UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q

☒ **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**

For the transition period from _____ to _____

Commission File Number: 001-35945

EPIZYME, INC.

(Exact name of registrant as specified in its charter)

Delaware	**26-1349956**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
400 Technology Square, Cambridge, Massachusetts	**02139**
(Address of principal executive offices)	**(Zip code)**

617-229-5872
(Registrant's telephone number, including area code)

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, $0.0001 par value	**EPZM**	**Nasdaq Global Select Market**

The number of shares outstanding of the registrant's common stock as of July 31, 2019: 91,036,622 shares.

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 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 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 ☒

Forward-looking Information

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. These statements may be identified by such forward-looking terminology as “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar statements or variations of such terms. Our forward-looking statements are based on a series of expectations, assumptions, estimates and projections about our company, are not guarantees of future results or performance and involve substantial risks and uncertainty. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. Our business and our forward-looking statements involve substantial known and unknown risks and uncertainties, including the risks and uncertainties inherent in our statements regarding:

- our plans to develop and commercialize novel epigenetic therapies for patients with cancer and other serious diseases;
- our ongoing and planned clinical trials, including the timing of initiation and enrollment in the trials, the timing of availability of data from the trials and the anticipated results of the trials;
- our ability to achieve anticipated milestones under our collaborations;
- the timing of and our ability to apply for, obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of our products;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position; and
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

All of our forward-looking statements are made as of the date of this Quarterly Report on Form 10-Q only. In each case, actual results may differ materially from such forward-looking information. We can give no assurance that such expectations or forward-looking statements will prove to be correct. An occurrence of or any material adverse change in one or more of the risk factors or risks and uncertainties referred to in this Quarterly Report on Form 10-Q or included in our other public disclosures or our other periodic reports or other documents or filings filed with or furnished to the Securities and Exchange Commission, or the SEC, could materially and adversely affect our business, prospects, financial condition and results of operations. Except as required by law, we do not undertake or plan to update or revise any such forward-looking statements to reflect actual results, changes in plans, assumptions, estimates or projections or other circumstances affecting such forward-looking statements occurring after the date of this Quarterly Report on Form 10-Q, even if such results, changes or circumstances make it clear that any forward-looking information will not be realized. Any public statements or disclosures by us following this Quarterly Report on Form 10-Q which modify or impact any of the forward-looking statements contained in this Quarterly Report on Form 10-Q will be deemed to modify or supersede such statements in this Quarterly Report on Form 10-Q.

Our management’s discussion and analysis of our financial condition and results of operations are based upon our unaudited condensed consolidated financial statements included in this Quarterly Report on Form 10-Q, which have been prepared by us in accordance with accounting principles generally accepted in the United States of America, or GAAP, for interim periods and with Regulation S-X promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act. This discussion and analysis should be read in conjunction with these unaudited condensed consolidated financial statements and the notes thereto as well as in conjunction with our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, or our Annual Report. The three months ended June 30, 2019 and 2018 are referred to as the second quarter of 2019 and 2018, respectively. Unless the context indicates otherwise, all references herein to our company include our wholly owned subsidiary.

PART I – FINANCIAL INFORMATION

Item 1. Financial Statements

EPIZYME, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS (UNAUDITED)
(Amounts in thousands, except per share data)

	June 30, 2019	December 31, 2018
ASSETS		
Current assets:		
Cash and cash equivalents	$ 45,932	$ 86,671
Marketable securities	285,048	153,633
Accounts receivable	13,273	20,067
Prepaid expenses and other current assets	14,106	12,164
Total current assets	358,359	272,535
Property and equipment, net	1,992	2,057
Operating lease assets	10,029	—
Restricted cash and other assets	1,032	909
Total assets	$ 371,412	$ 275,501
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 7,069	$ 4,780
Accrued expenses	17,713	19,700
Current portion of operating lease obligation	2,876	—
Current portion of deferred revenue	6,259	13,300
Other current liabilities	16	53
Total current liabilities	33,933	37,833
Operating lease obligation, net of current portion	7,950	—
Deferred revenue, net of current portion	3,806	3,806
Other long-term liabilities	38	853
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 5,000 shares authorized; 350 shares issued and outstanding (equivalent to 3,500 shares of common stock upon conversion at a 10:1 ratio)	37,432	—
Common stock, $0.0001 par value; 125,000 shares authorized; 91,016 shares and 79,175 shares issued and outstanding, respectively	9	8
Additional paid-in capital	952,524	819,779
Accumulated other comprehensive income (loss)	248	(54)
Accumulated deficit	(664,528)	(586,724)
Total stockholders' equity	325,685	233,009
Total liabilities and stockholders' equity	$ 371,412	$ 275,501

See notes to condensed consolidated financial statements.

EPIZYME, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(UNAUDITED)
(Amounts in thousands, except per share data)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Collaboration revenue	$ 5,900	$ 12,000	$ 13,791	$ 12,000
Operating expenses:				
Research and development	40,907	31,346	67,803	56,968
General and administrative	15,698	10,914	27,684	20,274
Total operating expenses	56,605	42,260	95,487	77,242
Operating loss	(50,705)	(30,260)	(81,696)	(65,242)
Other income, net:				
Interest income, net	2,253	1,143	3,911	2,042
Other (expense) income, net	(13)	(11)	(19)	7
Other income, net	2,240	1,132	3,892	2,049
Net loss	$ (48,465)	$ (29,128)	$ (77,804)	$ (63,193)
Other comprehensive income (loss):				
Unrealized gain (loss) on available-for-sale securities	216	46	302	23
Comprehensive loss	$ (48,249)	$ (29,082)	$ (77,502)	$ (63,170)
Reconciliation of net loss to net loss attributable to common stockholders:				
Net loss	$ (48,465)	$ (29,128)	$ (77,804)	$ (63,193)
Accretion of convertible preferred stock	—	—	(2,940)	—
Net loss attributable to common stockholders	$ (48,465)	$ (29,128)	$ (80,744)	$ (63,193)
Net loss per share attributable to common stockholders - basic and diluted	$ (0.53)	$ (0.42)	$ (1.04)	$ (0.91)
Weighted-average common shares outstanding used in net loss per share attributable to common stockholders - basic and diluted	90,876	69,490	77,315	69,438

See notes to condensed consolidated financial statements.

EPIZYME, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS (UNAUDITED)
(Amounts in thousands)

	Six Months Ended June 30,	
	2019	**2018**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (77,804)	$ (63,193)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	416	582
Stock-based compensation	7,939	6,311
Amortization of discount on investments	(1,759)	(565)
Changes in operating assets and liabilities:		
Accounts receivable	6,794	382
Contract asset	—	(12,000)
Prepaid expenses and other current assets	(1,942)	469
Accounts payable	2,092	3,988
Accrued expenses	(1,972)	619
Deferred revenue	(7,041)	—
Operating lease assets	1,255	—
Operating lease liabilities	(1,290)	—
Other assets	(123)	(18)
Other liabilities	(18)	196
Net cash used in operating activities	(73,453)	(63,229)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of available-for-sale securities	(297,904)	(165,688)
Maturities of available-for-sale securities	168,548	68,334
Purchases of property and equipment	(190)	(109)
Net cash used in investing activities	(129,546)	(97,463)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Payments under capital lease obligation	—	(129)
Proceeds from issuance of common stock, net of commissions	122,992	—
Proceeds from issuance of preferred stock, net of commissions	37,433	—
Proceeds from stock options exercised	1,739	1,604
Proceeds from issuance of shares under employee stock purchase plan	360	459
Payment of public offering costs	(264)	—
Net cash provided by financing activities	162,260	1,934
Net increase (decrease) in cash, cash equivalents and restricted cash	(40,739)	(158,758)
Cash, cash equivalents and restricted cash, beginning of period	87,133	227,126
Cash, cash equivalents and restricted cash, end of period	$ 46,394	$ 68,368
SUPPLEMENTAL CASH FLOW INFORMATION:		
Cash paid for income taxes	$ 45	$ 38
Purchases of property and equipment unpaid at period end	$ 208	$ 88

See notes to condensed consolidated financial statements.

EPIZYME, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDER'S EQUITY
(Amounts in thousands, except share amounts)

	Common Stock		Preferred Stock		Additional Paid-In	Accumulated	Accumulated Other Comprehensive	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Deficit	Income (Loss)	Equity
Balance at December 31, 2017	69,301,691	$ 7	—	$ —	$ 723,510	$ (488,097)	$ (49)	$ 235,371
Cumulative catch up related to the adoption of ASU 2016-09	—	—	—	—	—	25,003	—	25,003
Exercise of stock options and vesting of restricted stock units	152,734	—	—	—	1,500	—	—	1,500
Stock-based compensation	—	—	—	—	2,887	—	—	2,887
Issuance of shares under employee stock purchase plan	31,116	—	—	—	459	—	—	459
Unrealized gain on available for sale securities	—	—	—	—	—	—	(23)	(23)
Net loss	—	—	—	—	—	(34,065)	—	(34,065)
Balance at March 31, 2018	69,485,541	$ 7	—	$ —	$ 728,356	$ (497,159)	$ (72)	$ 231,132
Exercise of stock options and vesting of restricted stock units	9,460	—	—	—	105	—	—	105
Stock-based compensation	—	—	—	—	3,423	—	—	3,423
Unrealized gain on available for sale securities	—	—	—	—	—	—	46	46
Net loss	—	—	—	—	—	(29,128)	—	(29,128)
Balance at June 30, 2018	69,495,001	$ 7	—	$ —	$ 731,884	$ (526,287)	$ (26)	$ 205,578
Balance at December 31, 2018	79,175,380	$ 8	—	—	$ 819,779	$ (586,724)	$ (54)	$ 233,009
Issuance of common stock (net of commissions and offering costs of $284)	11,500,000	1	—	—	122,707	—	—	122,708
Issuance of series A convertible preferred stock, net of commissions and beneficial conversion charge	—	—	350,000	34,492	2,940	—	—	37,432
Accretion of series A convertible preferred stock	—	—	—	2,940	(2,940)	—	—	—
Exercise of stock options and vesting of restricted stock units	89,726	—	—	—	886	—	—	886
Stock-based compensation	—	—	—	—	3,211	—	—	3,211
Issuance of shares under employee stock purchase plan	37,972	—	—	—	360	—	—	360
Unrealized gain on available for sale securities	—	—	—	—	—	—	86	86
Net loss	—	—	—	—	—	(29,339)	—	(29,339)
Balance at March 31, 2019	90,803,078	$ 9	350,000	$ 37,432	$ 946,943	$ (616,063)	$ 32	$ 368,353
Exercise of stock options and vesting of restricted stock units	208,749	—	—	—	853	—	—	853
Stock-based compensation	—	—	—	—	4,681	—	—	4,681
Issuance of shares of common stock in lieu of board fees	3,812	—	—	—	47	—	—	47
Unrealized gain on available for sale securities	—	—	—	—	—	—	216	216
Net loss	—	—	—	—	—	(48,465)	—	(48,465)
Balance at June 30, 2019	91,015,639	$ 9	350,000	$ 37,432	$ 952,524	$ (664,528)	$ 248	325,685

See notes to condensed consolidated financial statements.

1. Overview

Epizyme, Inc. (collectively referred to with its wholly owned, controlled subsidiary, Epizyme Securities Corporation, as "Epizyme" or the "Company") is a late-stage biopharmaceutical company that is committed to rewriting treatment for cancer and other serious diseases through the discovery, development, and commercialization of novel epigenetic medicines. By focusing on the genetic drivers of disease, the Company's science seeks to match targeted medicines with the patients who need them. The Company is developing its lead product candidate, tazemetostat, an oral, first-in-class selective inhibitor of the EZH2 histone methyltransferase, or HMT, in a broad range of cancer types and settings, and developing its novel G9a program, EZM8266, for the treatment of sickle cell disease, or SCD.

Through June 30, 2019, the Company has raised, including amounts received under collaboration agreements, an aggregate of $1,155.1 million to fund its operations, of which $239.6 million was non-equity funding through its collaboration agreements, $839.5 million was from the sale of common stock and series A Convertible Preferred Stock in the Company's public offerings and $76.0 million was from the sale of redeemable convertible preferred stock in private financings prior to the Company's initial public offering in May 2013. As of June 30, 2019, the Company had $331.0 million in cash, cash equivalents and marketable securities.

The Company commenced active operations in early 2008. Since its inception, the Company has generated an accumulated deficit of $664.5 million through June 30, 2019, and will require substantial additional capital to fund its research and development and commercialization plans for tazemetostat, if approved. The Company is subject to risks common to companies in the biotechnology industry, including, but not limited to, risks of failure of clinical trials and preclinical studies, the need to obtain additional financing to fund the future development and commercialization of tazemetostat and the rest of its pipeline, the need to obtain marketing approval for its product candidates, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and ability to transition from clinical-stage manufacturing to commercial-stage production of products.

2. Summary of Significant Accounting Policies

Basis of Presentation

The condensed consolidated financial statements of the Company included herein have been prepared, without audit, pursuant to the rules and regulations of the Securities and Exchange Commission, or the SEC. Certain information and footnote disclosures normally included in financial statements prepared in accordance with accounting principles generally accepted in the United States of America have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these condensed consolidated financial statements should be read in conjunction with the financial statements and notes thereto included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2018, or the Annual Report.

The unaudited condensed consolidated financial statements include the accounts of Epizyme, Inc. and its wholly owned, controlled subsidiary, Epizyme Securities Corporation. All intercompany transactions and balances of subsidiaries have been eliminated in consolidation. In the opinion of management, the information furnished reflects all adjustments, all of which are of a normal and recurring nature, necessary for a fair presentation of the results for the reported interim periods. The Company considers events or transactions that occur after the balance sheet date but before the condensed consolidated financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The three months ended June 30, 2019 and 2018 are referred to as the second quarter of 2019 and 2018, respectively. The results of operations for interim periods are not necessarily indicative of results to be expected for the full year or any other interim period.

Certain reclassifications have been made to prior periods to conform to current period presentation. Reclassification of prior year amounts have been made to present capital lease liability in other current and other long-term liabilities in the consolidated Balance Sheets. There was no impact on total operating expenses or net income (loss) resulting from these reclassifications.

Significant Accounting Policies

During the quarter ended March 31, 2019, the Company adopted Accounting Standards Codification, Topic 842, *Leases*, or ASC 842, using the required modified retrospective approach and utilizing the effective date as its date of initial application, for which prior periods are presented in accordance with previous guidance in ASC 840, Leases, or ASC 840, as referenced below in this Note 2 under *Recently Adopted Accounting Pronouncements*. There were no material changes to the Company's significant accounting policies during the three months ended June 30, 2019, as compared to the significant accounting policies disclosed in Note 2, *Summary of Significant Accounting Policies*, of the Company's financial statements included in the Annual Report.

Going Concern

At each reporting period, the Company evaluates whether there are conditions or events that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the financial statements are issued. The Company is required to make certain additional disclosures if it concludes substantial doubt exists and it is not alleviated by the Company's plans or when its plans alleviate substantial doubt about the Company's ability to continue as a going concern.

The Company's evaluation entails analyzing prospective operating budgets and forecasts for expectations of the Company's cash needs, and comparing those needs to the current cash, cash equivalent and marketable securities balances. After considering the Company's current research and development plans, the building of commercial infrastructure and the timing expectations related to the progress of its programs, and after considering its existing cash, cash equivalents and marketable securities as of June 30, 2019, the Company did not identify conditions or events that raise substantial doubt about the Company's ability to continue as a going concern within one year from the date these financial statements were issued.

Pending Accounting Pronouncements

In June 2016, the Financial Accounting Standards Board, or FASB, issued ASU 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. The FASB has subsequently issued amendments to ASU 2016-13, which will be effective for the Company January 1, 2020. These standards require that credit losses be reported using an expected losses model rather than the incurred losses model that is currently used, and establishes additional disclosures related to credit risks. For available-for-sale securities with unrealized losses, these standards now require allowances to be recorded instead of reducing the amortized cost of the investment. The adoption of ASU 2016-13 is not expected to have a material effect on the Company's consolidated financial statements or disclosures.

In November 2018, the FASB issued ASU 2018-18, *Collaborative Arrangements, or ASC 808,* which clarifies certain transactions between collaborative arrangement participants should be accounted for as revenue when the collaborative arrangement participant is a customer in the context of a unit of account and precludes recognizing as revenue consideration received from a collaborative arrangement participant if the participant is not a customer. The ASU will be effective for the Company in the first quarter of fiscal 2021, with early adoption permitted. A retrospective adoption to the date the Company adopted ASC 606 is required by recognizing a cumulative-effect adjustment to the opening balance or retained earnings of the earliest period presented. The Company is currently evaluating the impact of the adoption of this standard on its financial statements.

Recently Adopted Accounting Pronouncements

Leases

In February 2016, the FASB issued ASU 2016-02, Leases, or ASC 842, which requires lessees to recognize a right-of-use asset and lease liability for most lease arrangements. The new standard is effective for annual reporting periods beginning after December 15, 2018. A modified retrospective transition approach is required to be applied to leases existing as of, or entered into after, the beginning of the earliest comparative period presented in the financial statements, with certain practical expedients available.

Effective January 1, 2019, the Company adopted ASC 842 using the required modified retrospective approach and utilizing the effective date as its date of initial application, for which prior periods are presented in accordance with the previous guidance in ASC 840, Leases, or ASC 840.

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on the unique facts and circumstances present in the arrangement. Most leases with a term greater than one year are recognized on the balance sheet as right-of-use assets and short-term and long-term lease liabilities, as applicable. The Company has elected not to recognize on the balance sheet leases with terms of 12 months or less. The Company typically only includes an initial lease term in its assessment of a lease arrangement. Options to renew a lease are not included in the Company's assessment unless there is reasonable certainty that the Company will renew.

Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of lease payments over the expected remaining lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The interest rate implicit in lease contracts is typically not readily determinable. As a result, the Company utilizes its incremental borrowing rate, which reflects the fixed rate at which the Company could borrow on a collateralized basis the amount of the lease payments in the same currency, for a similar term, in a similar economic environment. In transition to ASC 842, the Company utilized the remaining lease term of its leases in determining the appropriate incremental borrowing rates.

In accordance with ASC 842, components of a lease should be split into three categories: lease components (e.g., land, building, etc.), non-lease components (e.g., common area maintenance, consumables, etc.), and non-components (e.g., property taxes, insurance, etc.).

The fixed and in-substance fixed contract consideration (including any consideration related to non-components) must be allocated based on the respective relative fair values to the lease components and non-lease components.

Although separation of lease and non-lease components is required, certain expedients are available. Entities may elect the practical expedient to not separate lease and non-lease components by class of underlying asset. Rather, entities would account for each lease component and the related non-lease component together as a single component.

In adopting ASC 842, the Company elected to utilize the available package of practical expedients permitted under the transition guidance within the new standard, which does not require the reassessment of the following: i) whether existing or expired arrangements are or contain a lease, ii) the lease classification of existing or expired leases, and iii) whether previous initial direct costs would qualify for capitalization under the new lease standard.

The adoption of this standard resulted in the recognition of operating lease liabilities and right-of-use assets of $11.5 million and $10.7 million, respectively, on the Company's condensed consolidated balance sheet relating to its leases for its corporate headquarters in Cambridge, Massachusetts and other operating leases. The adoption of the standard did not have a material effect on the Company's condensed consolidated statements of operation and comprehensive loss or condensed consolidated statements of cash flows. As of June 30, 2019, the Company recognized operating lease liabilities and right-of-use assets under the new guidance of $10.8 million and $10.0 million, respectively, on the Company's balance sheet.

Compensation

In June 2018, the FASB issued ASU No. 2018-07, *Compensation – Stock Compensation, or ASC 718: Improvements to Nonemployee Share-Based Payment Accounting,* or ASU 2018-07. The guidance in this ASU expands the scope of ASC 718 to include share-based payment transactions for acquiring goods and services from nonemployees. The new standard is effective for annual reporting periods beginning after December 15, 2018, including interim reporting periods within each annual reporting period. The Company adopted ASU 2018-07 as of January 1, 2019. The impact on the Company's condensed consolidated financial statements was not material.

3. Cash

A reconciliation of cash, cash equivalents, and restricted cash reported within the condensed consolidated balance sheets that sum to the total of the same such amounts shown in the condensed consolidated statements of cash flows, is as follows:

	As of June 30,	
	2019	2018
	(In thousands)	
Cash and cash equivalents	$ 45,932	$ 67,906
Restricted cash, as part of other assets	462	462
Total cash, cash equivalents, and restricted cash shown in the consolidated statements of cash flows	$ 46,394	$ 68,368

The $0.5 million in restricted cash relates to a letter of credit as a security deposit for the office and laboratory lease at Technology Square in Cambridge, Massachusetts. The Company has recorded cash held to secure this letter of credit as restricted cash in restricted cash and other assets on the condensed consolidated balance sheet.

4. Marketable Securities

The following table summarizes the available-for-sale securities held at June 30, 2019 (in thousands):

Description	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper	$ 138,975	$ 109	$ —	$ 139,084
Corporate notes	143,825	139	—	143,964
U.S. government agency securities and U.S. treasuries	2,000	—	—	2,000
Total	$ 284,800	$ 248	$ —	$ 285,048

The following table summarizes the available-for-sale securities held at December 31, 2018 (in thousands):

Description	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper	$ 73,110	$ —	$ (22)	$ 73,088
Corporate notes	80,575	—	(30)	80,545
Total	$ 153,685	$ —	$ (52)	$ 153,633

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At June 30, 2019, the balance in the Company's accumulated other comprehensive loss was composed solely of activity related to the Company's available-for-sale marketable securities. There were no realized gains or losses recognized on the sale or maturity of available-for-sale securities during the three months ended June 30, 2019, and as a result, the Company did not reclassify any amounts out of accumulated other comprehensive loss for the same period.

The aggregate fair value of available-for-sale securities held by the Company in an unrealized loss position for less than twelve months as of June 30, 2019 was $9.4 million, which consisted of 1 commercial paper security and 2 corporate notes securities. The aggregate unrealized loss for those securities in an unrealized loss position for less than twelve months as of June 30, 2019 was less than $0.1 million.

The Company does not intend to sell and it is unlikely that the Company will be required to sell the above investments before recovery of their amortized cost bases, which may be maturity. The Company determined that there was no material change in the credit risk of any of its investments. As a result, the Company determined it did not hold any investments with any other-than-temporary impairment as of June 30, 2019. The weighted-average maturity of the Company's portfolio was approximately seven months at June 30, 2019.

5. Fair Value Measurements

The Company's financial instruments as of June 30, 2019 and December 31, 2018 consisted primarily of cash and cash equivalents, marketable securities and accounts receivable and accounts payable. As of June 30, 2019 and December 31, 2018, the Company's financial assets recognized at fair value consisted of the following:

	Fair Value as of June 30, 2019			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$ 37,071	$ 37,071	—	$ —
Marketable securities:				
Commercial paper	139,084	—	139,084	—
Corporate notes	143,964	—	143,964	—
U.S. government agency securities and U.S. treasuries	2,000	—	2,000	
Total	$ 322,119	$ 37,071	$ 285,048	$ —

	Fair Value as of December 31, 2018			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	$ 79,225	$ 50,785	$ 28,440	$ —
Marketable securities:				
Commercial paper	73,088	—	73,088	—
Corporate notes	80,545	—	80,545	—
Total	$ 232,858	$ 50,785	$ 182,073	$ —

Cash equivalents and marketable securities have been initially valued at the transaction price and subsequently valued, at the end of each reporting period, utilizing third-party pricing services or other market observable data.

The Company measures its cash equivalents at fair value on a recurring basis. The Company classifies some of its cash equivalents within Level 1 of the fair value hierarchy because they are valued using observable inputs that reflect quoted prices for identical assets in active markets. The Company measures its marketable securities at fair value on a recurring basis and classifies those instruments and some cash equivalents within Level 2 of the fair value hierarchy. The pricing services used by management utilize industry

standard valuation models, including both income and market based approaches and observable market inputs to determine the fair value of marketable securities and those cash equivalents classified within Level 2 of the fair value hierarchy.

6. Supplemental Balance Sheet Information

Accrued expenses consisted of the following:

	June 30, 2019	December 31, 2018
	(In thousands)	
Employee compensation and benefits	$ 3,871	$ 5,509
Research and development expenses	9,801	11,272
Professional services and other	4,041	2,919
Accrued expenses	$ 17,713	$ 19,700

7. Income Taxes

The Company did not record a federal or state income tax provision or benefit for the three months ended June 30, 2019 and 2018 due to the expected and known loss before income taxes to be incurred, or incurred, as applicable, for the years ended December 31, 2019 and 2018, as well as the Company's continued maintenance of a full valuation allowance against its net deferred tax assets, with the exception of the deferred tax asset related to alternative minimum tax credit.

8. Commitments and Contingencies

There have been no significant changes to the Company's commitments and contingencies in the three and six months ended June 30, 2019, as compared to those disclosed in Note 7, *Commitments and Contingencies*, included in its Annual Report.

9. Leases

The Company enters into lease arrangements for its facilities as well as certain equipment. A summary of the arrangements are as follows:

Operating Leases

The Company leases office and laboratory space at Technology Square in Cambridge, Massachusetts under a Lease Agreement, dated as of June 15, 2012, as amended, or the Lease, with ARE-TECH Square, LLC, a Delaware limited liability company, or Landlord, with a term that originally continued through May 31, 2018, and a Company option to extend the term of the lease at the then-current market rent, as defined in the Lease, through November 30, 2022.

In May 2017, the Company entered into a Third Amendment to Lease, or the Third Amendment, with the Landlord, and a Fourth Amendment to Lease with the Landlord, or the Fourth Amendment, and, together with the Third Amendment, the Amendments.

Under the Amendments, the Company extended the term of the lease to November 30, 2022 but retained the right to terminate the Lease, effective as of December 31, 2018, by giving written notice to the Landlord by December 31, 2017 and paying an early termination fee. The Company did not exercise this right. Under the Lease as amended, the Company has agreed to pay a monthly base rent of approximately $0.2 million for the period commencing December 1, 2017 through May 31, 2018, with an increase on June 1, 2018 of approximately $33,000 and annual increases of approximately $9,000 on December 1 of each subsequent year until December 1, 2021.

The Company has a $0.5 million letter of credit as a security deposit for this lease and has recorded cash held to secure this letter of credit as restricted cash and other assets on the consolidated balance sheet. In applying the ASC 842 transition guidance, the Company determined the classification of this lease to be operating and recorded a lease liability and a right-of-use asset on the ASC 842 effective date.

In addition, the Company has a capital lease related to computer hardware equipment, an operating lease for storage space in Colorado and an operating lease for office space in North Carolina. In applying the ASC 842 transition guidance, the Company determined the classification of the storage space and office space as operating leases and recorded lease liabilities and right-of-use assets on the ASC 842 effective date.

The Company is required to pay certain variable costs to the Landlord in addition to fixed rent. These costs include common area maintenance, real estate taxes, and parking.

The following table contains a summary of the lease costs recognized under Topic 842 and other information pertaining to the Company's operating leases for the three and six months ended June 30, 2019:

	Three Months Ended June 30, 2019	Six Months Ended June 30, 2019
	(In thousands)	
Lease cost		
Operating lease cost	$ 889	$ 1,777
Variable lease cost	305	628
Total lease cost	$ 1,194	$ 2,405
Other information		
Operating cash flows used for operating leases	$ 907	$ 1,812
Weighted average remaining lease term	3.4 years	3.4 years
Weighted average discount rate	8.55%	8.55%

Future minimum lease payments under the Company's non-cancelable operating leases as of June 30, 2019, are as follows:

	2019
	(In thousands)
2019	$ 1,825
2020	3,729
2021	3,622
2022	3,340
Thereafter	—
Total lease payments	$ 12,516
Less: imputed interest	(1,690)
Total operating lease liabilities at June 30, 2019	$ 10,826

10. Collaborations

Celgene

In April 2012, the Company entered into a collaboration and license agreement with Celgene Corporation, or Celgene. On July 8, 2015, the Company entered into an amendment and restatement of the collaboration and license agreement with Celgene.

Original Agreement Structure

Under the original agreement, the Company granted Celgene an exclusive license, for all countries other than the United States, to small molecule HMT inhibitors targeting the DOT1L HMT, including pinometostat, and an option, on a target-by-target basis, to exclusively license, for all countries other than the United States, rights to small molecule HMT inhibitors targeting any HMT targets, other than the EZH2 HMT, including tazemetostat, and targets covered by the Company's collaboration and license agreement dated January 8, 2011 with GlaxoSmithKline, or GSK. Under the original agreement, Celgene's option was exercisable during an option period that would have expired on July 9, 2015.

Under the original agreement, the Company received a $65.0 million upfront payment and $25.0 million from the sale of its series C redeemable convertible preferred stock to an affiliate of Celgene, of which $3.0 million was considered a premium and included as collaboration arrangement consideration for a total upfront payment of $68.0 million. In addition, the Company has received a $25.0 million clinical development milestone payment and $7.0 million of global development co-funding through June 30, 2019. The Company was also eligible to receive $35.0 million in an additional clinical development milestone payment and up to $100.0 million in regulatory milestone payments related to DOT1L as well as up to $65.0 million in payments, including a combination of clinical development milestone payments and an option exercise fee for each available target to which Celgene had the right to exercise its option during an initial option period that would have ended in July 2015 but was extended pursuant to the amended and restated agreement as discussed below under "Amended and Restated Agreement Structure" (each a "selected target"), and up to $100.0 million in regulatory milestone payments for each selected target. As to DOT1L and each selected target, the Company retained all product rights in the United States and was eligible to receive royalties for each target at defined percentages ranging from the mid-single digits to the mid-teens on net product sales outside of the United States subject to reduction in specified circumstances.

The Company was obligated to conduct and solely fund research and development costs of the Phase 1 clinical trials for pinometostat. For all remaining DOT1L program development costs, Celgene and the Company were to equally co-fund global development and each party was to solely fund territory-specific development costs for its territory.

Amended and Restated Agreement Structure

Under the amended and restated collaboration and license agreement:

- Celgene retained its exclusive license to small molecule HMT inhibitors targeting DOT1L, including pinometostat,
- Celgene's other option rights were narrowed to small molecule HMT inhibitors targeting three predefined targets, or the Option Targets,
- The exclusive licenses to HMT inhibitors targeting two of the Option Targets that Celgene may acquire were expanded to include the United States, with the exclusive license to HMT inhibitors targeting the third Option Target continuing to be for all countries other than the United States,
- Celgene's option period was extended for each of the Option Targets and Celgene's option is exercisable at the time of the Company's investigational new drug application, or IND, filing for an HMT inhibitor targeting the applicable Option Target, upon the payment by Celgene at such time of a pre-specified development milestone-based license payment,
- Celgene's license may be maintained beyond the end of Phase 1 clinical development for each of the Option Targets, upon payment by Celgene at such time of a pre-specified development milestone-based license payment, and
- The Company's research and development obligations with respect to each Option Target under the amended and restated agreement were extended for at least an additional three years, subject to Celgene exercising its option with respect to such Option Target at IND filing. Subject to the Company's opt-out rights, the Company's research and development obligations were expanded to include the completion of a Phase 1 clinical trial as to each Option Target following Celgene's exercise of its option at IND filing.

Under the amended and restated agreement, the Company received a $10.0 million upfront payment in exchange for the Company's extension of Celgene's option rights to the Option Targets and the Company's research and development obligations. In addition, the Company is eligible to earn an aggregate of up to $75.0 million in development milestones and license payments, up to $365.0 million in regulatory milestone payments and up to $170.0 million in sales milestone payments related to the three Option Targets. The Company is also eligible to receive royalties on each of the Option Targets as specified in the amended and restated agreement. The Company is also eligible to earn $35.0 million in an additional clinical development milestone payment and up to $100.0 million in regulatory milestone payments related to DOT1L. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or royalty payments from Celgene. Due to the varying stages of development of each target, the Company is not able to determine the next milestone that might be earned, if any.

The amended and restated agreement eliminated the right of first negotiation that the Company had granted to Celgene under the original agreement with respect to business combination transactions that the Company may desire to pursue with third parties.

The Company is primarily responsible for the research strategy under the collaboration. During each applicable option period the Company is required to use commercially reasonable efforts to carry out a mutually agreed-upon research plan for each Option Target. Subject to the Company's opt-out right for the DOT1L target and each of the Option Targets, the Company is required to conduct and solely fund development costs of the Phase 1 clinical trials for HMT inhibitors directed to such targets, including for pinometostat. After the completion of Phase 1 development, as to DOT1L and the Option Target for which the Company retains U.S. rights, Celgene and the Company will equally co-fund global development and each party will solely fund territory-specific development costs for its respective territory; and, as to the other two Option Targets, after the completion of Phase 1 development, Celgene will solely fund all development costs on a worldwide basis.

Accounting Considerations of the Amended and Restated Agreement

The Company assessed the amended arrangement in accordance with ASC 606 and concluded that the contract counterparty, Celgene, is a customer based on the arrangement structure, through the satisfaction of each target's performance obligations. As of the amendment, the Company identified the following performance obligations under the arrangement, whether satisfied or not:

- an exclusive license to small molecule HMT inhibitors targeting DOT1L, including pinometostat, combined with pre-IND research services for DOT1L;
- post-IND research and development services for DOT1L through a Phase 1 clinical trial;
- pre-IND research services for each Option Target; and
- material rights related to each of Celgene's options at the time of an IND filing to license HMT inhibitors targeting each Option Target.

The Company determined that the DOT1L license and pre-IND research and development activities for DOT1L were not distinct from one another, due to the limited economic benefit that Celgene would derive from the DOT1L license if it did not obtain the research services. After IND effectiveness, the Company concluded that the DOT1L license would be distinct apart from any remaining research and development services because Celgene, or other market participants, would have the ability to execute human clinical trials on the identified compound. Accordingly, the DOT1L license and pre-IND research services for DOT1L were accounted for as a combined performance obligation. The post-IND research and development services for DOT1L have been accounted for as a separate performance obligation.

The pre-IND research services for each Option Target were the only performance obligations not subject to the exercise of a customer option at the time of the amendment for each Option Target and therefore represent three separate performance obligations (one for each Option Target).

The Company evaluated the option rights at the time of an IND filing to determine whether they provide Celgene with material rights. The Company concluded that the options were issued at a discount, and therefore provide material rights. As such, the option rights at the time of an IND filing for each Option Target represent three separate performance obligations (one for each Option Target) as of the amendment of the arrangement. The license to each HMT inhibitor targeting each respective Option Target, the Company's research and development obligations through the completion of a Phase 1 clinical trial for each Option Target, and the option to maintain the license beyond the end of Phase 1 clinical development for each Option Target are all subject to Celgene's exercise of the option rights at the time of an IND filing and, therefore, are not considered performance obligations as of the amendment.

Under the agreement, the Company determined that the total transaction price was $103.0 million as of the amendment of the arrangement, comprised the following:

- $68.0 million total upfront payment received under the original agreement, as described above;
- $25.0 million clinical development milestone payment for DOT1L; and
- $10.0 million upfront payment under the amended and restated agreement.

The option exercise fees of $75.0 million in the aggregate, for the options at the time of IND and completion of Phase 1, that may be received are excluded from the transaction price until each customer option is exercised. The future potential milestone payments were excluded from the transaction price, as all milestone amounts were fully constrained. The Company will reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

The transaction price was allocated to the performance obligations based on the estimated stand-alone selling prices at the time of the amendment. For the DOT1L performance obligation that includes the license and pre-IND research services, the stand-alone selling price was determined considering the stage and status of the program and the technology involved and the level of development expected, as well as the expected cost and margin for the research services. For the post-IND research and development services for DOT1L and the pre-IND research services for each Option Target, the stand-alone selling price was determined considering the expected cost and a reasonable margin for the respective services. The material rights from the option rights at the time of an IND filing for each Option Target were valued based on the estimated discount at which the option is priced and the Company's estimated probability of the options' exercise as of the time of the amendment. The Company believes that a change in the assumptions used to determine its stand-alone selling price for the performance obligations most likely would not have a significant effect on the allocation of consideration received (or receivable) to the performance obligations that were not satisfied as of the adoption of ASC 606.

The Company allocated the following amounts of the total transaction price to the performance obligations as of the amendment date:

- $65.1 million, including the $25.0 million clinical development milestone payment for DOT1L, to the two DOT1L performance obligations, which were satisfied prior to the ASC 606 adoption date;
- $34.1 million to the three Pre-IND research services performance obligations related to the Option Targets, which were substantially satisfied as of the ASC 606 adoption date; and
- $3.8 million to the three material rights related to Celgene's option rights at the time of an IND filing for each Option Target, which shall not be satisfied until the option is exercised or one of the parties opts out of the arrangement.

All performance obligations, except for the three material rights were substantially satisfied as of the adoption of ASC 606 and therefore all of the transaction price allocated to those performance obligations has been recognized as revenue under ASC 606. Through June 30, 2019, the Company has recognized revenue of $99.2 million under the agreement as collaboration revenue in the Company's consolidated statements of operations and comprehensive loss and in accumulated deficit as a result of the cumulative-effect recognition upon adoption of ASC 606. The amounts received that have not yet been recognized as revenue, related to the material rights, are recorded in deferred revenue on the Company's condensed consolidated balance sheet. Deferred revenue related to the agreement amounted to $3.8 million as of June 30, 2019, all of which is included in noncurrent liabilities.

GSK

In January 2011, the Company entered into a collaboration and license agreement with GSK, to discover, develop and commercialize novel small molecule HMT inhibitors directed to available targets from the Company's platform. Under the terms of the agreement, the Company granted GSK exclusive worldwide license rights to HMT inhibitors directed to three targets. Additionally, as part of the research collaboration, the Company agreed to provide research and development services related to the licensed targets pursuant to agreed upon research plans during a research term that ended January 8, 2015. In March 2014, the Company and GSK amended certain terms of this agreement for the third licensed target, revising the license terms with respect to candidate compounds and amending the corresponding financial terms, including reallocating milestone payments and increasing royalty rates as to the third target. Subsequent to a GSK strategic portfolio prioritization, the Company received notice in October 2017 that GSK terminated the agreement with respect to the third target, effective December 31, 2017, which returned all rights to that target to the Company. The two other targets, PRMT5 and PRMT1, continue to be subject to the agreement and were not impacted by the termination with respect to the third target. The Company substantially completed all research obligations under this agreement by the end of the first quarter of 2015 and completed the transfer of the remaining data and materials for these programs to GSK in the second quarter of 2015.

Agreement Structure

Under the agreement, the Company has received and recognized as collaboration revenue a $20.0 million upfront payment, a $3.0 million payment upon the execution of the March 2014 agreement amendment, $6.0 million of fixed research funding, $9.0 million for research and development services and $51.0 million of preclinical and research and development milestone payments.

The preclinical and research and development milestone payments total includes a $10.0 million milestone payment earned in May 2017 related to the second target in the collaboration, upon GSK's initiation of good laboratory practices toxicology studies, as well as a $6.0 million clinical milestone following GSK's initiation of patient dosing in a Phase 1 clinical trial of a PRMT5 inhibitor that the Company discovered and licensed to GSK. In 2018, the Company recognized a $12.0 million milestone based on the Company's determination that it was earned in 2018 relating to the first dosing of a patient in a Phase 2 clinical trial of GSK3326595, a PRMT5 inhibitor discovered by us and licensed to GSK under the collaboration agreement, as well as a $8.0 million milestone payment earned in 2018 relating to the initiation of a patient dosing in a Phase 1 clinical trial of GSK3368715, a PRMT1 inhibitor discovered by us and licensed to GSK under the collaboration agreement. As of June 30, 2019, for the two remaining targets, the Company is eligible to receive up to $50.0 million in clinical development milestone payments, up to $197.0 million in regulatory milestone payments and up

to $128.0 million in sales-based milestone payments. As a result of the termination of the agreement as it relates to the third target, the Company will receive no additional payments related to that target. In addition, GSK is required to pay the Company royalties, at percentages from the mid-single digits to the low double-digits, on a licensed product-by-licensed product basis, on worldwide net product sales, subject to reduction in specified circumstances. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or royalty payments from GSK. GSK became solely responsible for development and commercialization for each licensed target in the collaboration when the research term ended on January 8, 2015.

Collaboration Revenue

Through June 30, 2019, the Company has earned a total of $89.0 million under the GSK agreement, which the Company recognized as collaboration revenue in the condensed consolidated statements of operations and comprehensive loss. The Company has a $12.0 million receivable as of June 30, 2019, under this agreement as a result of the achievement of a milestone in 2018. The receivable is overdue and the Company is continuing to work with GSK on collection. The Company continues to assess that it is probable that the receivable will be collected. The Company did not have any deferred revenue related to this agreement as of June 30, 2019 or June 30, 2018 and any future revenues will relate to milestone payments and royalties received under the agreement with respect to the two remaining targets, if any.

Eisai

In April 2011, the Company entered into a collaboration and license agreement with Eisai Co. Ltd., or Eisai, under which the Company granted Eisai an exclusive worldwide license to its small molecule HMT inhibitors directed to the EZH2 HMT, including the Company's product candidate tazemetostat, while retaining an opt-in right to co-develop, co-commercialize and share profits with Eisai as to licensed products in the United States.

As of December 31, 2014, the Company had completed its performance obligations under the original agreement.

In March 2015, the Company entered into an amended and restated collaboration and license agreement with Eisai, under which the Company reacquired worldwide rights, excluding Japan, to its EZH2 program, including tazemetostat. Under the amended and restated agreement, the Company is responsible for global development, manufacturing and commercialization outside of Japan of tazemetostat and any other EZH2 product candidates, with Eisai retaining development and commercialization rights in Japan, as well as a right to elect to manufacture tazemetostat and any other EZH2 product candidates in Japan and waived the right of first negotiation for the rest of Asia.

Under the original agreement, Eisai was solely responsible for funding all research, development and commercialization costs for EZH2 compounds. Under the amended and restated agreement, the Company is solely responsible for funding global development, manufacturing and commercialization costs for EZH2 compounds outside of Japan, including the remaining development costs due under a companion diagnostic agreement with Roche Molecular Systems Inc., or Roche Molecular, and Eisai is solely responsible for funding Japan-specific development and commercialization costs for EZH2 compounds.

The Company recorded the reacquisition of worldwide rights, excluding Japan, to the EZH2 program, including tazemetostat, under the amended and restated agreement with Eisai as an acquisition of an in-process research and development asset. As this asset was acquired without corresponding processes or activities that would constitute a business, had not achieved regulatory approval for marketing and, absent obtaining such approval, had no alternative future use, the Company recorded the $40.0 million upfront payment made to Eisai in March 2015 as research and development expense in the consolidated statements of operations and comprehensive loss. The Company has also agreed to pay Eisai up to $20.0 million in clinical development milestone payments, including a $10.0 million milestone upon the earlier of initiation of a first phase 3 clinical trial of any EZH2 product or the first submission of an NDA or Market Authorization Application, or MAA, up to $50.0 million in regulatory milestone payments, including a $25.0 million milestone payment upon regulatory approval of the first NDA or MAA, and royalties at a percentage in the mid-teens on worldwide net sales of any EZH2 product, excluding net sales in Japan. The Company is eligible to receive from Eisai royalties at a percentage in the mid-teens on net sales of any EZH2 product in Japan. In the second quarter of 2019, the Company submitted its first NDA to the U.S. Food and Drug Administration, or FDA, for the treatment of patients with epithelioid sarcoma, triggering the payment of the $10 million clinical development milestone to Eisai and the recording of this amount to research and development expense. The Company paid the $10.0 million clinical development milestone to Eisai in June 2019. During the three and six months ended June 30, 2019, Eisai purchased drug product from the Company at cost to facilitate development within Japan under the collaboration agreement and the Company recognized approximately $1.3 million and $2.3 million, respectively, as a reduction to research and development expense.

LYSA

In May 2016, the Company entered into a collaboration agreement with the Lymphoma Academic Research Organisation, or LYSARC, for the first planned combination trial of tazemetostat. LYSARC is the operational arm of the Lymphoma Study Association, or LYSA, a premier cooperative group in France dedicated to clinical and translational research for lymphoma. This

Phase 1b/2 study is evaluating tazemetostat in combination with R-CHOP, the standard of care first line combination treatment for diffuse large B-cell lymphoma, or DLBCL, as a first line treatment in elderly, high-risk patients with DLBCL and is being sponsored by LYSARC. LYSA is managing the study operations for the trial, and the Company is recognizing its share of the related expenses as those costs are incurred over the duration of the trial. In addition, the Company is planning an expansion of this trial to include a cohort of patients with high-risk front-line FL.

Genentech

In June 2016, the Company entered into a collaboration agreement with Genentech Inc., or Genentech, a member of the Roche Group, to conduct a Phase 1b clinical trial to investigate the anti-cancer effects of the Company's EZH2 inhibitor, tazemetostat, and Genentech's anti-PD-L1 cancer immunotherapy, atezolizumab, when used in combination. The trial is evaluating this combination regimen for the treatment of patients with relapsed or refractory DLBCL. Under the agreement, each company is supplying its respective anti-cancer agent to support the trial and sharing equally in the trial costs. Genentech is managing the study operations for the trial, and the Company is recognizing its share of the related expenses as those costs are incurred over the duration of the trial.

In June 2017, the Company announced an expansion of the clinical collaboration with Genentech to investigate the combination of tazemetostat with atezolizumab in a Phase 1b/2 clinical trial for the treatment of patients with relapsed or refractory metastatic non-small cell lung cancer, or NSCLC. The trial will be part of MORPHEUS, Genentech's open-label, multi-center, randomized umbrella trial evaluating the efficacy and safety of multiple immunotherapy-based treatment combinations for metastatic NSCLC. This trial was initiated at the end of 2017, but before patients had been enrolled in the study, recruitment was halted due to the partial hold placed on tazemetostat studies by the FDA in April 2018 following a safety report from one patient in the dose-ranging portion of the Phase 1 study who developed a secondary case of T-cell lymphoblastic lymphoma, or T-LBL. Due to the hold and strategic reprioritizations, in early 2019 the companies announced that they jointly opted not to move forward with the NSCLC combination study.

Roche Molecular

In December 2012, Eisai and the Company entered into an agreement with Roche Molecular under which Eisai and the Company engaged Roche Molecular to develop a companion diagnostic to identify patients who possess certain activating mutations of EZH2. In October 2013, this agreement was amended to include additional mutations in EZH2. The development costs due under the amended agreement with Roche Molecular were the responsibility of Eisai until the execution of the amended and restated collaboration and license agreement with Eisai in March 2015, at which time the Company assumed responsibility for the remaining development costs due under the agreement. In December 2015, the Company entered into a second amendment to the companion diagnostic agreement with Roche Molecular. The agreement was further amended in March 2018. Under the amended agreement, the Company is responsible for remaining development costs of $10.4 million due under the agreement and Eisai has agreed to reimburse the Company $0.9 million of this amount related to a regulatory milestone for Japan. As of June 30, 2019, the Company is responsible for the remaining development costs of $4.9 million due under the agreement. The Company expects the remaining development costs under the amended agreement to be incurred and paid through 2020.

Under the agreement with Roche Molecular, Roche Molecular is obligated to use commercially reasonable efforts to develop and to make commercially available the companion diagnostic. Roche Molecular has exclusive rights to commercialize the companion diagnostic.

The agreement with Roche Molecular will expire when the Company is no longer developing or commercializing tazemetostat. The Company may terminate the agreement by giving Roche Molecular 90 days' written notice if the Company discontinues development and commercialization of tazemetostat or determines, in conjunction with Roche Molecular, that the companion diagnostic is not needed for use with tazemetostat. Either the Company or Roche Molecular may also terminate the agreement in the event of a material breach by the other party, in the event of material changes in circumstances that are contrary to key assumptions specified in the agreement or in the event of specified bankruptcy or similar circumstances. Under specified termination circumstances, Roche Molecular may become entitled to specified termination fees.

Boehringer Ingelheim

In November 2018, the Company entered into a collaboration and license agreement with Boehringer Ingelheim International GmbH, or Boehringer Ingelheim, to discover, research, develop and commercialize small molecule compounds that are inhibitors of an undisclosed histone acetyl transferase, or HAT, target and an undisclosed helicase target, along with associated predictive biomarkers, or the Target Projects. Under the terms of the agreement, the Company granted to Boehringer Ingelheim an exclusive, world-wide license to the undisclosed target inhibitors technology. The agreement also includes reciprocal licenses to utilize each other's know-how, patents and technologies for activities under the agreement. Further, each party is granted the license to develop, manufacture, commercialize and otherwise exploit any compound or product that successfully achieves start of lead optimization, or SoLO. The Company is also obligated to provide research and development services through SoLO approval for both Target Projects, and to serve on the Joint Steering Committee throughout the contractual term of the contract. The parties will jointly research and develop the first target program and will share commercialization activities within the United States. Boehringer Ingelheim will assume responsibility for commercialization outside of the United States. Boehringer Ingelheim is responsible for worldwide development and commercialization of the second target program.

Agreement Structure

Under the terms of the agreement, the Company received a $15.0 million upfront payment and $1.3 million in research funding for the costs to be incurred by the Company in connection with its research activities. As of June 30, 2019, $3.7 million in research funding will be received in the remainder of 2019, payable quarterly in three equal installments. At its discretion, Boehringer Ingelheim has the option to extend the research period by up to one year, subject the Company's agreement to the specified research activities and additional research funding. The Company is eligible to receive up to $80.5 million in clinical development milestone payments, up to $106.5 million in regulatory milestone payments and up to $93.5 million in sales-based milestone payments. In addition, Boehringer Ingelheim is required to pay the Company tiered royalties, on a product by product, and country by country basis, at percentages ranging from the mid-single digits to low-double digits. Royalties will be payable on net product sales for therapies directed at the second target both in the United States and the rest of the world and net product sales outside of the United States for therapies directed at the first target.

During the six months ended June 30, 2019, it became probable that a significant reversal of cumulative revenue would not occur for a $5.5 million development milestone for selection of a lead optimization candidate for the shared program targeting enzymes within helicase families under the agreement. In the second quarter of 2019, we achieved the milestone and received $5.5 million from Boehringer Ingelheim and the associated consideration was added to the estimated transaction price, which will be recognized over the remaining performance period through December 31, 2019.

The next potential milestone payment that the Company might be entitled to receive under this agreement is a $5.5 million milestone, for the second Target Project, for the SoLO Approval for a compound, as defined in the agreement. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone or royalty payments from Boehringer Ingelheim.

Accounting Considerations of the Agreement

The Company assessed the arrangement in accordance with ASC 606 and concluded that the contract counterparty, Boehringer Ingelheim, is a customer based on the arrangement structure, through the satisfaction of each target's performance obligations. The Company identified the following performance obligations under the arrangement:

- the combination of the Epizyme license to the first undisclosed target inhibitor technology, and associated research and development services through the research period; and,
- the combination of the Epizyme license to the second undisclosed target inhibitor technology, associated research and development services through the research period.

The Company determined that each Epizyme license was not distinct from the associated research and development services due to the limited economic benefit that Boehringer Ingelheim would derive from the Epizyme license if the research services were not provided by the Company. Accordingly, the Epizyme licenses and associated research and development services, for each Target Project, are each accounted for as a combined performance obligation.

Under the agreement, the Company determined as of June 30, 2019 that the total transaction price is $25.5 million, comprised of the following:

- $15.0 million total upfront payment received under the agreement;
- $5.0 million research funding payment to be received in 2019; and

- $5.5 million development milestone for selection of a lead optimization candidate for the shared program targeting enzymes within helicase families.

The future potential milestone payments are excluded from the transaction price, as the achievement of the milestone events are highly uncertain. As such, all milestone payments are fully constrained. The Company will reevaluate the transaction price at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur, and, if necessary, adjust its estimate of the transaction price.

The Company determined that a 50/50 allocation of transaction price between the two performance obligations is appropriate considering the following factors: (i) the standalone selling price of research and development components, estimated using the cost plus margin approach; and based on cost plus 10%; (ii) the license rights granted for each program (world-wide or ex-US only) and their potential market opportunities; (iii) the total potential milestone payments for each program; and (iv) the expected revenue recognition pattern for each program, which is expected to be relatively consistent. Therefore, $10.0 million is allocated to the first undisclosed target license and associated research services and $10.0 million is allocated to the second undisclosed target license and associated research services and will be recognized through December 31, 2019.

The development milestones, will be allocated to each performance obligation as described in the contract. The milestone payments are defined by program and are directly attributable to distinct achievements in each program. The recognition of revenue for each milestone will be based on progress to date in satisfying the applicable performance obligation. During the six months ended June 30, 2019, the Company allocated the $5.5 million development milestone for selection of a lead optimization candidate for the shared program targeting enzymes within helicase families to the first Target Project.

Collaboration Revenue

Through June 30, 2019, the Company has recognized $15.5 million in total collaboration revenue under its agreement with Boehringer Ingelheim including $5.9 million and $13.8 million in the three and six months ended June 30, 2019. As of June 30, 2019, the Company had deferred revenue of $6.3 million related to this agreement.

The Company will reevaluate the likelihood of achieving future milestones at the end of each reporting period. If the performance obligations have not been satisfied at the point at which the risk of significant revenue reversal is resolved, the transaction price will be adjusted and a cumulative catch up based on performance to date will be recorded. If performance obligations have been satisfied, the milestone revenue from the arrangement will be recognized as revenue in the period the risk of significant reversal is relieved.

11. Convertible Preferred Stock

On March 6, 2019, the Company entered into an Underwriting Agreement, or the Preferred Stock Agreement, that related to the public offering of 350,000 shares of Series A Convertible Preferred Stock, par value of $0.001 per share, or Series A Preferred Stock, for a purchase price to the public of $115.00 per share. All of the Series A Preferred Stock was sold by the Company for net proceeds of $37.4 million.

Upon issuance, each share of Series A Preferred Stock included an embedded beneficial conversion feature because the market price of the Company's common stock on the date of issuance of the Series A Preferred Stock was $12.34 per share. As a result, the Company recorded the intrinsic value of the beneficial conversion feature of $2.9 million as a discount on the Series A Preferred at issuance. Because the Series A Preferred Stock is immediately convertible upon issuance and does not include mandatory redemption provisions, the discount on the Series A Preferred Stock was immediately accreted.

The Company evaluated the Series A Preferred Stock for liability or equity classification in accordance with the provisions of ASC 480, Distinguishing Liabilities from Equity, and determined that equity treatment was appropriate because the Series A Preferred Stock did not meet the definition of the liability instruments defined thereunder for convertible instruments. Specifically, the Series A Preferred Stock is not mandatorily redeemable and does not embody an obligation to buy back the shares outside of the Company's control in a manner that could require the transfer of assets. Additionally, the Company determined that the Series A Preferred Stock would be recorded as permanent equity, not temporary equity, based on the guidance of ASC 480 given that the holders of equally and more subordinated equity would be entitled to also receive the same form of consideration upon the occurrence of the event that gives rise to the redemption or events of redemption are within the control of the company.

Voting Rights

Shares of Series A Preferred Stock will generally have no voting rights except as required by law and except that the consent of the holders of a majority of our outstanding shares of Series A Preferred Stock will be required to amend the terms of the Series A Preferred Stock or take certain other actions with respect to the Series A Preferred Stock.

Dividends

Shares of Series A Preferred Stock will be entitled to receive dividends equal to (on an as-if-converted-to-common stock basis), and in the same form and manner as, dividends actually paid on shares of the Company's common stock.

Liquidation Rights

Subject to the prior and superior rights of the holders of any senior securities of the Company, upon liquidation, dissolution or winding up of the Company, whether voluntary or involuntary, each holder of shares of Series A Preferred Stock shall be entitled to receive, in preference to any distributions of any of the assets or surplus funds of the Company to the holders of common stock, an amount equal to $0.001 per share of Series A Preferred Stock, plus an additional amount equal to any dividends declared but unpaid on such shares, before any payments shall be made or any assets distributed to holders of any class of common stock.

If, upon any such liquidation, dissolution or winding up of the Company, the assets of the Company shall be insufficient to pay the holders of shares of the Series A Preferred Stock the amount required under the preceding sentence, then all remaining assets of the Company shall be distributed ratably to holders of the shares of the Series A Preferred Stock in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

Conversion

Each share of Series A Preferred Stock shall be convertible, at any time and from time to time from and after the issuance date, at the option of the holder thereof, into a number of shares of common stock equal to 10 shares of common stock, provided that the holder will be prohibited from converting Series A Preferred Stock into shares of the Company's common stock if, as a result of such conversion, the holder, together with its affiliates and attribution parties, would own more than 9.99% of the total number of shares of common stock then issued and outstanding. The holder can change this requirement to a higher or lower percentage, not to exceed 9.99% of the number of shares of common stock outstanding, upon 61 days' notice to the Company.

Redemption

The Company is not obligated to redeem or repurchase any shares of Series A Preferred Stock. Shares of Series A Preferred Stock are not entitled to any redemption rights or mandatory sinking fund or analogous fund provisions.

12. Stock-Based Compensation

Total stock-based compensation expense related to stock options, restricted stock units, shares issued under the employee stock purchase plan, and shares granted to non-employee directors in lieu of board fees was $4.7 million and $3.4 million for the three months ended June 30, 2019 and 2018, respectively, and $7.9 million and $6.3 million for the six months ended June 30, 2019 and 2018, respectively.

Stock-based compensation expense is classified in the condensed consolidated statements of operations and comprehensive loss as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
	(In thousands)		(In thousands)	
Research and development	$ 1,732	$ 1,222	$ 2,897	$ 2,346
General and administrative	2,996	2,202	5,042	3,965
Total	$ 4,728	$ 3,424	$ 7,939	$ 6,311

Stock Options

The weighted-average grant date fair value of options, estimated as of the grant date using the Black-Scholes option pricing model, was $8.56 and $10.08 per option for those options granted during the three months ended June 30, 2019 and 2018, respectively, and $6.57 and $10.34 per option for those options granted during the six months ended June 30, 2019 and 2018, respectively. Key assumptions used to apply this pricing model were as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
Risk-free interest rate	2.0%	2.8%	2.4%	2.6%
Expected life of options	6.0 years	6.0 years	6.0 years	6.0 years
Expected volatility of underlying stock	71.3%	71.9%	71.8%	71.5%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%

The following is a summary of stock option activity for the six months ended June 30, 2019:

	Number of Options	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
	(In thousands)		(In years)	(In thousands)
Outstanding at December 31, 2018	5,153	$ 14.48		
Granted	3,011	10.16		
Exercised	(203)	8.57		
Forfeited or expired	(666)	14.42		
Outstanding at June 30, 2019	7,295	$ 12.87	8.32	$ 11,818
Exercisable at June 30, 2019	2,446	$ 15.53	6.74	$ 2,852

As of June 30, 2019, there was $33.3 million of unrecognized compensation cost related to stock options that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 2.97 years.

Restricted Stock Units

As of June 30, 2019, 238,166 restricted stock units, or RSUs, were granted to executives. The awards granted to executives are service-based. Assuming all service conditions are achieved, 25% of the RSUs would vest annually for four years.

	Number of Service Based RSU Shares (in thousands)	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2018	—	$ —
Granted	238	9.47
Vested	—	—
Forfeited	—	—
Outstanding at June 30, 2019	238	$ 9.47

Compensation expense totaling $0.2 million was recognized for the service-based RSUs for the six months ended June 30, 2019.

As of June 30, 2019, there was $1.8 million of unrecognized compensation cost related to service-based RSUs that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 3.6 years.

As of June 30, 2019, the Company granted 483,400 RSUs to executives and employees. The awards granted are performance-based. Assuming all performance conditions are achieved, 20% of the RSUs would vest on June 30, 2019, 30% would vest on December 31, 2019, 20% would vest on March 31, 2020, and the remaining 30% of the RSUs would vest on September 30, 2020.

	Number of Performance Based RSU Shares (in thousands)	Weighted Average Grant Date Fair Value
Outstanding at December 31, 2018	—	$ —
Granted	483	12.14
Vested	(95)	12.14
Forfeited	(10)	11.94
Outstanding at June 30, 2019	378	$ 12.15

Compensation expense totaling $1.2 million was recognized for the performance-based RSUs for the six months ended June 30, 2019.

There was $4.7 million of unrecognized compensation cost related to performance-based RSUs that are expected to vest as of June 30, 2019.

As of June 30, 2019, there were 616,486 RSUs outstanding.

13. Loss Per Share

Basic and diluted loss per share allocable to common stockholders are computed as follows:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
	(In thousands except per share data)		(In thousands except per share data)	
Net loss	$ (48,465)	$ (29,128)	$ (77,804)	$ (63,193)
Accretion of convertible preferred stock	—	—	(2,940)	—
Net loss attributable to common stockholders	$ (48,465)	$ (29,128)	$ (80,744)	$ (63,193)
Weighted average shares outstanding	90,876	69,490	77,315	69,438
Basic and diluted loss per share allocable to common stockholders	$ (0.53)	$ (0.42)	$ (1.04)	$ (0.91)

The following common stock equivalents were excluded from the calculation of diluted loss per share allocable to common stockholders because their inclusion would have been anti-dilutive:

	Three Months Ended June 30,		Six Months Ended June 30,	
	2019	2018	2019	2018
	(In thousands)		(In thousands)	
Stock options	7,295	5,818	7,295	5,818
Restricted stock units	616	—	616	—
Shares issuable under employee stock purchase plan	26	20	26	20
Preferred stock (if converted)	3,500	—	3,500	—
	11,437	5,838	11,437	5,838

14. Related Party Transactions

Celgene has made a series of equity investments in the Company, owning 3,674,640 shares of common stock representing 4.0% of the Company's outstanding common stock as of June 30, 2019. Refer to Note 10, *Collaborations,* for additional information regarding the Company's original agreement with Celgene entered into in April 2012 and the amended and restated agreement with Celgene entered into in July 2015.

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

Our management's discussion and analysis of our financial condition and results of operations are based upon our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q, which have been prepared by us in accordance with accounting principles generally accepted in the United States, or GAAP, and with Regulation S-X promulgated under the Securities Exchange Act of 1934, as amended. This discussion and analysis should be read in conjunction with these condensed consolidated financial statements and the notes thereto included elsewhere in this Quarterly Report on Form 10-Q. Some of the information contained in this discussion and analysis or set forth elsewhere in this Quarterly Report on Form 10-Q, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in Part II, Item 1A. *Risk Factors* of this Quarterly Report on Form 10-Q, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a late-stage biopharmaceutical company that is committed to rewriting treatment for people with cancer and other serious diseases through the discovery, development, and commercialization of novel epigenetic medicines. By focusing on the genetic drivers of disease, our science seeks to match targeted medicines with the patients who need them. We are developing our lead product candidate, tazemetostat, an oral, first-in-class, selective small molecule inhibitor of the EZH2 histone methyltransferase, or HMT, for the treatment of a broad range of cancer types in multiple treatment settings, and developing our novel G9a program, EZM8266, for the treatment of sickle cell disease, or SCD.

We have taken a "pipeline in a product" approach to developing tazemetostat with a broad clinical development program through company-sponsored studies and collaborations. This program is evaluating tazemetostat as both a monotherapy and combination treatment in hematological malignancies and solid tumors for both late and early lines of treatment. Tazemetostat has shown meaningful clinical activity as a monotherapy in multiple cancer indications and has been generally well-tolerated across clinical trials to date.

In our solid tumor program, we are evaluating tazemetostat's treatment potential in adults and children with molecularly defined solid tumors, including INI1- and SMARCA4-negative tumors, which we collectively refer to as INI1-negative tumors. We are conducting a multi-cohort global Phase 2 trial of tazemetostat in adults with INI1-negative tumors, including epithelioid sarcoma or metastatic chordoma. In the second quarter of 2019, we submitted a New Drug Application, or NDA, to the U.S. Food & Drug Administration, or FDA, for accelerated approval of tazemetostat for patients with metastatic or locally advanced epithelioid sarcoma not eligible for curative surgery. In July 2019, the NDA was accepted by the FDA for priority review with a Prescription Drug User Fee Act (PDUFA) target action date of January 23, 2020. Priority review is granted to investigational therapies that treat a serious condition and, if approved, would provide a significant improvement in the safety or effectiveness. This submission was based primarily on the clinical activity observed in the 62-patient cohort of epitheliod sarcoma patients in our ongoing Phase 2 trial, which was presented at the International Conference on Malignant Lymphoma in June 2019, and the safety and tolerability observed with tazemetostat in that trial and across our clinical development program. To support subsequent full approval of tazemetostat for epithelioid sarcoma, we plan to initiate a global, randomized, controlled confirmatory trial in the front-line treatment setting comparing tazemetostat in combination with doxorubicin versus doxorubicin plus placebo. This trial is expected to enroll approximately 150 patients and will include a safety run-in anticipated to begin in the second half of this year.

The Phase 2 study cohort of chordoma patients is ongoing, and we are evaluating tazemetostat in the dose-expansion portion of a Phase 1 study in pediatric patients with INI1-negative tumors.

In our hematological malignancy program, we are conducting a multi-cohort, global Phase 2 study evaluating tazemetostat's treatment potential in patients with relapsed or refractory non-Hodgkin lymphoma, or NHL. Two cohorts are evaluating tazemetostat as a monotherapy for patients with relapsed or refractory FL, one of the most prevalent forms of NHL, both with and without EZH2 activating mutations. In December 2018, we completed target enrollment of FL patients in our study, with 54 patients with wild-type EZH2 and 45 patients with EZH2 activating mutations. Based on interactions with the FDA, we believe we have identified a path to submission for accelerated approval of tazemetostat in FL patients with either an EZH2 activating mutation or wild-type EZH2, whose disease has progressed following two or more lines of systemic therapy. We are targeting submission of an NDA for accelerated approval for tazemetostat for FL in this population in the fourth quarter of 2019, subject to the results of our ongoing trial in this indication.

As part of an accelerated approval strategy for FL, we plan to conduct a a confirmatory program for tazemetostat for the treatment of patients with follicular lymphoma. We anticipate that the trial will be a randomized, controlled clinical trial comparing tazemetostat in combination with the FDA-approved chemo-free regimen known as R^2 (REVLIMID® plus a rituximab product) versus placebo plus R^2 in FL patients who have been treated with at least one prior systemic therapy. The trial design is pending final alignment with the FDA, but we expect to begin the safety run-in portion of the trial in the second half of this year.

Our goal is to be able to bring tazemetostat to patients with FL in all lines of treatment. We hope to leverage the confirmatory program to expand tazemetostat into the second-line treatment setting for patients with FL, both with and without EZH2 activating mutations. Based on clinical activity observed with tazemetostat in combination with R-CHOP as a front-line treatment for patients

with diffuse large B-cell lymphoma, or DLBCL, we are evaluating the opportunity to investigate this combination as a front-line treatment for patients with FL. In collaboration with The Lymphoma Study Association, or LYSA, we are planning to evaluate tazemetostat with R-CHOP as a front-line treatment for high-risk FL patients. In addition, we are finalizing plans for an investigator-sponsored study to evaluate the combination of tazemetostat plus rituximab for the treatment of patients with FL in the third line or later settings.

We also plan to evaluate tazemetostat in combination with standards of care for the potential treatment of castration-resistant prostate cancer, and with a PARP inhibitor for the treatment of platinum-resistant solid tumors, such as small-cell lung cancer, triple-negative breast cancer and ovarian cancer.

We own the global development and commercialization rights to tazemetostat outside of Japan. Eisai Co. Ltd, or Eisai, holds the rights to develop and commercialize tazemetostat in Japan. We intend to build a focused field presence and marketing capabilities to commercialize tazemetostat for the epithelioid sarcoma and follicular lymphoma indications in the United States. We have begun building the infrastructure necessary to support the launch and marketing of tazemetostat for epithelioid sarcoma, and believe we can adequately address this patient population through a modest field force of less than 25 professionals. For geographies outside the United States, we are evaluating the most efficient path to reach patients, including through potential collaborations.

Tazemetostat is covered by claims of U.S. and European composition of matter patents, which are expected to expire in 2032, exclusive of any patent term or other extensions. Tazemetostat has been granted Fast Track designation by the FDA in patients with relapsed or refractory FL, with or without activating EZH2 mutations, relapsed or refractory DLBCL with EZH2 activating mutations and metastatic or locally advanced epithelioid sarcoma who have progressed on or following an anthracycline-based treatment regimen. The FDA has also granted orphan drug designation to tazemetostat for the treatment of patients with FL, malignant rhabdoid tumors, or MRT, soft tissue sarcoma, or STS, and mesothelioma. The orphan drug designation for the treatment of MRT applies to INI1-negative MRT as well as SMARCA4-negative malignant rhabdoid tumor of ovary, or MRTO.

Beyond tazemetostat, we are building an early pipeline to further support our leadership in epigenetics. We are developing our wholly-owned G9a candidate, EZM8266, for the treatment of people with sickle cell disease. We have completed IND-enabling studies for this program and plan to begin clinical evaluation with a safety and dose-finding study in the second half of 2019. In November 2018, we entered a strategic collaboration with Boehringer Ingelheim International GmbH, or Boehringer Ingelheim, focused on the research, development and commercialization of novel small molecule inhibitors, discovered by us, directed toward two previously unaddressed epigenetic targets as potential therapies for people with cancer. Specifically, these targets are enzymes within the helicase and histone acetyltransferase, or HAT, families that when dysregulated have been linked to the development of cancers that currently lack therapeutic options. We also have collaborations with Glaxo Group Limited (an affiliate of GlaxoSmithKline), or GSK, focused on the development of PRMT inhibitors discovered by us, and with Celgene Corporation and Celgene RIVOT Ltd., an affiliate of Celgene Corporation, which we collectively refer to as Celgene, focused on the development of pinometostat and small molecule inhibitors directed to three HMT targets.

In April 2018, the FDA placed a partial clinical hold on new patient enrollment in the United States in our ongoing clinical trials of tazemetostat, following a safety report from one patient in the dose-ranging portion of the Phase 1 study who developed a secondary case of T-cell lymphoblastic lymphoma, or T-LBL. This child had metastatic poorly differentiated chordoma and entered our study with a poor prognosis following several prior treatments. The patient was on a high dose of tazemetostat for 15 months and achieved an objective response. Following the T-LBL diagnosis, the patient discontinued tazemetostat and began a standard treatment for T-LBL. This remains the only case of T-LBL that we have seen in approximately 800 patients treated with tazemetostat. In September 2018, the FDA lifted the partial clinical hold.

To better understand the potential risk of T-LBL in our trials, and the overall benefit-risk of tazemetostat across hematological malignancies and solid tumors in both adults and children, we conducted a comprehensive assessment of tazemetostat based on published literature and the clinical experience with tazemetostat to date. A panel of external scientific and medical experts reviewed and validated the findings for the assessment, and we submitted the assessment to the FDA as part of our complete response submission.

To resolve the partial clinical hold in the United States, we reconsented all patients in our clinical trials and updated our informed consent form based on the safety report. We also aligned with the FDA on certain amendments to our tazemetostat study protocols focused on increasing patient monitoring and putting in place risk-mitigation strategies designed to reduce the risk of potential future secondary malignancies.

In November 2018, Germany's Federal Institute for Drugs and Medical Devices lifted the partial clinical hold that it had imposed in Germany, and in January 2019, the partial clinical hold was lifted in France. We have re-activated clinical trial sites and have resumed enrollment in our tazemetostat clinical trials in the United States, and for adult clinical trials in Germany and France.

We commenced active operations in early 2008, and since inception, have incurred significant operating losses. As of June 30, 2019, our accumulated deficit totaled $664.5 million. As a late-stage biopharmaceutical company, we expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We expect our expenses to increase in connection with our ongoing activities, including our continued execution on our clinical development and commercialization plans for tazemetostat, if approved.

Collaborations

Refer to Note 10, *Collaborations*, 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 Boehringer Ingelheim, Celgene, GSK, Eisai and Roche Molecular Systems Inc., or Roche Molecular.

Results of Operations

Collaboration Revenue

The following is a comparison of collaboration revenue for the three and six months ended June 30, 2019 and 2018:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2019	2018	Change	2019	2018	Change
	(In millions)			(In millions)		
Collaboration revenue	$ 5.9	$ 12.0	$ (6.1)	$ 13.8	$ 12.0	$ 1.8

In the three and six months ended June 30, 2019 we recognized $5.9 million and $13.8 million, respectively, in collaboration revenue. This collaboration revenue was earned as part of our Boehringer Ingelheim collaboration. Under the agreement we received $15.0 million in an upfront payment from Boehringer Ingelheim for our license to inhibitor technology of two undisclosed targets, $5.5 million for a development milestone for the selection of a lead optimization candidate for the shared program targeting enzymes within helicase families and $1.3 million in research funding in the second quarter of 2019. We expect to receive $3.7 million in research funding for costs to be incurred in the remainder of 2019. Through June 30, 2019, the Company has recognized $15.5 million in total collaboration revenue under its agreement with Boehringer Ingelheim. The remaining consideration will be recognized in 2019 as services are performed.

We recognized $12.0 million of collaboration revenue in the three and six months ended June 30, 2018. Collaboration revenue in the three and six months ended June 30, 2018 reflects a $12.0 million milestone earned in 2018 based on our determination that the milestone was achieved under the GSK agreement. This milestone relates to the first dosing of a patient in a Phase 2 clinical trial of GSK3326595, a PRMT5 inhibitor discovered by us and licensed to GSK under the collaboration agreement.

Research and Development

The following is a comparison of research and development expenses for the three and six months ended June 30, 2019 and 2018:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2019	2018	Change	2019	2018	Change
	(In millions)			(In millions)		
Research and development	$ 40.9	$ 31.3	$ 9.6	$ 67.8	$ 57.0	$ 10.8

During the three months ended June 30, 2019, total research and development expenses increased by $9.6 million compared to the three months ended June 30, 2018. During the six months ended June 30, 2019, total research and development expenses increased by $10.8 million as compared to the six months ended June 30, 2018. The increases in the three and six months ended June 30, 2019 primarily relates to the payment of a $10 million clinical development milestone to Eisai, increases in tazemetostat manufacturing costs and the build out of our regulatory and late stage development groups, offset by decreases in clinical trial expenses.

The following table illustrates the components of our research and development expenses:

	Three Months Ended June 30,		Six Months Ended June 30,	
Product Program	**2019**	**2018**	**2019**	**2018**
	(In millions)		(In millions)	
External research and development expenses:				
Tazemetostat and related EZH2 programs	$ 25.2	$ 16.6	$ 36.9	$ 27.8
Pinometostat and related DOT1L programs	0.1	0.0	0.1	0.0
Discovery and preclinical stage product programs, collectively	4.3	4.3	9.2	8.3
Unallocated personnel and other expenses	11.3	10.4	21.6	20.9
Total research and development expenses	$ 40.9	$ 31.3	$ 67.8	$ 57.0

External research and development expenses for tazemetostat and related EZH2 programs increased $8.6 million and $9.1 million during the three and six months ended June 30, 2019, respectively, compared to the three and six months ended June 30, 2018 due to an increase in tazemetostat manufacturing costs, offset by decreased clinical trial expenses.

External research and development expenses for pinometostat and related DOT1L programs increased $0.1 million for both the three and six months ended June 30, 2019, respectively, compared to the three and six months ended June 30, 2018. There were no costs incurred related to pinometostat for the three and six months ended June 30, 2018. The costs incurred in the three and six months ended June 30, 2019 are primarily associated with costs attributed to the Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institute, or NCI, to evaluate tazemetostat in clinical trials in a variety of hematologic malignancies and solid tumors.

External research and development expenses for discovery and preclinical stage product programs remained consistent during the three months ended June 30, 2019 compared to the three months ended June 30, 2018. External research and development expenses for discovery and preclinical stage product programs increased by $0.9 million during the six months ended June 30, 2019 compared to the six months ended June 30, 2018, primarily related to increased development activities related to our novel G9a program, EZM8266, for the potential treatment of sickle cell disease, and offset by reduced spending for discovery research activities.

Unallocated personnel and other expenses are comprised of compensation expenses for our full-time research and development employees and other general research and development expenses. Unallocated personnel and other expenses increased by $0.9 million and $0.7 million during the three and six months ended June 30, 2019, respectively, compared to the three and six months ended June 30, 2018, as a result of allocation of expenses to projects and increases in facilities and equipment related expenses offset by an increase in unallocated personnel costs.

We expect that research and development expenses will remain consistent throughout the remainder of 2019, as we continue our clinical trial expenses for tazemetostat and focus on our G9a program and our most promising discovery stage research programs.

General and Administrative

The following is a comparison of general and administrative expenses for the three and six months ended June 30, 2019 and 2018:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2019	**2018**	**Change**	**2019**	**2018**	**Change**
	(In millions)			(In millions)		
General and administrative	$ 15.7	$ 10.9	$ 4.8	$ 27.7	$ 20.3	$ 7.4

For the three months ended June 30, 2019, our general and administrative expenses increased $4.8 million compared to the three months ended June 30, 2018. During the six months ended June 30, 2019, our general and administrative expenses increased by $7.4 million as compared to the six months ended June 30, 2018. The increases in expenses for the three and six months ended June 30,

2019 compared to the three and six months ended June 30, 2018 are due to increased pre-commercialization activities, including the build out of our medical affairs and commercial organizations, and increased personnel related expenses.

We expect that general and administrative expenses will increase during the remainder of 2019, as we continue to increase our pre-commercial activities for tazemetostat.

Other Income, Net

The following is a comparison of other income, net for the three and six months ended June 30, 2019 and 2018:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2019	2018	Change	2019	2018	Change
	(In thousands)			(In thousands)		
Other income, net						
Interest income, net	$ 2,253	$ 1,143	$ 1,110	$ 3,911	$ 2,042	$ 1,869
Other (expense) income, net	(13)	(11)	(2)	(19)	7	(26)
Other income, net	$ 2,240	$ 1,132	$ 1,108	$ 3,892	$ 2,049	$ 1,843

Other income, net consists of interest income earned on our cash equivalents and marketable securities, net of imputed interest expense paid under our capital lease obligation. The increase in other income is principally due to net interest income, which increased $1.1 million and $1.9 million during the three and six months ended June 30, 2019, respectively, compared to the three and six months ended June 30, 2018. The increased net interest income is primarily due to active management of the Company's investment portfolio, an increase in investment yields, and an increased cash balance as a result of our October 2018 and March 2019 public offerings.

Income Tax Expense

We did not record a federal or state income tax provision or benefit for the three and six months ended June 30, 2019 and 2018 due to the expected and known loss before income taxes to be incurred, or incurred, as applicable, for the years ended December 31, 2019 and 2018, as well as our continued maintenance of a full valuation allowance against our net deferred tax assets, with the exception of the deferred tax asset related to alternative minimum tax credit.

Liquidity and Capital Resources

In March 2019, we raised approximately $122.7 million in net proceeds (after deducting underwriting discounts and commissions and estimated offering expenses, but excluding any expenses and other costs reimbursed by the underwriters) from the sale of 11,500,000 shares of our common stock in a public offering at a price of $11.50 per share. We also raised approximately $37.4 million in net proceeds (after deducting underwriting discounts and commissions and estimated offering expenses, but excluding any expenses and other costs reimbursed by the underwriters) from the sale of 350,000 shares of series A convertible preferred stock in a public offering at a price of $115 per share. The series A convertible preferred stock is convertible into 3,500,000 shares of our common stock.

In October 2018, we raised approximately $81.6 million in net proceeds (after deducting underwriting discounts and commissions and offering expenses, but excluding any expenses and other costs reimbursed by the underwriters) from the sale of 9,583,334 shares of our common stock in a public offering at a price of $9.00 per share.

Through June 30, 2019, we have raised an aggregate of $1,155.1 million to fund our operations, of which $239.6 million was non-equity funding through our collaboration agreements, $839.5 million was from the sale of common stock and series A convertible preferred stock in our public offerings and $76.0 million from the sale of redeemable convertible preferred stock, prior to our initial public offering. As of June 30, 2019, we had $331.0 million in cash, cash equivalents, and marketable securities.

In addition to our existing cash, cash equivalents and marketable securities, we may receive research and development co-funding and are eligible to earn a significant amount of option exercise and milestone payments under our collaboration agreements. Our ability to earn these payments and the timing of earning these payments is dependent upon the outcome of our research and development activities and is uncertain at this time.

Funding Requirements

Our primary uses of capital are clinical trial costs, third party research and development services, expenses related to preparation for commercialization, compensation and related expenses, laboratory and related supplies, our potential future milestone payment obligations to Eisai and Roche Molecular under the amended Eisai collaboration agreement and Roche Molecular companion diagnostic agreement, legal and other regulatory expenses and general overhead costs.

Because our product candidates are in various stages of clinical and preclinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates or whether, or when, we may achieve profitability. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity or debt financings and collaboration arrangements. Except for any obligations of our collaborators to make license, milestone or royalty payments under our agreements with them, we do not have any committed external sources of liquidity. To the extent that we raise additional capital through the future sale of equity or debt, the ownership interest of our stockholders may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. Debt financing and preferred equity 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 additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise any additional funds that may be needed through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Outlook

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that our existing cash, cash equivalents and marketable securities as of June 30, 2019, will be sufficient to fund our planned operating expenses and capital expenditure requirements into the first quarter of 2021, without giving effect to any potential option exercise fees or milestone payments we may receive under our collaboration agreements. We have based this estimate on assumptions that may prove to be wrong, particularly as the process of testing drug candidates in clinical trials is costly and the timing of progress in these trials is uncertain. As a result, we could use our capital resources sooner than we expect.

Cash Flows

The following is a summary of cash flows for the six months ended June 30, 2019 and 2018:

	Six Months Ended June 30,		
	2019	2018	Change
	(In millions)		
Net cash used in operating activities	$ (73.5)	$ (63.2)	$ (10.3)
Net cash used in investing activities	(129.5)	(97.5)	(32.0)
Net cash provided by financing activities	162.3	1.9	160.4

Net Cash Used in Operating Activities

Net cash used in operating activities during the six months ended June 30, 2019 primarily relates to our net loss of $77.8 million, changes in working capital of $2.3 million, and net depreciation and amortization of $1.3 million, partially offset by non-cash stock-based compensation of $7.9 million.

Net cash used in operating activities for the six months ended June 30, 2018 primarily relates to our net loss of $63.2 million and changes in working capital of $6.4 million, partially offset by non-cash stock-based compensation of $6.3 million.

Net Cash Used in Investing Activities

Net cash used in investing activities during the six months ended June 30, 2019 reflects $297.9 million of purchases of available-for-sale securities and $0.2 million of purchases of property and equipment, offset by maturities of available-for-sale securities of $168.5 million.

Net cash used in investing activities during the six months ended June 30, 2018 reflects $165.7 million of purchases of available-for-sale securities, partially offset by maturities of available-for-sale securities of $68.3 million and purchases of property and equipment of $0.1 million.

Net Cash Provided by Financing Activities

Net cash provided by financing activities of $162.3 million during the six months ended June 30, 2019 primarily reflects cash received from the issuance of common and preferred stock of $160.4 million, stock option exercises of $1.8 million, and the purchases of shares under our employee stock purchase plan of $0.4 million, partially offset by payments of public offering costs of $0.3 million.

Net cash provided by financing activities of $1.9 million during the six months ended June 30, 2018 primarily reflects cash received from stock option exercises of $1.6 million, and the purchases of shares under our employee stock purchase plan of $0.4 million, partially offset by the payments under our capital lease obligation of $0.1 million.

Contractual Obligations

There were no material changes to our contractual obligations and commitments described under "Management's Discussion and Analysis and Results of Operations" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based upon our condensed consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these condensed consolidated financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and disclosures of contingent assets and liabilities as of the date of the balance sheets and the reported amounts of collaboration revenue and expenses during the reporting periods. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances at the time such estimates are made. Actual results and outcomes may differ materially from our estimates, judgments and assumptions. We periodically review our estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates are reflected in the condensed consolidated financial statements prospectively from the date of the change in estimate.

We define our critical accounting policies as those accounting principles generally accepted in the United States of America that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations as well as the specific manner in which we apply those principles. Management has determined that our most critical accounting policies are those relating to revenue recognition, stock-based compensation and research and development expenses, including our accounting for clinical trial expense and accruals. As our clinical development plan for tazemetostat progresses, we expect research and development expenses and, in particular, our accounting for clinical trial accruals to be an increasingly important critical accounting policy.

During the quarter ended March 31, 2019, we adopted ASC 842 using the modified retrospective approach, resulting in a change in our lease accounting policy, as described in Note 2, *Summary of Significant Accounting Policies—Recently Adopted Accounting Pronouncements,* in the accompanying Notes to Condensed Consolidated Financial Statements included in Item 1 of this Quarterly Report on Form 10-Q. During the three months ended June 30, 2019, there have been no material changes to our critical accounting policies disclosed in our Annual Report on Form 10-K for our fiscal year ended December 31, 2018.

Recently Adopted Accounting Pronouncements

For detailed information regarding recently issued accounting pronouncements and the expected impact on our condensed consolidated financial statements, see Note 2, *Summary of Significant Accounting Policies—Recently Adopted Accounting Pronouncements*, in the accompanying Notes to Condensed Consolidated Financial Statements included in Item 1 of this Quarterly Report on Form 10-Q.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of June 30, 2019, we had cash and cash equivalents and marketable securities of $331.0 million consisting of money market funds, corporate bonds, and commercial paper. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. We estimate that a hypothetical 100-basis point change in market interest rates would impact the fair value of our investment portfolio as of June 30, 2019 by $0.5 million.

We contract with contract research organizations and manufacturers globally. Transactions with these providers are predominantly settled in U.S. dollars and, therefore, we believe that we have only minimal exposure to foreign currency exchange risks. We do not hedge against foreign currency risks.

Item 4. Controls and Procedures

Disclosure Controls and Procedures

We have established disclosure controls and procedures designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934, as amended, or the Exchange Act, is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer and the principal financial officer, to allow timely decisions regarding required disclosure.

Our management, under the supervision and with the participation of the principal executive officer (our Chief Executive Officer) and the principal financial officer (our Chief Strategy and Business Officer) has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Quarterly Report on Form 10-Q. Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on such evaluation, our Chief Executive Officer and Chief Strategy and Business officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of June 30, 2019.

PART II — OTHER INFORMATION

Item 1A. Risk Factors

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Annual Report on Form 10-K and in other documents that we file with the SEC, in evaluating our company and our business. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks facing our company. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations.

Risks Related to the Discovery and Development of Our Product Candidates

We are dependent on the successful development and commercialization of our lead product candidate, tazemetostat. If we are unable to develop, obtain marketing approval for or successfully commercialize this product candidate, either alone or through a collaboration, or if we experience significant delays in doing so, our business could be harmed.

We currently have no products approved for sale and are investing a significant portion of our efforts and financial resources to fund the development and commercialization of our lead product candidate, tazemetostat. In May 2019, we submitted our first new drug application, or NDA, to the U.S. Food and Drug Administration, or FDA, for accelerated approval of tazemetostat for the treatment of patients with metastatic or locally advanced epithelioid sarcoma not eligible for curative surgery. The FDA has accepted the NDA for accelerated approval for filing and granted priority review. However, the FDA may conclude after review of our data that our application is insufficient to obtain marketing approval of tazemetostat on an accelerated basis or at all. We and our collaborators are conducting clinical trials of other of our product candidates. However, these development programs are early stage, and all of our other product candidates are still in preclinical development. As a result, our prospects are substantially dependent on our ability, or the ability of any future collaborator, to develop, obtain marketing approval for and successfully commercialize tazemetostat in one or more disease indications. The success of tazemetostat and any other product candidate will depend on several factors, including the following:

- successful enrollment in, and completion of, clinical trials;
- safety, tolerability and efficacy profiles that are satisfactory to the FDA, the European Medicines Agency, or EMA, or any comparable foreign regulatory authority for marketing approval;
- timely receipt of marketing approvals from applicable regulatory authorities and the patient populations for which the approvals are granted;
- the extent of any required post-marketing approval commitments to applicable regulatory authorities;
- making arrangements with third-party manufacturers for, or establishing, clinical and commercial manufacturing capabilities;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;
- acceptance of the products, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- protecting our rights in our intellectual property portfolio; and
- maintaining a continued acceptable safety profile of the products following approval.

Many of these factors are beyond our control, including clinical development, the regulatory review process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any collaborator. If any of these factors adversely affects the development or commercialization of tazemetostat or any other product candidate, we may not be able to successfully develop or commercialize our product candidates on a timely basis or at all, which would materially harm our business.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. 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 are conducting multiple clinical trials of tazemetostat. In addition, Glaxo Group Limited (an affiliate of GlaxoSmithKline), or GSK, has initiated a Phase 2 expansion clinical trial for a PRMT5 inhibitor that it has licensed from us and has initiated patient dosing in a Phase 1 clinical trial of GSK3368715, a PRMT1 inhibitor. The risk of failure for each of these product candidates 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 regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans.

Product candidates are subject to preclinical safety studies, which may be conducted prior to or concurrently with clinical testing, as well as continued clinical safety assessment throughout clinical testing. The outcomes of these safety studies or assessments may delay the launch of or enrollment in clinical studies. For example, in the course of our preclinical safety studies of tazemetostat, we observed the development of lymphoma in Sprague Dawley rats. As a result of these findings, coupled with our limited clinical experience in follicular lymphoma, or FL, at the time of the IND submission in December 2015, we were unable to conduct our Phase 2 trial of tazemetostat in FL patients in the United States until the beginning of 2017. In addition, in April 2018, following a safety report of a pediatric patient who developed a secondary T-cell lymphoma in our ongoing Phase 1 clinical trial of tazemetostat in pediatric patients, the FDA issued a partial clinical hold on new enrollment of patients in our ongoing clinical trials of tazemetostat. In the second quarter of 2018, the French National Agency for Medicines and Health Products Safety and Germany's Federal Institute for Drugs and Medical Devices each placed a comparable partial clinical hold on new patient enrollment. In September 2018, the FDA lifted the partial clinical hold on new patient enrollment in the United States and in November 2018, Germany's Federal Institute for Drugs and Medical Devices lifted the partial clinical hold in Germany, and in January 2019, the partial clinical hold was lifted in France. We have re-activated clinical trial sites in the United States, Germany, and France, resuming enrollment in our tazemetostat clinical trials at those sites. If we or our collaborators are unable to fully and adequately address matters such as the partial clinical hold when they arise, we may be unable to conduct clinical trials of our product candidates, our trials may be limited to certain patient populations or our ability to conduct other trials in the United States or in other countries may be delayed.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. In our FL program, we have engaged in discussions with the FDA regarding the classification of FL patients as EZH2 mutant or wild-type patients. If the FDA does not agree with our classification of patients, particularly the wild-type patients in our studies, the FDA may disagree with our data in our patient population subsets, which could affect our ability to obtain regulatory approval of tazemetostat for one or both of the FL patient populations.

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

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- clinical trials of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- preclinical testing may produce results based on which we may decide, or regulators may require us, to conduct additional preclinical studies before we proceed with certain clinical trials, limit the scope of our clinical trials, halt ongoing clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- we may have to limit the scope of, suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we 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 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 or a risk evaluation mitigation strategy that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

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

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. In particular, because certain of our product candidates may be focused on specific patient populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. In addition, some of our competitors have ongoing clinical trials for product candidates that may treat the broader patient populations within which our product candidates are being developed for the treatment of a subset of identifiable patients with cancer and other diseases, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. For instance, our ongoing clinical trials of tazemetostat in adult and pediatric patients with INI1-negative tumors are targeting rare patient populations.

Patient enrollment is affected by other factors including:

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

- the proximity and availability of clinical trial sites for prospective patients; and
- the ability to identify specific patient population for molecularly defined study cohort(s).

For example, in April 2018, following a safety report of a pediatric patient who developed a secondary T-cell lymphoma, the FDA issued a partial clinical hold on new enrollment of patients in our ongoing clinical trials of tazemetostat. In the second quarter of 2018, the French National Agency for Medicines and Health Products Safety and Germany's Federal Institute for Drugs and Medical Devices each took similar actions. In September 2018, the FDA lifted the partial clinical hold on new patient enrollment in the United States, in November 2018, Germany's Federal Institute for Drugs and Medical Devices lifted the partial clinical hold in Germany, and in January 2019, the partial clinical hold was lifted in France. We have re-activated clinical trial sites in the United States, Germany, and France, resuming enrollment in our tazemetostat clinical trials at those sites.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could 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, and could delay or prevent our ability to obtain marketing approval, which may cause the value of our company to decline and limit our ability to obtain additional financing.

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

If our product candidates are associated with undesirable side effects in preclinical testing or clinical trials or have characteristics that are unexpected in clinical trials or preclinical testing, we may need to abandon their development or limit development to more narrow 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. In pharmaceutical development, many compounds that initially show promise in early-stage testing for treating cancer are later found to cause side effects that prevent further development of the compound.

Our research and development is focused on the creation of novel epigenetic therapies for patients with cancer and other diseases, which is a rapidly evolving area of science, and the approach we are taking to discover and develop drugs is novel and may never lead to marketable products.

The discovery of novel epigenetic therapies for patients with cancer and other serious diseases is an emerging field, and the scientific discoveries that form the basis for our efforts to discover and develop product candidates are relatively new. Although epigenetic regulation of gene expression plays an essential role in biological function, few drugs premised on epigenetics have been discovered. Moreover, those drugs based on an epigenetic mechanism that have received marketing approval are in different target classes than the chromatin modifying protein, or CMP, inhibitors where our research and development is principally focused. Although preclinical studies suggest that genetic alterations can result in changes to the activity of CMPs making them oncogenic, to date no company has translated these biological observations into systematic drug discovery that has yielded a drug that has received marketing approval. We believe that our first three inhibitors of histone methyltransferases, or HMTs, in the clinic are all the first molecules against these targets to enter clinical development. Therefore, we do not know if our approach of inhibiting HMTs or other CMPs to treat patients with cancer and other serious diseases will be successful.

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 products 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 products. 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 required to develop a companion diagnostic and if we or our collaborators are unable to successfully develop diagnostics for our therapeutic product candidates when needed, or experience significant delays in doing so, we may not achieve marketing approval or realize the full commercial potential of our therapeutic product candidates.

We may develop, or we may work with collaborators, to develop diagnostics for our therapeutic product candidates to identify patients for our clinical trials who have the specific cancers that we are seeking to treat as appropriate and when existing, available technology may not be sufficient to identify those patients. We do not have experience or capabilities in developing or commercializing diagnostics and plan to rely in large part on third parties to perform these functions. For example, we have entered into an agreement with Roche Molecular to develop and commercialize a diagnostic for use with tazemetostat for NHL patients with EZH2 activating mutations. Companion diagnostics are subject to regulation by the FDA and similar regulatory authorities outside of the United States as medical devices and require separate regulatory approval prior to commercialization. If any third parties that we engage to assist us are unable to successfully develop companion diagnostics that are needed 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 their safe and effective use depends on a companion diagnostic; and
- we may not realize the full commercial potential of any therapeutic product candidates that receive marketing approval if, among other reasons, we are unable to appropriately identify patients with the specific genetic alterations targeted by our therapeutic product candidates.

If any of these events were to occur, our business would be harmed, possibly materially.

We may not be successful in our efforts to use and expand our proprietary drug discovery platform to build a pipeline of product candidates.

A key element of our strategy is to use and expand our proprietary drug discovery platform to build a pipeline of small molecule inhibitors of HMT and other CMP targets and progress these product candidates through clinical development for the treatment of a variety of different types of cancer and other diseases. Although our research and development efforts to date have resulted in a pipeline of programs directed to specific HMT and other CMP targets, we may not be able to develop product candidates that are safe and effective CMP inhibitors. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including as a result of being shown to have harmful side effects or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our technological approach, we will not be able to obtain product revenues in future periods, which likely would result in significant harm to our financial position and adversely affect our stock price.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception. We expect to incur losses over the next several years and may never achieve or maintain profitability.

Since inception, we have incurred significant operating losses. Our net loss was $48.5 million for the six months ended June 30, 2019, $123.6 million for the year ended December 31, 2018, $134.3 million for the year ended December 31, 2017, and $110.2 million for the year ended December 31, 2016. As of June 30, 2019, we had an accumulated deficit of $664.5 million. To date, we have financed our operations primarily through our collaborations, our public offerings, and private placements of our preferred stock. All of our revenue to date has been collaboration revenue. We have devoted substantially all of our financial resources and efforts to research and development, including clinical and preclinical studies. We are still in the early to middle stages of development of our product candidates, and we have not completed development of any product candidates. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will continue to increase over the next several years if and as we:

- continue our Phase 2 clinical trial of tazemetostat for the treatment of patients with NHL, including relapsed or refractory FL cohorts in the trial;
- continue our Phase 2 clinical trial of tazemetostat for the treatment of adult patients with certain molecularly defined solid tumors, including the epithelioid sarcoma cohort in the trial;

- continue our Phase 1 clinical trial of tazemetostat for the treatment of pediatric patients with certain molecularly-defined solid tumors;
- continue our clinical trials of tazemetostat in combination with R-CHOP in first line elderly patients with DLBCL and in combination with Genentech Inc.'s anti-PD-L1 cancer immunotherapy, atezolizumab, in patients with relapsed or refractory DLBCL being conducted by our collaborators;
- design and conduct a new combination trial of tazemetostat in FL;
- pay any milestone payments provided for and achieved under the amended and restated collaboration and license agreement with Eisai Co Ltd, or Eisai;
- complete IND-enabling studies for EZM8266, a G9a inhibitor designed to treat patients with sickle cell disease, and prepare for a Phase 1 study;
- establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;
- grow our medical affairs organization to support the commercialization efforts of any product candidate that is approved;
- conduct research and development under our collaboration and license agreements with Celgene and Boehringer Ingelheim International GmbH, or Boehringer Ingelheim;
- continue the research and development of our other product candidates, as well as for Celgene Corporation, or Celgene, under our amended and restated collaboration and license agreement;
- seek to discover and develop additional product candidates or to expand our product candidates into additional lines of treatment;
- prepare NDA submissions as we seek regulatory approvals for any product candidates that successfully complete clinical trials;
- maintain, expand and protect our intellectual property portfolio;
- hire additional clinical, quality control, manufacturing and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

To become and remain profitable, we must succeed in developing, and eventually commercializing, a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the FDA, the EMA, or other regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

Even 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 depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could cause our stockholders to lose all or part of their investment in our company.

We will need substantial additional funding. If we are unable to raise capital when needed, we could 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 to fund our tazemetostat development program; make any milestone payments provided for and achieved under the amended and restated collaboration and license agreement with Eisai; prepare for commercialization of tazemetostat; continue our collaboration with Celgene; and continue research and development and initiate clinical trials of, and seek regulatory approval for, any future product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. 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 acceptable terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that our existing cash, cash equivalents and marketable securities as of June 30, 2019, will be sufficient to fund our planned operating expenses and capital expenditure requirements into the first quarter of 2021, without giving effect to milestone payments we may receive under our collaboration agreements. We have based these expectations on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Our future capital requirements will depend on many factors, including:

- the progress and results of our ongoing and planned clinical trials of tazemetostat;
- the number and development requirements of additional indications for tazemetostat and other product candidates that we may pursue, including the scope, progress, results and costs of discovery research, preclinical development, laboratory testing and clinical trials for such product candidates;
- the costs, timing and outcome of regulatory review of tazemetostat and other product candidates we may pursue;
- our ongoing collaboration with Celgene;
- milestones, option exercise fees, license fees, and other revenues, if any, we may receive under our collaboration agreements;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution for any of our product candidates for which we receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- the extent to which we acquire or in-license other products 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 regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Commercial revenues, if any, will not be derived until and unless we can achieve sales of commercially available products. 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. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

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 revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings and license and development agreements with collaboration partners. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our existing 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 and preferred equity 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 additional funds through collaborations, strategic alliances or marketing, distribution 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, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

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

We commenced active operations in early 2008, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and, beginning in 2012, conducting clinical trials. All but four of the product candidates discovered by us are still in preclinical development. We have not yet demonstrated our ability to obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

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

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

Risks Related to the Commercialization of Our Product Candidates

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

In July 2019, the FDA accepted for submission our first NDA for accelerated approval of tazemetostat for the treatment of patients with metastatic or locally advanced epithelioid sarcoma not eligible for curative surgery. In addition, based on recent interactions with the FDA, we believe we have identified a potential path for accelerated approval of tazemetostat as a monotherapy for relapsed or refractory FL in both EZH2 mutant and wild-type FL patient populations, where patients' disease has progressed following two or more lines of therapy. Subject to the results of the FL cohorts in our ongoing global Phase 2 study of tazemetostat in NHL, we are targeting submission of an NDA for tazemetostat for this indication in the fourth quarter of 2019.

It is possible that the FDA or any other regulatory authority may refuse to accept our applications for substantive review, or that the FDA or other regulatory authority may conclude after review of our data that our application is insufficient to obtain marketing approval of tazemetostat on an accelerated basis or at all. If the FDA does not agree that we have sufficient data to seek accelerated approval or does not accept or approve one or more of our submitted or planned NDAs for tazemetostat, we may be required to study tazemetostat in additional patients or conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data to regulators before our application can be resubmitted or will be reconsidered. If the FDA grants accelerated approval for our submitted or our planned NDAs, we will need to conduct a confirmatory program in each indication, which may involve Phase 3 trials that may be expensive and time-consuming and may not confirm such benefit and subject the NDAs to withdrawal.

We are planning to submit our NDA for accelerated approval for tazemetostat for relapsed or refractory FL in both EZH2 mutant and wild-type FL patient populations following two prior systemic therapies. If the FDA only accepts or approves our application for the mutant FL patient population, we may be required to study tazemetostat in additional wild-type FL patients or conduct additional clinical trials or preclinical studies and submit that data to regulators and resubmit an application for that patient population. Depending on the extent of these or any other required trials or studies, submission of our planned NDAs or acceptance or approval of these NDAs for tazemetostat 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 to accept or approve any NDAs for tazemetostat. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing tazemetostat in the United States and/or abroad, generating revenue and achieving and sustaining profitability. If our confirmatory program does not verify clinical benefit, we may have to withdraw our accelerated approval indication. If any of these outcomes occurs, either to tazemetostat or to any future product candidate for which we may seek marketing approval, we may be forced to abandon our development efforts for tazemetostat or such future product candidates, which could significantly harm our business.

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;

- the availability of third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects;
- any safety events that may have occurred in connection with the development of the product candidate; and
- any restrictions on the use of our products together with other medications.

If we are unable to establish sales, marketing and distribution capabilities, we may not be successful in commercializing our product candidates if and when they are approved.

To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales and marketing organization.

We have recently begun building the infrastructure necessary to support the successful commercial launch and marketing of tazemetostat and other product candidates that may receive marketing approval. There are risks involved with establishing our own sales, marketing and distribution capabilities. 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. These efforts 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 products on our own include:

- our inability to recruit, train 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 products;
- the lack of complementary products 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 are unable to establish our own sales, marketing and distribution capabilities and enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are acceptable 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 products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will likely face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of many of the disease indications for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. 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. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Specifically, there are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. Companies that are developing new epigenetic treatments for cancer that target histone methyltransferases, or HMTs, and protein arginine methyltransferases, or PRMTs, include GSK, Johnson & Johnson, Pfizer, Inc., Daiichi Sankyo Company Limited, and Constellation Pharmaceuticals. Further, companies which are known to have EZH2 inhibitor programs or related programs include: Constellation Pharmaceuticals, developing an EZH2 inhibitor (CPI-1205, Phase 1/2 castration-resistant prostate cancer, solid tumors), Novartis AG, developing an EED inhibitor which indirectly blocks EZH2 (MAK683, Phase

1/2, advanced malignancies), Daiichi Sankyo, developing a EZH1/EZH2 dual inhibitor (valemetostat, DS-3201, Phase 1, relapsed or refractory non-Hodgkin lymphomas, AML, and ALL, as well as Phase 2 for small cell lung cancer), and Pfizer, developing EZH2 inhibitor PF-06821497, Phase 1, relapsed or refractory SCLC, castration-resistant prostate cancer, follicular lymphoma and diffuse large B-cell lymphoma. In July 2017, GSK discontinued their EZH2 inhibitor program, GSK2816126, which had been in Phase 1 development in solid tumors and hematological malignancies. In addition, many companies are developing cancer therapeutics that work by targeting epigenetic mechanisms other than HMTs, and some including Celgene, Merck & Co., Inc., Secura Bio, Spectrum Pharmaceuticals, and Otsuka, are now marketing cancer treatments that work by targeting epigenetic mechanisms other than HMTs. There are a number of companies currently evaluating investigational agents in the relapsed and refractory follicular lymphoma patient setting. To the best of our knowledge there are no competitive products in development for epithelioid sarcoma

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

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

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

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a 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 might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

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

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

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

- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend any 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 products that we may develop.

We currently hold $20.0 million in product liability insurance coverage in the aggregate, with a per incident limit of $20.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. 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.

Risks Related to Our Dependence on Third Parties

Our existing therapeutic collaborations are important to our business, and future collaborations may also be important to us. If we are unable to maintain any of these collaborations, or if these collaborations are not successful, our business could be adversely affected.

Our resources for drug development are limited and we are actively building our sales, marketing, medical affairs and supply chain infrastructure. Accordingly, we have entered into therapeutic collaborations with other companies that we believe can provide such capabilities, including our collaboration and license agreements with Celgene, GSK, and Boehringer Ingelheim. We also rely on Genentech to manage our combination trial of tazemetostat and atezolizumab in relapsed or refractory DLBCL, and on the Lymphoma Study Association to manage our combination study of tazemetostat and R-CHOP in newly diagnosed, elderly, high risk patients with DLBCL. With our reacquisition of tazemetostat rights under our amended and restated collaboration and license agreement with Eisai, we do not have access to Eisai's capabilities for tazemetostat except with Eisai in Japan. Our collaborations have provided us with important funding for our development programs and product platform and we expect to receive additional funding under these collaborations in the future. Our existing therapeutic collaborations, and any future collaborations we enter into, may pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not have the ability or the development capabilities to perform their obligations as expected;

- collaborators may not pursue commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that may divert resources or create competing priorities;
- 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;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- 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 intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

If our therapeutic collaborations do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product platform and product candidates could be delayed and we may need additional resources to develop product candidates and our product platform. All of the risks relating to product development, regulatory approval and commercialization described in our Annual Report on Form 10-K also apply to the activities of our therapeutic collaborators.

Our existing therapeutic collaborations contain restrictions on our engaging in activities that are the subject of the collaboration with third parties for specified periods of time. For example, under our collaboration agreement with Celgene, subject to specified exceptions, we may not, during the option period, research, develop or commercialize inhibitors directed to DOT1L and the three option targets covered by the agreement outside of the collaboration. These restrictions may have the effect of preventing us from undertaking development and other efforts that may appear to be attractive to us.

Additionally, subject to its contractual obligations to us, if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

For some of our product candidates or for some CMP targets, we may in the future collaborate with pharmaceutical and biotechnology companies for development and potential commercialization of therapeutic products. We face significant competition in seeking appropriate collaborators. Our ability to 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. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, 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 fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform and our business may be materially and adversely affected.

Failure of our third-party collaborators to successfully commercialize diagnostics, developed for use with our therapeutic product candidates, if and when needed, could harm our ability to commercialize these product candidates.

We do not plan to develop diagnostics internally and, as a result, we are dependent on the efforts of our third-party collaborators to successfully commercialize diagnostics when existing, available technology may not be sufficient to identify patients for treatment with our therapeutic product candidates. For example, we may rely on Roche Molecular to develop a companion diagnostic for detecting activating mutations in EZH2 in the tazemetostat in NHL program. Our collaborators:

- may not perform their obligations as expected or have difficulty responding to accelerated approval time lines alongside the therapeutic product development;
- may encounter production difficulties that could constrain the supply of the diagnostics;
- may encounter delays or have difficulty obtaining regulatory approval for the diagnostic in target markets;
- may have difficulties gaining acceptance of the use of the diagnostics in the clinical community;
- may not pursue commercialization of any diagnostics that achieve regulatory approval;
- may elect not to continue or renew commercialization programs based on changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition, that divert resources or create competing priorities;
- may not commit sufficient resources to the marketing and distribution of such product or products; and
- may terminate their relationship with us.

If diagnostics for use with our therapeutic product candidates fail to gain market acceptance, our ability to derive revenues from sales of our therapeutic product candidates could be harmed. If our collaborators fail to commercialize these diagnostics, we may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use in connection with our therapeutic product candidates or do so on commercially reasonable terms, which could adversely affect and delay the development or commercialization of our therapeutic product candidates.

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

We currently rely on third-party clinical research organizations to conduct our ongoing clinical trials and plan to rely on third-party clinical research organizations or third-party research collaborative groups to conduct our planned clinical trials. We do not plan to independently conduct clinical trials of any future product candidates. We expect to continue to rely on third parties, such as clinical research organizations, research collaborative groups, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. These agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities might be delayed.

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

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

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials and our commercial operations. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, 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 commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We do not have any manufacturing facilities and rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates receive marketing approval. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts.

We also expect to rely on third-party manufacturers or third-party collaborators for the manufacture of commercial supply of any other product candidates for which our collaborators or we obtain marketing approval. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third-party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

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

Our product candidates and any products 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 or a second source for bulk drug substance. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. 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 products may adversely affect our future profit margins and our ability to commercialize any products 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 protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully commercialize our technology and products may be impaired.

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 technology and products. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

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. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. 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 at all. Therefore, we cannot know with certainty whether 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. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. 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.

In the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other non-United States jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates. We intend to seek patent term extensions for any of our issued patents in any jurisdiction where they are available, however there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

Patent reform legislation such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the U.S. Patent and Trademark Office during patent prosecution and additional procedures to attack the validity of a patent at U.S. Patent and Trademark Office administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. In addition, under the Leahy-Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, we may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. For example, we are involved in an opposition proceeding against one of our European patents, the claims of which cover a method for determining whether a cancer patient is a candidate for treatment with an EZH2 inhibitor based on their EZH2 mutation status. 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 products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage.

Our competitors may be able to circumvent our owned or licensed 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 owned and licensed 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 freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, 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 products. 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 owned and licensed patent portfolio 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 or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or 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.

We may need to license certain intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property, including patent rights, that are important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we may be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially.

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

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, litigation regarding intellectual property rights with respect to our products and technology. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. For example, with respect to tazemetostat, we are aware of U.S. patents held by a third party, which could be construed to cover tazemetostat and its use in certain clinical indications.

In the event that an owner of one or more of these patents were to bring an infringement action against us, we believe we have defenses that we could assert in such event, and additionally in the U.S. Patent & Trademark Office, including the invalidity of the relevant claims of such patents. However, we may not be successful in asserting these defenses, including proving invalidity, and could be found to infringe one or more of these third party's patents.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

If we fail to comply with our obligations in our intellectual property licenses and funding arrangements with third parties, we could lose rights that are important to our business.

We are party to license and research agreements that impose, and we may enter into additional licensing and funding arrangements with third parties that may impose, diligence, development and commercialization timelines, milestone payment, royalty, insurance and other obligations on us. Under our existing licensing and funding agreements, we are obligated to pay royalties on net product sales of product candidates or related technologies to the extent they are covered by the agreements. We also had diligence and development obligations under those agreements that we have satisfied. If we fail to comply with our obligations under current or future license and funding agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market any product that is covered by these agreements or may face other penalties under the agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or reinstated agreements with less favorable terms, or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or 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 prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. 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. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise 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 product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. 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 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 of 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, we would have no right to prevent them, or those to whom they communicate it, 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, our competitive position would be harmed.

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

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

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export and import are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside of the United States. We have not received marketing approval for any of our product candidates in the United States or in any other jurisdiction.

In July 2019, the FDA accepted for submission our first NDA for accelerated approval of tazemetostat for the treatment of patients with metastatic or locally advanced epithelioid sarcoma not eligible for curative surgery, and we plan to submit an NDA to the FDA for tazemetostat for the treatment of relapsed and refractory FL in patients who have received at least two prior systemic therapies in the fourth quarter of 2019, subject to the results of our ongoing Phase 2 trial in this indication. Failure to obtain marketing approval for tazemetostat or any other product candidate will prevent us from commercializing the product candidate. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party clinical research organizations to assist us in this process.

Securing marketing approval requires the submission of extensive preclinical, clinical and manufacturing data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety, efficacy and quality. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. 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. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed.

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. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

We submitted our NDA for accelerated approval of tazemetostat in patients with epithelioid sarcoma and we plan to submit our NDA for accelerated approval of tazemetostat in patients with relapsed or refractory FL who have received at least two prior systemic therapies in both EZH2 mutant and wild-type FL patient populations. In order to obtain accelerated approval, we must demonstrate that tazemetostat provides meaningful therapeutic benefit over existing treatments. In addition, as a condition of accelerated approval, we will need to perform post-marketing confirmatory trials to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoints, and if the studies are unsuccessful, tazemetostat may be subject to withdrawal procedures. In the case of our planned FL submission, if tazemetostat is approved in both EZH2 mutant and wild-type FL patient populations, the FDA could use these post-marketing studies to withdraw our approval if the confirmatory studies fail to demonstrate a clinical benefit.

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

We may not be able to obtain, or may be delayed in obtaining, orphan drug exclusivity for our product candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs 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 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.

We have obtained orphan drug designations for tazemetostat for the treatment of patients with FL, chordoma, malignant rhabdoid tumors, or MRT, soft tissue sarcoma, or STS, and mesothelioma. The orphan drug designation for the treatment of MRT applies to INI1-negative MRT as well as SMARCA4-negative malignant rhabdoid tumor of ovary, or MRTO. We have also obtained orphan drug designations for tazemetostat for the treatment of patients with FL, DLBCL and malignant mesothelioma in Europe. We may not receive orphan drug designation for these product candidates for other indications, or for any other future clinical candidates we may develop.

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 drug for the same indication for that time period. The applicable period is seven years in the United States and ten years in Europe. The exclusivity period in Europe can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug 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 drug to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 18, 2017, 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. In addition, FDARA amended section 505B "Research into pediatric uses for drugs and biological products" of the Federal Food, Drug and Cosmetic Act (21USC 355c). Previously, drugs that had been granted orphan drug designation were exempt from the requirements of the Pediatric Research Equity Act. Under the amended section 505B, beginning on August 17, 2020, the submission of a pediatric assessment, waiver or deferral will be required for certain molecularly targeted cancer indications with the submission of an NDA application or supplement to an NDA application. Under FDARA, products with orphan drug designation that fall under this category will no longer be exempt from the pediatric research requirement. Follicular lymphoma qualifies for an automatic full pediatric waiver by the FDA because it rarely or never occurs in pediatric patients. However, our other indications in development or future product candidates may require a pediatric assessment, which could result in delays in obtaining orphan drug exclusivity and increased costs and delays in obtaining regulatory approval.

A Fast Track designation by the FDA, such as the Fast Track designation we received for tazemetostat, may not lead to a faster development or regulatory review or approval process.

We have announced that we have received Fast Track designation from the FDA for tazemetostat for patients with relapsed or refractory FL, with or without activating EZH2 mutations, relapsed or refractory DLBCL with EZH2 activating mutations, and metastatic or locally advanced epithelioid sarcoma who have progressed on or following an anthracycline-based treatment regimen. We intend to seek Fast Track designation for tazemetostat for other indications and for our other product candidates as appropriate. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track designation. Drugs that have received Fast Track designation from the FDA are eligible for expedited development and priority review, and the opportunity for a rolling review, under certain circumstances. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure that the FDA would decide to grant it. Even if we do receive Fast Track designation, as we have for tazemetostat, we may not experience a faster development process, review or approval compared to conventional FDA procedures. We or the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program.

A breakthrough therapy designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs and biologics that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. Even if we receive breakthrough therapy designation, the receipt of such designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed in those jurisdictions.

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

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union 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 European Union. If no formal withdrawal agreement can be reached between the United Kingdom and the European Union, then it is expected that the United Kingdom's membership of the European Union would automatically terminate on the deadline, which has been extended to October 31, 2019 to allow the parties to negotiate a withdrawal agreement. Such negotiations have proven to be extremely difficult to date. Discussions between the United Kingdom and the European Union will continue to focus on withdrawal issues and transition agreements. However, limited progress to date in these negotiations and ongoing uncertainty within the government of the United Kingdom sustains the possibility of the United Kingdom leaving the European Union 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 European Union directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. 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 European Union 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 European Union for our product candidates, which could significantly and materially harm our business.

If we are required by the FDA to obtain approval of a companion diagnostic in connection with approval of a candidate therapeutic product, and we do not obtain or there are delays in obtaining FDA approval of a diagnostic device, we will not be able to commercialize the product candidate and our ability to generate revenue will be materially impaired.

According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared for that indication. Under the Federal Food, Drug, and Cosmetic Act, companion diagnostics are regulated as medical devices, and the FDA has generally required companion diagnostics intended to select the patients who will respond to cancer treatment to obtain Premarket Approval, or a PMA, for the diagnostic. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. A PMA is not guaranteed and may take considerable time, and the FDA may ultimately respond to a PMA submission with a "not approvable" determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval. As a result, if we are required by the FDA to obtain approval of a companion diagnostic for a candidate therapeutic product, and we do not obtain or there are delays in obtaining FDA approval of a diagnostic device, we may not be able to commercialize the product candidate on a timely basis or at all and our ability to generate revenue will be materially impaired.

Any product candidate for which we obtain marketing approval could be subject to post-marketing 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 products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, 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 manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. As a condition of accelerated approval, the FDA may require a sponsor to perform post-marketing confirmatory study(ies) to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a risk evaluation and mitigation strategy. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure 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 products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

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

- restrictions on such products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;

- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions or the imposition of civil or criminal penalties; or
- litigation involving patients using our products.

Non-compliance with European Union and United Kingdom 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 European Union's and the United Kingdom's requirements regarding the protection of personal information can also lead to significant penalties and sanctions. 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, or 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.

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 products 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 $5,500 to $11,000 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.

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 European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union 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 European Union 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 European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Efforts to ensure that our business with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. We do not have a fully developed compliance program and are in the process of establishing a more robust compliance infrastructure to address our needs in this area. We may fail to establish appropriate compliance measures, and even with a stronger program in place, 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 is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

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

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In March 2010, the U.S. Congress enacted the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the PPACA, a sweeping law which included changes to the coverage and reimbursement of drug products under government healthcare programs.

Among the provisions of the PPACA of importance to our potential product candidates are the following:

- an annual, nondeductible 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 False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- 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;
- requirements to report financial arrangements with physicians and teaching hospitals;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Further, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. In January 2013, the American Taxpayer Relief Act of 2012 became law, which, among other things, reduced Medicare payments to several 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.

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.

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

The Trump administration has also taken executive actions to undermine or delay implementation of the PPACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. One Executive Order directs federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA 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 PPACA. Several state Attorneys General filed suit to stop the Trump administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. In addition, Centers for Medicare & Medicaid Services, or CMS, has 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 PPACA 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, or PA, and step therapy, or 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 will be accepted, and if so, what effect such changes will have on our business. 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 PPACA 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 PPACA marketplace, providers, and potentially our business, are not yet known.

Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the PPACA is an essential and inseverable feature of the PPACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the PPACA 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 has recently represented to the Court of Appeals considering this judgment that it does not oppose the district court's ruling. It is unclear how this decision and any subsequent appeals and other efforts to repeal and replace the PPACA will impact the PPACA and our business. Litigation and legislation over the PPACA are likely to continue, with unpredictable and uncertain results.

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 Trump 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 Trump administration issued a plan to lower drug prices. Under this blueprint for action, the Trump 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 drugs could be negotiated for a lower price by Medicare Part D plans, and improving 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.

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 Trump administration have stated that they will address such costs through new legislative and administrative measures.

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

Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. 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 candidate 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, or our business could be harmed, possibly materially.

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 harm 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 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 for failure to comply with such laws and regulations.

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. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. 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, standards 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.

Our internal information systems, or those of any collaborators, contractors, consultants, vendors, business partners or other third parties, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

We collect, store and transmit large amounts of confidential information, including personal information and information relating to intellectual property, on internal information systems and through the information systems of our collaborators, contractors, consultants, vendors, business partners or other third parties.

Despite the implementation of security measures, our internal information systems and those of third parties are vulnerable to damage from computer viruses, malware, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, our collaborators, contractors, consultants, vendors, business partners and other third parties, or from cyber-attacks by malicious third parties over the Internet or through other mechanisms. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, ransomware, denial of service attacks, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. Cyber-attacks also could include phishing attempts or e-mail fraud to cause payments or information to be transmitted to an unintended recipient.

While we have not experienced any such material system failure, accident, cyber-attack or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs, clinical trials and business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions, in addition to possibly requiring substantial expenditures of resources to remedy. For example, the loss of clinical trial data from clinical trials could result in delays or termination of our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, as risks with respect to our information systems continue to evolve, we will incur additional costs to maintain the security of our information systems and comply with evolving laws and regulations pertaining to cybersecurity and related areas. 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, including regulatory fines and other losses with respect to privacy claims, enrollment in our clinical trials could be negatively affected, our competitive position and reputation could be harmed and the further development and commercialization of our product candidates could be delayed.

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on the research and development, clinical and business expertise of our executive officers as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment letter agreements with our executive officers, each of them may terminate their employment with us at any time. For instance, since January 1, 2017, our former Executive Vice President and Chief Financial Officer, our former Chief Business Officer, our former President of Research and Chief Scientific Officer, and our former Executive Vice President and Chief Medical Officer have terminated their employment with us. We do not maintain “key person” insurance for any of our executives or other employees.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies, universities and research institutions for similar personnel. 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 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. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and implement sales, marketing and distribution 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, if any of our product candidates receives marketing approval, sales, marketing and distribution. 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 expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Our Common Stock

Provisions in our corporate charter documents, under Delaware law and in our collaboration agreements could make an acquisition of our company, 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 certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their 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 only one of three classes of directors is elected each year;
- 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 our board of directors;
- 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 “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 specified provisions of our certificate of incorporation 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.

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 sell their shares at all. Any 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 has been and may in the future be volatile and fluctuate substantially.

Our stock price has been and may in the future be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. From January 1, 2018 until July 31, 2019, the sale price of our common stock as reported on the Nasdaq Global Select Market ranged from a high of $21.40 to a low of $5.14. The market price for our common stock may be influenced by many factors, including:

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

We have broad discretion over the use of our cash and cash equivalents and may not use them effectively.

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

The Tax Cuts and Jobs Act of 2017 could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act of 2017, which significantly revised the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. 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.

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

As a public company, and particularly now that we are no longer an emerging growth company as of January 1, 2019, we will continue to incur significant legal, accounting and other expenses. 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. Our management and other personnel will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and make some activities more time-consuming and costly.

We cannot predict or estimate the amount of additional costs we may incur to continue to operate as a public company, nor can we predict the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. Now that we are no longer an emerging growth company, we are also required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we have and will need to continue to dedicate internal resources, engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. If we or our auditors identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be 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.

If securities or industry analysts do not continue to publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock may be impacted, in part, by the research and reports that securities or industry analysts publish about us or our business. There can be no assurance that analysts will cover us, continue to cover us or provide favorable coverage. If one or more analysts downgrade our stock or change their opinion of our stock, our share price may decline. In addition, if one or more analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which could cause our share price or trading volume to decline.

There is no public market for our series A convertible preferred stock.

There is no established public trading market for our series A convertible preferred stock, and we do not expect a market to develop. In addition, we do not intend to apply for listing of the series A convertible preferred stock on any national securities exchange or other nationally recognized trading system. Without an active market, the liquidity of the series A convertible preferred stock will be limited.

Item 6. Exhibits

The exhibits filed as part of this Quarterly Report on Form 10-Q are as follows:

Exhibit Number	Description of the Exhibit
10.1	Employment Offer Letter between the Company and Paolo Tombesi, dated July 1, 2019.(1)
10.2	Non-Employee Director Compensation Program.(1)
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.(1)
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.(1)
32.1	Certifications pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002, by Robert B. Bazemore, President and Chief Executive Officer of the Company, and Matthew Ros, Principal Financial Officer of the Company.(1)
101.INS	XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.
101.SCH	XBRL Schema Document.
101.CAL	XBRL Calculation Linkbase Document.
101.LAB	XBRL Labels Linkbase Document.
101.PRE	XBRL Presentation Linkbase Document.
101.DEF	XBRL Definition Linkbase Document.

(1) Filed with this Form 10-Q.

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.

Dated: August 9, 2019

EPIZYME, INC.

By: /s/ Matthew Ros
Matthew Ros
Chief Strategy & Business Officer
(Principal Financial Officer)

July 1, 2019

Mr. Paolo Tombesi
(delivered via email)

Dear Paolo:

It is my pleasure to extend to you this offer of employment with Epizyme, Inc. (the "Company"). I am pleased to set forth below the terms of your employment with the Company:

1. **Employment.** You will be employed to serve on a full-time basis as the Company's Chief Financial Officer, commencing on a date on or around August 19, 2019, as may be mutually agreed by you and the Company (such date being the "Start Date"). As Chief Financial Officer, you will be responsible for such duties as are consistent with such position, plus such other duties as may from time to time be assigned to you by the Company. You shall report to me and you agree to devote your full business time, best efforts, skill, knowledge, attention and energies to the advancement of the Company's business and interests and to the performance of your duties and responsibilities as an employee of the Company. You agree to abide by the rules, regulations, instructions, personnel practices and policies of the Company and any changes therein that may be adopted from time to time by the Company.

2. **Base Salary.** Your base salary will be at the rate of $18,958.33 per semi-monthly pay period (which if annualized equals $455,000), less all applicable taxes and withholdings, to be paid in installments in accordance with the Company's regular payroll practices. Such base salary may be adjusted from time to time in accordance with normal business practices and in the sole discretion of the Company.

3. **Discretionary Bonus.** Following the end of each fiscal year and subject to the approval of the Company's Board of Directors or a committee of the Board of Directors (the "Board"), you may be eligible for a retention and performance bonus, based on your performance and the Company's performance during the applicable fiscal year, as determined by the Company in its sole discretion. Your target bonus is 40% of your annualized base salary. Such target bonus may be adjusted from time to time in accordance with normal business practices and in the sole discretion of the Company. You must be an active employee of the Company on the date any bonus is

distributed in order to be eligible for and to earn a bonus award, as it also serves as an incentive to remain employed by the Company.

4. **Equity.** On your Start Date, you will receive a stock option grant under the Company's 2013 Stock Incentive Plan (the "Plan") for the purchase of 132,225 shares of common stock of the Company at an exercise price per share equal to the fair market value of one share of Common Stock on the date of the grant as determined by the Company in its sole discretion. The stock option grant shall be subject to all terms and other provisions set forth in the Plan and in a separate stock option agreement, including the vesting schedule. The stock option agreement will provide that the option will vest over a four-year period with the first quarter of the underlying shares vesting on the first anniversary of the Start Date and the remaining three-fourths of the underlying shares vesting monthly in 36 equal monthly installments following the first anniversary of the Start Date until fully vested on the fourth anniversary of the Start Date.

   In addition, you will receive a restricted stock unit award under the Plan with respect to 28,217 shares of common stock of the Company. Each restricted stock unit represents the right to receive one share of common stock of the Company upon vesting. The restricted stock units shall be subject to all terms and other provisions set forth in the Plan and in a separate restricted stock unit agreement, including the vesting schedule. The restricted stock unit agreement will provide that the restricted stock units will vest over a four-year period with one quarter of such restricted stock units vesting annually on the anniversary date of the restricted stock unit grant.

   You will also receive a restricted stock unit award under the Plan and as set forth in the "RSU Rewards Program" with respect to 16,000 shares of common stock of the Company (the "Performance RSUs"). The Performance RSUs will be subject to all terms and other provisions set forth in the Plan and in a separate restricted stock unit agreement, including vesting schedule. The vesting schedule will detail the milestones and projected associated timeframes.

   You may also be eligible for other grants of stock or stock options as determined by and in the sole discretion of the Board. Nothing in this section shall affect your status as an employee at will, as set forth below.

5. **Relocation.** You will also receive a one-time payment of $100,000 for relocation expenses on the first payroll after the Start Date, less all applicable taxes and withholdings. If you resign from the Company voluntarily for any reason or are terminated by the Company for Cause (as defined under the Company's Executive Severance and Change in Control Plan) on or prior to the first anniversary of the Start Date, you will be responsible to repay to the Company 100% of the relocation one-time payment ($100,000) less applicable taxes. We will provide temporary corporate housing through December 2019, prior to your actual move to the greater Boston area in order to facilitate your relocation. Expenses for travel from and to your present residence in New Jersey to the greater Boston area will be reimbursed or provided

during the time period of temporary corporate housing. Any taxes that may be associated with travel, hotel, and temporary housing benefit will be paid on your behalf by the Company. Any amounts owed by you to the Company under this Section 5 as a result of you ceasing to be an employee of the Company shall be repaid within 60 days of the date you cease to be an employee of the Company, and the Company shall have the right to offset such amounts against any amounts it owes you under this letter, the Company's Executive Severance and Change in Control Plan or otherwise.

6. **Benefits.** You may participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, provided that you are eligible under (and subject to all provisions of) the plan documents that govern those programs. Benefits are subject to change at any time in the Company's sole discretion.

7. **Vacation.** You will be eligible for a maximum of three (3) weeks of paid vacation per calendar year to be taken at such times as may be approved in advance by the Company. The number of vacation days for which you are eligible shall accrue at the rate of 1.25 days per month that you are employed during such calendar year. Your accrual and use of vacation time will be pursuant to Company policy, as established and as may be modified in the sole discretion of the Company from time to time.

8. **Invention, Non-Disclosure, Non-Competition and Non-Solicitation Obligations.** In exchange for your employment with the Company pursuant to the terms and conditions herein, you hereby acknowledge and affirm your obligations set forth in the enclosed Invention and Non-Disclosure Agreement to be executed for the benefit of the Company, which obligations remain in full force and effect and is a condition to your employment with the Company.

9. **At-Will Employment.** This letter shall not be construed as an agreement, either express or implied, to employ you for any stated term, and shall in no way alter the Company's policy of employment at-will, under which both the Company and you remain free to end the employment relationship for any reason, at any time, with or without cause or notice. Similarly, nothing in this letter shall be construed as an agreement, either express or implied, to pay you any compensation or grant you any benefit beyond the end of your employment with the Company, except as otherwise explicitly set forth herein. This letter supersedes all prior understandings, whether written or oral, relating to the terms of your employment.

10. **Severance Benefits.** In recognition of your position with and value to the Company, and to provide you with assurance in the event of certain employment terminations, you have been selected to participate in the Company's Executive Severance and Change in Control Plan, as amended from time to time, a copy of which is enclosed with this letter.

If this letter correctly sets forth the terms under which you will be employed by the Company, please sign and return to me (via hard copy or scanned copy), no later than July 8, 2019, the enclosed duplicate of this letter and the Invention and Non-Disclosure Agreement.

Sincerely,

By: 

Robert Bazemore
President and Chief Executive Officer

The foregoing correctly sets forth the terms of my at-will employment with Epizyme, Inc. I am not relying on any representations other than those set forth above.

_____ _____

Paolo Tombesi Date

Exhibit 10.2

EPIZYME, INC.

Non-Employee Director Compensation Program

Under Epizyme, Inc.'s (the "Company") director compensation program, the Company pays its non-employee directors retainers in cash. Each non-employee director receives a cash retainer for service on the board of directors and for service on each committee on which the director is a member, as well as additional fees for service as chairman of the board or chairman of each committee. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter and are as follows:

	Member Annual Fee	Chairman Additional Annual Fee
Board of Directors	$ 40,000	$ 35,000
Audit Committee	$ 7,500	$ 15,000
Compensation Committee	$ 6,250	$ 12,500
Nominating and Corporate Governance Committee	$ 4,500	$ 9,000

The Company also reimburses its non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending its board of director and committee meetings.

The Company's non-employee director compensation program also includes a stock-for-fees policy, under which directors have the right to elect to receive common stock in lieu of cash fees. Any common stock issued pursuant to the stock-for-fees program will be issued as a fully vested stock award under the Company's 2013 Stock Incentive Plan on the last day of each fiscal quarter (the date on which cash fees are paid). The number of shares to be issued to a director will be determined by dividing the cash fees for which the director has elected to receive common stock, by the closing price of the common stock on the last trading day of the quarter.

In addition, under the Company's director compensation program, each non-employee director receives, upon his or her initial election to its board of directors, an option to purchase the number of shares of the Company's common stock that have a Black-Scholes value as of the date of grant equal to $300,000; provided, that, in no event shall the number of shares of common stock issuable upon any such initial election exceed 50,000. Each of these options will vest as to 25% of the shares of common stock underlying such option on the one-year anniversary of the grant date and as to an additional 2.0833% of the shares of common stock underlying such option at the end of each successive month following the first anniversary of the grant date until the fourth anniversary of the grant date, subject to the non-employee director's continued service as a director. Further, under the Company's director compensation program, on the date of each annual meeting of stockholders, each non-employee director that had served on its board of directors for at least six months will receive an option to purchase the number of shares of Company's common stock that have a Black-Scholes value as of the date of grant equal to $150,000; provided, that, in no year shall the number of shares of common stock issuable upon such option exceed 25,000. Each of these options will vest in full on the one-year anniversary of the grant date, subject to the non-employee director's continued service as a director. All options issued to the Company's non-employee directors under its director compensation program will become exercisable in full upon a change in control of the Company. The exercise price of these options will be equal to the fair market value of the Company's common stock on the date of grant.

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO RULE 13a-14(a) / RULE 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

I, Robert B. Bazemore, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Epizyme, 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 9, 2019

/s/ Robert B. Bazemore

Robert B. Bazemore
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO RULE 13a-14(a) / RULE 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

I, Matthew Ros, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of Epizyme, 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 9, 2019

/s/ Matthew Ros

Matthew Ros
Chief Strategy & Business Officer

Exhibit 32.1

**CERTIFICATIONS OF CEO AND CFO PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

In connection with this Quarterly Report on Form 10-Q of Epizyme, Inc. (the "Company") for the period ended June 30, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned, Robert B. Bazemore, President and Chief Executive Officer of the Company, and Matthew Ros, Chief Strategy & Business Officer, hereby certifies, pursuant to 18 U.S.C. (section) 1350, as adopted pursuant to (section) 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

(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.

Dated: August 9, 2019

/s/ Robert B. Bazemore

Robert B. Bazemore
President and Chief Executive Officer
(Principal Executive Officer)

/s/ Matthew Ros

Matthew Ros
Chief Strategy & Business Officer
(Principal Financial Officer)