause (i) above (or demand rejected through Tenant's failure to timely respond), then Landlord may enter into a lease for the Additional First Offer Space providing for an effective Annual Fixed Rent equal to or less than seven and onehalf percent (7.5%) less than that specified in Landlord's Additional ROFO Notice. For clarity, in the event that Landlord proposes to enter into a lease for the Additional First Offer Space providing for an effective Annual Fixed Rent greater than seven and one-half percent (7.5%) less than that specified in Landlord's Additional ROFO Notice, Landlord shall notify Tenant of such terms by sending an additional Landlord's Additional ROFO Notice that will be subject to the terms of the preceding paragraph."

7. Parking. Tenant's parking privileges may be relocated by Landlord to Landlord's other parking facilities located at 55 Franklin Street, Cambridge, Massachusetts and/or 30 Pilgrim Street, Cambridge, Massachusetts as Landlord shall designate upon reasonable prior notice to Tenant from Landlord. In the event that Tenant's parking privileges are so relocated, Tenant's parking privileges at such new location shall be consistent with the terms set forth in Section 2.4 of the Lease.

8. Notice Addresses. Landlord's Address for Notices set forth in Exhibit A to the Lease is hereby amended to provide that notices Landlord shall be as follows (and to MIT in the event of a notice of default to Landlord):

Forest City 88 Sidney Street, LLC
c/o Brookfield Properties (USA II) LLC
350 Massachusetts Avenue
Cambridge, Massachusetts 02139
Attention: Asset Manager

with a simultaneous copy to:

Forest City 88 Sidney Street, LLC
c/o Brookfield Properties (USA II) LLC
250 Vesey Street
New York, NY 10281-1023
Attention: General Counsel

9. Brokers. Tenant represents and warrants that it has not dealt with any broker in connection with the consummation of this Third Amendment other than Jones Lang LaSalle New England LLC, and CBRE, New England (the "**Brokers**"), and in the event any claim is made against Landlord relative to dealings by Tenant with any brokers other than the Brokers, Tenant shall defend the claim against Landlord with counsel of Tenant's selection, first approved by Landlord (which approval shall not be unreasonably withheld), and shall save harmless and indemnify Landlord on account of loss, cost or damage which may arise by reason of such claim. Landlord represents and warrants that it has not dealt with any broker in connection with the consummation of this Third Amendment other than the Brokers, and in the event any claim is made against Tenant relative to dealings by Landlord with any brokers, Landlord shall defend the claim against Tenant with counsel of Landlord's selection, first approved by Tenant (which approval shall not be unreasonably withheld), and shall save harmless and indemnify Tenant on account of loss, cost or damage which may arise by reason of such claim. Landlord shall be responsible for the payment of a commission to the Brokers in connection with this Third Amendment pursuant to a separate agreement between Landlord and the Broker.

10. Counterparts. This Third Amendment may be executed in any number of multiple counterparts, each of which shall be deemed an original, but all of which shall constitute one and the same instrument.

11. Ratification of Lease. Except as expressly supplemented, amended or modified by this Third Amendment, the Lease is hereby ratified and confirmed in all respects, and shall continue in full force and effect. In the event of any inconsistency between the terms of this Agreement and the Lease, the terms of this Agreement shall control. From and after the Effective Date, all references to the Lease shall mean the Lease as modified by this Third Amendment.

12. Successors and Assigns. This Third Amendment shall be binding upon and inure to the benefit of the parties hereto, their respective successors and assigns.

13. Authority. Landlord and Tenant each represent and warrant that the persons signing this Agreement have full right and authority to enter into this Third Amendment. This Third Amendment shall be subject to the consent of Landlord's mortgagee and Ground Lessor.

[SIGNATURE PAGE FOLLOWS]

IN WITNESS WHEREOF, the parties hereto have executed this Third Amendment as of the day and year first written above:

LANDLORD:

UP 64 SIDNEY STREET, LLC,
a Delaware limited liability company

By: /s/ Michael Farley
Michael Farley, Senior Vice President

TENANT:

AGIOS PHARMACEUTICALS, INC.,
a Delaware corporation

AGIOS PHARMACEUTICALS, I
By: /s/ Andrew Hirsch
Name: Andrew Hirsch
Title: Chief Financial Officer

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: August 1, 2019

/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: August 1, 2019

/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, 2019, 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: August 1, 2019

/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, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned, Andrew Hirsch, Chief Financial Officer of the Company, hereby certifies, pursuant to 18 U.S.C. Section 1350, that, to his knowledge on the date hereof:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: August 1, 2019

/s/ Andrew Hirsch

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