

Epizyme, Inc.  
Form 10-Q  
August 07, 2017  
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**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, 2017**

**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**  
**(State or other jurisdiction of**  
**incorporation or organization)**

**26-1349956**  
**(I.R.S. Employer**  
**Identification No.)**

**400 Technology Square, Cambridge, Massachusetts**  
**(Address of principal executive offices)**

**02139**  
**(Zip code)**

**617-229-5872**

**(Registrant's telephone number, including area code)**

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See 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 (Do not check if a smaller reporting company)

Smaller reporting company

Emerging growth company

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

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

The number of shares outstanding of the registrant's common stock as of August 1, 2017: 58,466,534 shares.



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**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, 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 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 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,

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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 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 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, 2016, or our Annual Report. The three months ended June 30, 2017 and 2016 are referred to as the second quarter of 2017 and 2016, respectively. Unless the context indicates otherwise, all references herein to our company include our wholly-owned subsidiary.

**Table of Contents****PART I FINANCIAL INFORMATION****Item 1. Financial Statements****EPIZYME, INC.****CONDENSED CONSOLIDATED BALANCE SHEETS (UNAUDITED)****(Amounts in thousands except per share data)**

	<b>June 30, 2017</b>	<b>December 31, 2016</b>
<b>ASSETS</b>		
Current Assets:		
Cash and cash equivalents	\$ 88,529	\$ 77,895
Marketable securities	104,475	164,297
Accounts receivable	25	23
Prepaid expenses and other current assets	8,631	6,457
Total current assets	201,660	248,672
Property and equipment, net	2,985	3,124
Restricted cash and other assets	665	645
Total Assets	\$ 205,310	\$ 252,441
<b>LIABILITIES AND STOCKHOLDERS EQUITY</b>		
Current Liabilities:		
Accounts payable	\$ 9,594	\$ 4,994
Accrued expenses	16,143	16,007
Current portion of capital lease obligation	427	620
Other current liabilities	15	
Total current liabilities	26,179	21,621
Capital lease obligation, net of current portion		110
Deferred revenue, net of current portion	28,809	28,809
Other long-term liabilities	282	201
Commitments and contingencies		
Stockholders Equity:		
Common stock \$0.0001 par value; 125,000 shares authorized; 58,433 shares and 58,050 shares issued and outstanding, respectively	6	6
Additional paid-in capital	564,428	555,473
Accumulated other comprehensive loss	(60)	(106)
Accumulated deficit	(414,334)	(353,673)
Total stockholders equity	150,040	201,700

Total Liabilities and Stockholders	Equity	\$ 205,310	\$ 252,441
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See notes to consolidated financial statements.



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

	<b>Three Months Ended June 30,</b>		<b>Six Months Ended June 30,</b>	
	<b>2017</b>	<b>2016</b>	<b>2017</b>	<b>2016</b>
Collaboration revenue	\$ 10,000	\$ 473	\$ 10,000	\$ 945
Operating expenses:				
Research and development	27,292	21,450	51,987	39,190
General and administrative	11,170	7,424	19,439	13,270
<b>Total operating expenses</b>	<b>38,462</b>	<b>28,874</b>	<b>71,426</b>	<b>52,460</b>
Loss from operations	(28,462)	(28,401)	(61,426)	(51,515)
Other income, net:				
Interest income, net	428	404	866	624
Other income	10	16	14	31
Other income, net	438	420	880	655
<b>Net loss</b>	<b>\$ (28,024)</b>	<b>\$ (27,981)</b>	<b>\$ (60,546)</b>	<b>\$ (50,860)</b>
Other comprehensive income (loss):				
Unrealized gain on available for sale securities	34	25	46	25
<b>Comprehensive loss</b>	<b>\$ (27,990)</b>	<b>\$ (27,956)</b>	<b>\$ (60,500)</b>	<b>\$ (50,835)</b>
Loss per share allocable to common stockholders:				
Basic	\$ (0.48)	\$ (0.49)	\$ (1.04)	\$ (0.90)
Diluted	\$ (0.48)	\$ (0.49)	\$ (1.04)	\$ (0.90)
Weighted average shares outstanding:				
Basic	58,377	57,352	58,298	56,250
Diluted	58,377	57,352	58,298	56,250

See notes to consolidated financial statements.

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## EPIZYME, INC.

## CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS (UNAUDITED)

(Amounts in thousands)

	<b>Six Months Ended, June 30,</b>	
	<b>2017</b>	<b>2016</b>
<b>CASH FLOWS FROM OPERATING ACTIVITIES:</b>		
Net loss	\$ (60,546)	\$ (50,860)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	824	791
Stock-based compensation	5,778	5,126
Amortization of discount on investments	(69)	(27)
Changes in operating assets and liabilities:		
Accounts receivable	(2)	202
Prepaid expenses and other current assets	(1,947)	(3,095)
Accounts payable	4,600	(980)
Accrued expenses	138	(393)
Deferred revenue		(944)
Restricted cash and other assets	(20)	116
Other liabilities	96	(86)
<b>Net cash used in operating activities</b>	<b>(51,148)</b>	<b>(50,150)</b>
<b>CASH FLOWS FROM INVESTING ACTIVITIES:</b>		
Purchases of available for sale securities	(80,846)	(199,441)
Maturities of available for sale securities	140,552	
Purchases of property and equipment	(683)	(319)
<b>Net cash provided by (used in) investing activities</b>	<b>59,023</b>	<b>(199,760)</b>
<b>CASH FLOWS FROM FINANCING ACTIVITIES:</b>		
Payment under capital lease obligation	(303)	(274)
Proceeds from public offering, net of commissions	1,587	130,067
Proceeds from stock options exercised	1,128	1,498
Issuance of shares under employee stock purchase plan	347	150
Payment of public offering costs		(374)
<b>Net cash provided by financing activities</b>	<b>2,759</b>	<b>131,067</b>
Net increase (decrease) in cash and cash equivalents	10,634	(118,843)
Cash and cash equivalents, beginning of period	77,895	208,323
Cash and cash equivalents, end of period	\$ 88,529	\$ 89,480

**SUPPLEMENTAL CASH FLOW INFORMATION:**

Purchases of property and equipment unpaid at period end	\$		\$
Unrealized gain on investments	\$	46	\$
Cumulative catch up related to the adoption of ASU 2016-09 (Note 2)	\$	115	\$

See notes to consolidated financial statements.

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**Table of Contents****EPIZYME, INC.****NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS (UNAUDITED)****1. Overview**

Epizyme, Inc. (collectively referred to with its wholly owned, controlled subsidiary, Epizyme Securities Corporation, as "Epizyme" or the "Company") is a clinical stage biopharmaceutical company that discovers, develops and plans to commercialize novel epigenetic therapies for patients with cancer and other diseases. The Company's lead product candidate, tazemetostat, is a potent and selective inhibitor of EZH2, an enzyme that plays an important role in various cancers. The Company owns the global development and commercialization rights to tazemetostat outside of Japan. Eisai Co. Ltd. ("Eisai") holds the rights to develop and commercialize tazemetostat in Japan, and holds a limited right of first negotiation for the rest of Asia.

The Company has additional programs in development, including pinometostat, a clinical program that is subject to a collaboration with Celgene Corporation and Celgene RIVOT Ltd., an affiliate of Celgene Corporation ("Celgene") (refer to Note 8, *Collaborations*), three preclinical programs for small molecule histone methyltransferase, or HMT, inhibitors that are subject to a collaboration with Celgene, one clinical and two preclinical programs for small molecule HMT inhibitors that are subject to a collaboration with Glaxo Group Limited, an affiliate of GlaxoSmithKline ("GSK") (refer to Note 8, *Collaborations*), and multiple novel targets for which the Company retains worldwide global development and commercialization rights.

Through June 30, 2017, the Company has raised an aggregate of \$740.3 million to fund its operations, of which \$217.8 million was non-equity funding through its collaboration agreements, \$446.5 million was from the sale of common stock in the Company's public offerings, which includes \$1.6 million during the six months ended June 30, 2017 and \$76.0 million 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, 2017, the Company had \$193.0 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 \$414.3 million through June 30, 2017, and will require substantial additional capital to fund its research and development. 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 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 ("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, 2016 (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 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, 2017 and 2016 are referred to as the second quarter of 2017 and 2016, 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.

***Significant Accounting Policies***

There have been no material changes to the Company's significant accounting policies during the six months ended June 30, 2017, 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.

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**Table of Contents*****Recent Accounting Pronouncements***

In May 2014, the Financial Accounting Standards Board ( FASB ) issued Accounting Standards Update ( ASU ) 2014-09, *Revenue From Contracts With Customers*. ASU 2014-09 amends Accounting Standards Codification ( ASC ) 605, *Revenue Recognition*, by outlining a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers. In addition, the FASB recently issued ASUs 2016-10 and 2016-12, which provide clarifying amendments to ASU 2014-09. ASU 2014-09 and its related amendments will be effective for the Company for interim and annual periods beginning after December 15, 2017. The Company expects to adopt ASU 2014-09, as amended, effective January 1, 2018. The Company plans on utilizing the modified retrospective approach to implement this standard and is in the process of evaluating its collaboration agreements with Celgene, GSK and Eisai (as the Eisai agreement relates to the receipt of royalties on the sale of any EZH2 product in Japan) to determine the impact the adoption of this standard may have on its consolidated financial statements and internal control over financial reporting.

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 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 with early adoption permitted. The Company is currently evaluating the potential changes to the Company's future financial reporting and disclosures that may result from adopting this ASU.

In August 2016, the FASB issued ASU 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments*. The new standard clarifies certain aspects of the statement of cash flows, including the classification of debt prepayment or debt extinguishment costs, settlement of zero-coupon debt instruments or other debt instruments with coupon interest rates that are insignificant in relation to the effective interest rate of the borrowing, contingent consideration payments made after a business combination, proceeds from the settlement of insurance claims, proceeds from the settlement of corporate-owned life insurance policies, distributions received from equity method investees and beneficial interests in securitization transactions. The new standard also clarifies that an entity should determine each separately identifiable source or use within the cash receipts and cash payments on the basis of the nature of the underlying cash flows. In situations in which cash receipts and payments have aspects of more than one class of cash flows and cannot be separated by source or use, the appropriate classification should depend on the activity that is likely to be the predominant source or use of cash flows for the item. The new standard will be effective for the Company on January 1, 2018. The adoption of this standard is not expected to have a material impact on the Company's consolidated statements of cash flows.

In November 2016, the FASB issued ASU 2016-18, *Restricted Cash*, or ASU 2016-18, which requires an entity to reconcile and explain the period-over-period change in total cash, cash equivalents and restricted cash within its statements of cash flows. ASU 2016-18 is effective for fiscal years, and interim periods within, beginning after December 15, 2017. Early adoption is permitted. A reporting entity must apply the amendments in ASU 2016-18 using a full retrospective approach. The Company is currently evaluating the impact the adoption of the ASU will have on its consolidated financial statements.

In May 2017, the FASB issued ASU 2017-09, *Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting*, which clarifies when to account for a change to the terms or conditions of a share-based payment award as a modification. The new standard does not change the accounting for modifications but clarifies that modification accounting guidance should only be applied if the fair value, vesting conditions, or classification of the award changes as a result of the change in terms or conditions. The new standard is effective for fiscal years, and interim periods within, beginning after December 15, 2017. Early adoption is permitted. A reporting entity must apply the amendments in the ASU prospectively to an award modified on or after the adoption date. The Company is currently evaluating the impact the adoption of the ASU will have on its consolidated financial statements.

***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 security balances. After considering the Company's current research and development plans 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, 2017, 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.



**Table of Contents****Share-Based Payment**

As of January 1, 2017, the Company adopted ASU 2016-09, *Improvements to Employee Share-Based Payment Accounting*. The standard revised the accounting for share-based compensation arrangements, including the accounting for income taxes, forfeitures, and statutory tax withholding requirements, as well as classification in the statement of cash flows. Under this guidance, a company recognizes all excess tax benefits and tax deficiencies as income tax expense or benefit in the income statement when the awards vest or are settled. The amendments also removed the requirement to delay the recognition of an excess tax benefit until it reduces current taxes payable. In addition, cash flows related to excess tax benefits will no longer be separately classified as a financing activity apart from other income tax cash flows. The standard also allows the Company to repurchase more of an employee's shares for tax withholding purposes without triggering liability accounting, clarifies that all cash payments made on an employee's behalf for withheld shares should be presented as a financing activity on the cash flows statement, and provides an accounting policy election to account for forfeitures as they occur. Upon adoption, the Company recognized previously unrecognized excess tax benefits using the modified retrospective transition method, which increased deferred tax assets and the valuation allowance by \$25.7 million and charged \$0.1 million to retained earnings, with a corresponding credit to additional paid-in-capital related to the Company's election to account for forfeitures as they occur. The adoption of the standard did not materially impact the Company's stock-based compensation expense.

**3. Marketable Securities**

The following table summarizes the available for sale securities held at June 30, 2017 (in thousands):

<b>Description</b>	<b>Amortized Cost</b>	<b>Unrealized Gains</b>	<b>Unrealized Losses</b>	<b>Fair Value</b>
Commercial paper	\$ 43,570	\$	\$ (17)	\$ 43,553
Corporate notes	57,973		(43)	57,930
U.S. government agency securities and U.S. Treasuries	2,992			2,992
Total	\$ 104,535	\$	\$ (60)	\$ 104,475

The following table summarizes the available for sale securities held at December 31, 2016 (in thousands):

<b>Description</b>	<b>Amortized Cost</b>	<b>Unrealized Gains</b>	<b>Unrealized Losses</b>	<b>Fair Value</b>
Commercial paper	\$ 68,407	\$	\$ (32)	\$ 68,375
Corporate notes	70,489		(81)	70,408
U.S. government agency securities and U.S. Treasuries	25,507	7		25,514
Total	\$ 164,403	\$ 7	\$ (113)	\$ 164,297

The amortized cost of available for sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At June 30, 2017, 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 and six months ended June 30, 2017, 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, 2017 was \$88.4 million. The aggregate unrealized loss for those securities in an unrealized loss position for less than twelve months as of June 30, 2017 was \$0.1 million. 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, 2017. The weighted average maturity of the Company's portfolio was approximately two months at June 30, 2017.

#### **4. Fair Value Measurements**

The Company's financial instruments as of June 30, 2017 and December 31, 2016 consisted primarily of cash and cash equivalents, marketable securities and accounts receivable and accounts payable. As of June 30, 2017 and December 31, 2016, the Company's financial assets recognized at fair value consisted of the following:

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	<b>Fair Value as of June 30, 2017</b>			
	<b>Total</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
	<b>(In thousands)</b>			
Cash equivalents	\$ 63,592	\$ 52,054	\$ 11,538	\$
Marketable securities:				
Commercial paper	43,553		43,553	
Corporate notes	57,930		57,930	
U.S. government agency securities and treasuries	2,992		2,992	
<b>Total</b>	<b>\$ 168,067</b>	<b>\$ 52,054</b>	<b>\$ 116,013</b>	<b>\$</b>

	<b>Fair Value as of December 31, 2016</b>			
	<b>Total</b>	<b>Level 1</b>	<b>Level 2</b>	<b>Level 3</b>
	<b>(In thousands)</b>			
Cash equivalents	\$ 62,854	\$ 59,862	\$ 2,992	\$
Marketable securities:				
Commercial paper	68,375		68,375	
Corporate notes	70,408		70,408	
U.S. government agency securities and treasuries	25,514		25,514	
<b>Total</b>	<b>\$ 227,151</b>	<b>\$ 59,862</b>	<b>\$ 167,289</b>	<b>\$</b>

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 cash equivalents that the Company classifies within Level 1 of the fair value hierarchy are classified within Level 1 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 some cash equivalents.

**5. Supplemental Balance Sheet Information**

Accrued expenses consisted of the following:

	<b>June 30, 2017</b>	<b>December 31, 2016</b>
	<b>(In thousands)</b>	
Employee compensation and benefits	\$ 3,165	\$ 4,100
Research and development expenses	9,200	10,925
Professional services and other	3,778	982

Accrued expenses	\$ 16,143	\$ 16,007
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## 6. Income Taxes

The Company did not record a federal or state income tax provision or benefit for the three and six months ended June 30, 2017 and 2016 due to the expected loss before income taxes to be incurred for the years ended December 31, 2017 and 2016, as well as the Company's continued maintenance of a full valuation allowance against its net deferred tax assets.

## 7. 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, 2017, as compared to those disclosed in Note 7, *Commitments and Contingencies*, included in its Annual Report, except as summarized below.

A \$1.5 million payment obligation was incurred and paid in the six months ended June 30, 2017 upon the achievement of a milestone under the companion diagnostic agreement with Roche Molecular Systems, Inc. ( Roche Molecular ).

**Table of Contents***Lease*

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 (the *Lease* ) with ARE-TECH Square, LLC, a Delaware limited liability company (the *Landlord* ) with a term that originally continued through May 31, 2018, which included an 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 (the *Third Amendment* ) with the Landlord, and a Fourth Amendment to Lease with the Landlord (the *Fourth Amendment*, and, together with the Third Amendment, the *Amendments* ). The Amendments each amend the Lease.

Under the Amendments, the Company extended the term of the Lease at the Company's headquarters in Cambridge, Massachusetts to November 30, 2022, subject to the Company's 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. Under the Lease, 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 and annual increases December 1 of each subsequent year until December 1, 2021.

Under the Lease as amended by the Amendments, the Company is responsible for aggregate minimum rent payments of \$18.6 million, of which approximately \$0.5 million was paid prior to June 30, 2017. The remaining future minimum rent payments from July 1, 2017 through November 30, 2022 are as follows (in thousands):

July 1, 2017 - December 31, 2017	\$ 1,384
2018	3,074
2019	3,335
2020	3,435
2021	3,538
2022	3,332
<b>Total</b>	<b>\$ 18,098</b>

**8. Collaborations***Celgene*

In April 2012, the Company entered into a collaboration and license agreement with 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 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, 2017. 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 (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.

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*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 (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 (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.

#### *Collaboration Revenue*

Through June 30, 2017, the Company has recognized \$74.3 million of total collaboration revenue since the inception of the collaboration, including \$0.5 million and \$0.9 million in the three and six months ended June 30, 2016, respectively. No revenue from the collaboration was earned in the three and six months ended June 30, 2017. The Company recognized total global development co-funding as a reduction to research and development expense of less than \$0.1 million in the three months ended June 30, 2016. No global development co-funding was recognized in the three months ended June 30, 2017. The Company recognized total global development co-funding as a reduction to research and development expense of less than \$0.1 million in the six months ended June 30, 2017 and 2016. As of both June 30, 2017 and December 31, 2016, the Company had deferred revenue of \$28.8 million related to this agreement.



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**Table of Contents*****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. 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 recorded 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 \$31.0 million of preclinical research and development milestone payments, which includes a \$10.0 million milestone payment earned in May 2017 upon GSK's initiation of good laboratory practices toxicology studies for a first-in-class methyltransferase inhibitor discovered by the Company and licensed to GSK and paid in the three months ended June 30, 2017. As of June 30, 2017, the Company was eligible to receive up to \$8.0 million in additional preclinical research and development milestone payments, up to \$103.0 million in clinical development milestone payments, up to \$278.0 million in regulatory milestone payments and up to \$218.0 million in sales-based milestone payments. 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. Due to the varying stages of development of each licensed target, the Company is not able to determine the next milestone that might be achieved under this agreement, if any. 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, 2017, the Company has earned a total of \$69.0 million under the GSK agreement, which the Company recognized as collaboration revenue in the condensed consolidated statements of operations and comprehensive loss. The Company recognized \$10.0 million of collaboration revenue in the three months ended June 30, 2017 related to achievement of the milestone described in the preceding paragraph. The Company did not have any deferred revenue related to this agreement as of June 30, 2017 or December 31, 2016 and any future revenues will relate to any milestone payments and royalties received under the agreement, if any.

***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. As of June 30, 2017, the Company is responsible for the remaining development costs of \$10.5 million due under the agreement. The Company expects the remaining development costs under the agreement to be incurred and paid through 2019.

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.

**Table of Contents****9. Stock-Based Compensation**

Total stock-based compensation expense related to stock options, restricted stock units and the employee stock purchase plan was \$3.0 million and \$2.8 million for the three months ended June 30, 2017 and 2016, respectively, and \$5.8 million and \$5.1 million for the six months ended June 30, 2017 and 2016, respectively.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
	(In thousands)			
Research and development	\$ 1,509	\$ 1,366	\$ 2,901	\$ 2,613
General and administrative	1,512	1,387	2,877	2,513
<b>Total</b>	<b>\$ 3,021</b>	<b>\$ 2,753</b>	<b>\$ 5,778</b>	<b>\$ 5,126</b>

**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 \$10.13 and \$7.27 per option for those options granted during the three months ended June 30, 2017 and 2016, respectively, and \$8.54 and \$6.43 per option for those options granted during the six months ended June 30, 2017 and 2016, respectively. Key assumptions used to apply this pricing model were as follows:

	Three Months Ended June 30		Six Months Ended June 30	
	2017	2016	2017	2016
Risk-free interest rate	1.8%	1.3%	1.8%	1.2%
Expected life of options	6 years	6 years	6 years	6 years
Expected volatility of underlying stock	74.4%	79.0%	74.5%	78.9%
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, 2017:

	Number of Options (In thousands)	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Outstanding at December 31, 2016	4,059	\$ 14.32		
Granted	1,860	12.99		

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Exercised	(181)	6.24		
Forfeited or expired	(631)	12.62		
Outstanding at June 30, 2017	5,107	\$ 14.33	8.19	\$ 16,501
Exercisable at June 30, 2017	1,763	\$ 16.74	6.55	\$ 6,191

As of June 30, 2017, there was \$27.7 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 2.9 years.

**Table of Contents****Restricted Stock Units**

The following is a summary of restricted stock unit activity for the six months ended June 30, 2017:

	Number of Units (in thousands)	Weighted Average Grant Date Fair Value per Unit
Outstanding at December 31, 2016	64	\$ 12.20
Granted		
Vested	(15)	12.20
Outstanding at June 30, 2017	49	\$ 12.20

As of June 30, 2017, there was \$0.6 million of unrecognized compensation cost related to restricted stock units that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 1.6 years.

**10. 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,	
	2017	2016	2017	2016
	(In thousands except per share data)			
Net loss	\$ (28,024)	\$ (27,981)	\$ (60,546)	\$ (50,860)
Weighted average shares outstanding	58,377	57,352	58,298	56,250
Basic and diluted loss per share allocable to common stockholders	\$ (0.48)	\$ (0.49)	\$ (1.04)	\$ (0.90)

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,	
	2017	2016	2017	2016
	(In thousands)			
Stock options	5,107	3,927	5,107	3,927
Unvested restricted stock units	49	79	49	79
Shares issuable under employee stock purchase plan	32	24	32	24

5,188 4,030 5,188 4,030

## 11. Related Party Transactions

Celgene has made a series of equity investments in the Company, owning 3,674,640 shares of common stock representing 6.3% of the Company's outstanding common stock as of June 30, 2017. Refer to Note 8, *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.

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**Table of Contents****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 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 Exchange Act. This discussion and analysis should be read in conjunction with these 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.

***Management Overview***

We are a clinical-stage biopharmaceutical company that discovers, develops and plans to commercialize novel epigenetic therapies for patients with cancer and other diseases. We are leaders in discovering and developing small molecule inhibitors of a class of enzymes known as histone methyltransferases, or HMTs, as well as other chromatin modifying proteins, or CMPs. CMPs mediate selective and reversible modifications to chromatin, a complex of chromosomal DNA and histone proteins that controls gene expression. This chromatin remodeling and its resultant control of gene expression are part of a larger regulatory system, commonly referred to as epigenetics. Genetic alterations within CMPs or that indirectly affect CMPs can result in changes to their activity and drive multiple types of cancer, including hematological cancers and solid tumors, as well as other diseases. We believe that inhibiting altered CMPs presents the opportunity to create, develop and commercialize multiple targeted therapeutics.

Our lead product candidate, tazemetostat, is an oral, first-in-class potent and selective inhibitor of the EZH2 HMT, an enzyme that is implicated in a wide range of cancers. In our clinical trials of tazemetostat in patients with relapsed or refractory non-Hodgkin lymphoma, or NHL, and in patients with certain molecularly defined solid tumors, tazemetostat showed meaningful clinical activity as a monotherapy, and was generally well tolerated. We are conducting a broad clinical development program for tazemetostat as both a monotherapy and combination treatment, in relapsed/refractory and front-line disease, across a number of subtypes of NHL and in patients with and without EZH2 activating mutations. We are also testing tazemetostat in several different types of molecularly defined solid tumors in adults and children, including INI1- and SMARCA4-negative tumors, which we collectively refer to as INI1-negative tumors, and in adults with mesothelioma characterized by BAP1 loss-of-function.

In June 2017 at the American Society of Clinical Oncology Annual Meeting, or ASCO 2017, we presented interim data from the two arms of our five-arm Phase 2 clinical trial of tazemetostat as a monotherapy in adults with molecularly defined solid tumors that had reached the pre-specified futility analysis, which were the epithelioid sarcoma and synovial sarcoma arms. In addition, in June 2017 at the 14<sup>th</sup> International Conference on Malignant Lymphoma, or ICML 2017, we presented interim efficacy, safety and biomarker data from all five monotherapy arms of our Phase 2 clinical trial investigating tazemetostat as a potential treatment for adult patients with relapsed or refractory NHL. We met with the U.S. Food and Drug Administration, or FDA, in May 2017 to discuss our solid tumor data and identify a path to submission for accelerated approval of tazemetostat based on the 60 patient epithelioid sarcoma cohort in our Phase 2 study. We plan to meet with regulatory authorities in the second half of 2017, beginning with the FDA, to seek to identify the paths to registration for tazemetostat as a monotherapy in NHL.

We are actively studying tazemetostat in combination with other anti-cancer agents as part of our broad development plan for tazemetostat. We have entered into collaborations to evaluate tazemetostat in combination with other therapies approved for, or being investigated for, the treatment of diffuse large B-cell lymphoma, or DLBCL, an aggressive form of NHL. We have initiated an immuno-oncology Phase 1b study in collaboration with Genentech, a member of the Roche Group, to investigate the combination of tazemetostat and Genentech's anti-PD-L1 cancer immunotherapy, atezolizumab (Tecentriq®). The study is evaluating this combination regimen for the treatment of patients with relapsed or refractory DLBCL. In June 2017, we expanded our clinical collaboration with Genentech. Tazemetostat administered in combination with atezolizumab will be evaluated in a Phase 1b/2 clinical study for the treatment of patients with relapsed/refractory metastatic non-small cell lung cancer, or NSCLC. The study will be part of MORPHEUS, Genentech's open-label, multi-center, randomized umbrella study evaluating the efficacy and safety of multiple immunotherapy-based treatment combinations for metastatic NSCLC. We have initiated a Phase 1b/2 clinical trial in collaboration with the Lymphoma Study Association, or LYSA, a premier cooperative French lymphoma group, to evaluate tazemetostat in combination with R-CHOP in a front line setting in newly diagnosed, elderly, high-risk patients with DLBCL. R-CHOP is the standard of care front-line combination treatment for patients with DLBCL. In March 2017, we opened an additional arm of our ongoing Phase 2 NHL study to investigate tazemetostat in combination with prednisolone for patients with relapsed or refractory DLBCL. In 2017, we also plan to begin a combination study of tazemetostat in patients with follicular lymphoma, or FL, an indolent and currently incurable form of NHL. In addition, under our cooperative research and development agreement, or CRADA, with a National Cancer Institute, or NCI, a sponsored study of tazemetostat for the treatment of ovarian cancer is in the planning stages. In



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addition, the NCI has initiated its Pediatric MATCH study, which includes a phase 2 evaluation of tazemetostat as one of its treatment arms. This multi-institutional study will evaluate tazemetostat as a monotherapy for pediatric patients with advanced solid tumors, including CNS tumors, NHL or histiocytic disorders with EZH2 activating mutations, or loss of function mutations in the SWI/SNF complex subunits SMARCB1 or SMARCA4.

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, and holds a limited right of first negotiation for the rest of Asia. Tazemetostat is covered by claims of U.S. composition of matter patents, which are expected to expire in 2032. Tazemetostat has been granted Fast Track designation by the FDA in patients with DLBCL with EZH2 activating mutations and relapsed or refractory FL patients, with or without activating EZH2 mutations, and orphan drug designation by the FDA for the treatment of malignant rhabdoid tumors, or MRT, and soft tissue sarcoma, or STS. 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 collaboration agreements with Celgene Corporation and Celgene RIVOT Ltd., an affiliate of Celgene Corporation, which we collectively refer to as Celgene, Glaxo Group Limited (an affiliate of GlaxoSmithKline), or GSK, and Eisai. We also have a collaboration with Roche Molecular Systems, Inc., or Roche Molecular, to develop a companion diagnostic for use with tazemetostat to identify NHL patients with EZH2 activating mutations. These collaborations provide us with access to considerable scientific, development, regulatory and commercial capabilities. As of June 30, 2017, we had received \$217.8 million in non-equity funding under these collaborations.

Since our inception, we have pioneered the discovery and development of novel epigenetic medicines. We have discovered and developed three first-in-class experimental medicines that are in clinical trials, including tazemetostat. In addition to tazemetostat, we plan to evaluate pinometostat, an inhibitor of the DOT1L HMT that is the subject of our collaboration with Celgene, under our CRADA with the Cancer Therapy Evaluation Program, or CTEP, of the NCI as a combination therapy for patients with acute leukemias. Under our collaboration with GSK, GSK is evaluating GSK3326595, a protein arginine methyltransferase 5, or PRMT5, inhibitor invented by us and licensed to GSK under the collaboration, in a Phase 1 clinical trial in patients with solid tumors and NHL. We have additional small molecule HMT inhibitors that are being developed under our collaborations with Celgene and GSK. We have also identified multiple novel epigenetic targets for which we are developing small molecule inhibitors in preclinical drug discovery. We own the global development and commercialization rights to these programs. All of our novel targets have been identified internally using our proprietary drug discovery platform, and all of our small molecule inhibitors have been discovered internally.

We commenced active operations in early 2008, and since inception, have incurred significant operating losses. As of June 30, 2017, our accumulated deficit totaled \$414.3 million. As a clinical stage 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 as we execute on our clinical development plans for tazemetostat.

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**Development Program Update**

The following table summarizes our current pipeline:

- <sup>1</sup> Eisai holds rights to tazemetostat in Japan
- <sup>2</sup> Study not yet initiated
- <sup>3</sup> Part of the MORPHEUS umbrella study
- <sup>4</sup> Celgene holds ex-US rights to pinometostat
- <sup>5</sup> GSK holds global development and commercialization rights
- <sup>6</sup> Celgene holds option to license ex-US rights for one target and global rights for the other two targets

**Tazemetostat Clinical Program**

***Tazemetostat NHL Clinical Program***

We are executing a broad clinical development program for tazemetostat as both a monotherapy and combination treatment in relapsed/refractory and front-line NHL, as summarized below.

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*Tazemetostat Monotherapy Clinical Trials for NHL*

We are evaluating tazemetostat in a global Phase 2 study in up to 340 patients with relapsed or refractory NHL across six cohorts. Five of the arms are investigating tazemetostat as a monotherapy, and the sixth arm is investigating tazemetostat in combination with prednisolone, a standard agent in a variety of NHL combination treatment regimens. Patients are dosed with tazemetostat at 800 mg twice daily with tablets taken orally. The three arms enrolling patients with DLBCL are enrolling 60 patients each, the two arms enrolling patients with FL are enrolling 45 patients each, and the prednisolone combination arm is enrolling 70 patients. The monotherapy study cohorts are as follows:

DLBCL with Germinal Center B-cell, or GCB, subtype and EZH2 mutations;

DLBCL with GCB subtype and wild-type EZH2;

DLBCL with non-GCB subtype;

FL with EZH2 mutations; and

FL with wild-type EZH2.

The prednisolone combination arm is enrolling both GCB and non-GCB DLBCL patients with wild-type EZH2.

The primary endpoint of the study is overall response rate. Secondary endpoints include duration of response, progression free survival, overall survival, safety and population pharmacokinetics. In January 2017, we completed enrollment in the three arms of the study with wild-type DLBCL and FL. We are continuing to enroll the two remaining arms for GCB DLBCL and FL patients with EZH2 mutations.

In June 2017, at ICML 2017, we presented interim efficacy and safety data from the study, as well as data from a 62-gene panel biomarker study of tazemetostat in patients with various subtypes of NHL.

**Follicular Lymphoma Efficacy Data**

FL, an indolent form of NHL, is considered to be incurable with existing treatments and is characterized by cycles of relapse that become increasingly difficult to treat with each disease progression. We estimate that approximately 40,000 FL patients in the United States and major European countries alone are treated with these systemic therapies each year, of which an estimated 20% have an EZH2 activating mutation. There are no approved treatments indicated for patients with FL with an EZH2 mutation.

As of June 1, 2017, we had enrolled 19 FL patients with EZH2 activating mutations in the Phase 2 trial, of which 13 were evaluable for efficacy. Enrollment of FL patients with wild-type EZH2 was completed in late 2016 with a total of 54 patients, all of which were evaluable for efficacy. More than 75% of evaluable FL patients had three or more prior treatments, and approximately 50% of patients in each group were refractory to their last therapy.

For FL patients with EZH2 activating mutations, 12 of 13 patients experienced a partial or complete response, representing an objective response rate of 92%. One of the 12 experienced a complete response, or CR (8%), and 11 experienced a partial response, or PR (85%). Median time to first response was 11.9 weeks, with a range of 6.9 to 35.9 weeks. For FL patients with wild-type EZH2, 14 of 54 patients experienced a PR or CR, representing an objective response rate of 26%. Three of the 14 experienced a CR (6%) and 11 experienced a PR (20%). An additional 12 patients (22%) experienced stable disease, or SD, and remained on treatment as of the data cutoff date. Median time to first response was 15.2 weeks, with a range of 8.1 to 32.1 weeks.

*Diffuse Large B-Cell Lymphoma Efficacy Data*

DLBCL is an aggressive form of NHL that, once diagnosed, typically requires immediate treatment. We estimate that approximately 80,000 patients in the United States and major European countries alone are actively treated with systemic therapies to manage their disease every year. Approximately 40% of DLBCL patients are diagnosed with germinal center lymphoma and an estimated 20% of those patients have an EZH2 activating mutation. Forty to 50% of patients will relapse on their first-line treatment, which is most commonly the chemotherapy regimen R-CHOP, and there are few treatment options for patients who relapse or become refractory to chemotherapy.

As of June 1, 2017, we had enrolled 22 DLBCL patients with EZH2 activating mutations, of which 17 patients were evaluable for efficacy. Enrollment of DLBCL patients with wild-type EZH2 (germinal center and non-germinal center) was completed in early 2017 with 120 patients, of which 119 were evaluable for efficacy.

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For DLBCL patients with EZH2 activating mutations, 5 of 17 patients experienced a confirmed objective response (all partial), representing an objective response rate of 29%. Median time to first response was 8.3 weeks, with a range of 4.6 to 48.1 weeks. For DLBCL patients with wild-type EZH2, 18 of 119 patients experienced a PR or CR, representing an overall response rate of 15%. Ten of the 18 experienced a CR (8%) and eight experienced a PR (7%). Median time to first response was 8.5 weeks, with a range of 5.3 to 24.7 weeks.

**Tazemetostat NHL Safety Data**

Safety data from patients in this Phase 2 trial (n=210), as of the data cutoff date, demonstrated a favorable tolerability profile in the trial, consistent with the experience observed in a safety database exceeding 400 patients from tazemetostat clinical trials to date. Across all cohorts of this trial, dose reductions and discontinuations due to treatment-related adverse events were low, at only 3% and 2%, respectively. The majority of treatment-emergent adverse events were grade 1 or 2, with only 18% of grade 3 or higher being considered treatment-related.

**Tazemetostat Combination Clinical Trials for NHL**

In addition to evaluating tazemetostat as a monotherapy for NHL, we are investigating the combination of tazemetostat with other cancer agents in both the relapsed/refractory and front-line settings.

**Atezolizumab.** Based on preclinical evidence showing that EZH2 inhibition may enhance the activity of checkpoint inhibitors, we entered into a collaboration agreement with Genentech to conduct a global Phase 1b study combining tazemetostat with atezolizumab, a PD-L1 inhibitor. The global study was initiated in the fourth quarter of 2016 and is being conducted by Genentech. The study will enroll approximately 45 patients with relapsed or refractory DLBCL. Primary endpoints in the trial include safety and combination tolerability with the objective of establishing a recommended Phase 2 dose. Secondary and exploratory endpoints include overall response, objective response, duration of response, pharmacokinetics and preliminary biomarker assessment.

**R-CHOP.** We are studying tazemetostat in combination with R-CHOP, the current standard of care for newly-diagnosed patients with DLBCL, in collaboration with LYSA. We have generated preclinical data showing synergy between tazemetostat and the chemotherapy and steroid components of R-CHOP. This multi-center Phase 1b/2 study in front-line, elderly high-risk patients with DLBCL will enroll up to 133 patients. Primary endpoints in the trial include CR rate as well as safety and tolerability of the combination. Secondary endpoints include overall response rate and progression free survival. The trial was initiated in the fourth quarter of 2016.

**Prednisolone.** In March 2017, we opened an additional arm of our ongoing Phase 2 NHL study to investigate tazemetostat in combination with prednisolone for patients with relapsed or refractory DLBCL. We determined to conduct this combination trial based on substantial preclinical synergy data with prednisolone, a standard agent in a variety of NHL treatment regimens, including R-CHOP. The objective of this new arm of the ongoing Phase 2 NHL study is to evaluate the clinical synergy of the agents and to explore the potential of prednisolone to slow progression in patients with aggressive disease.

**FL combination.** We have seen extensive preclinical synergy of tazemetostat with a number of targeted agents and chemotherapies used for, or in development for the treatment of, FL. In 2017, we plan to begin a combination study of tazemetostat in patients with FL.

***Tazemetostat Clinical Program in Molecularly Defined Solid Tumors***

We are conducting a registration-supporting, global Phase 2 study of tazemetostat in patients with INI1-negative solid tumors and synovial sarcoma. This study is enrolling up to 220 patients. The patients in the trial are stratified into one of five cohorts: epithelioid sarcoma, rhabdoid tumors, other INI1-negative tumors, renal medullary carcinoma, and synovial sarcoma, with the epithelioid sarcoma cohort enrolling up to 100 patients and the other four cohorts each enrolling up to 30 patients.

Patients in the five-arm Phase 2 study in molecularly defined solid tumors are dosed at 800 mg twice daily with tablets taken orally. The primary endpoint for the epithelioid sarcoma arm is a composite endpoint including overall response rate and disease control rate. The primary endpoint for the synovial sarcoma arm is disease control, defined as a CR, PR or SD, at 16 weeks. The primary endpoint for the other cohorts is overall response rate. Secondary endpoints include duration of response, overall survival, progression-free survival, or PFS, overall survival and safety and pharmacokinetics.

The epithelioid sarcoma cohort in Epizyme's Phase 2 study represents the largest prospective study of epithelioid sarcoma with any approved or investigational treatment to date. The cohort was initially designed to enroll 30 patients, and was expanded in December 2016 to enroll an additional 30 patients based on encouraging early activity. In July 2017, the expansion cohort reached full enrollment. We plan to further expand the study to enroll up to an additional 40 patients to explore the effect of tazemetostat treatment on immune responsiveness by obtaining paired tumor biopsies in these patients.

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Epithelioid sarcoma is an ultra-rare and aggressive soft tissue sarcoma, characterized by a loss of the INI1 protein. It is most commonly diagnosed in young adults (20-40 years old) and is often fatal. There is no established standard-of-care for treating these patients, who are typically resistant to chemotherapy.

In June 2017, at ASCO 2017, we presented interim data from 31 patients in the initial epithelioid sarcoma cohort, as of the data cutoff date of May 1, 2017. In these patients, tazemetostat treatment resulted in a 32% disease control rate, or DCR, the primary endpoint. DCR is comprised of confirmed objective responses measured in accordance with Response Evaluation Criteria In Solid Tumors, or RECIST 1.1, guidelines for any duration or disease stabilization of 32 weeks or more. As of the data cutoff date, four patients (13%) had achieved confirmed objective responses (all partial), and the time to response ranged from two months to six months. The median duration of response was seven months and ongoing. Prolonged disease stabilization of 32 weeks or more was observed in six patients (19%), including two patients having SD for more than 15 months.

We also presented data from the synovial sarcoma arm of the study at ASCO 2017. Unlike the cancers in the other four arms of the study, synovial sarcoma is characterized by a functional dysregulation of INI1, rather than by a complete loss of INI1. The synovial sarcoma arm of the Phase 2 trial has been fully enrolled at approximately 30 patients. The data presented show tazemetostat treatment resulted in SD as the best response in 10 patients (30%) with five patients (15%) meeting the primary endpoint of disease stabilization for 16 weeks or longer. Although this arm of the study surpassed its interim futility hurdle, we concluded that the activity of tazemetostat in this cohort was insufficient to continue further investigation of tazemetostat in this population as a monotherapy.

We are also conducting a global Phase 1 dose-escalation and expansion study of tazemetostat in approximately 110 children with INI1-negative solid tumors. In this trial, we are using an oral suspension formula of tazemetostat. We have completed the dose escalation portion of the study, and have advanced to the dose expansion stage. The primary endpoint of the study is safety, with the objective of establishing the recommended Phase 2 dose in pediatric patients. Secondary endpoints include pharmacokinetics, objective response rate, duration of response, PFS and overall survival.

***Tazemetostat Mesothelioma Clinical Program***

We are conducting a global Phase 2 monotherapy trial of tazemetostat in relapsed or refractory patients with mesothelioma characterized by BAP1 loss-of-function. This trial will enroll up to 67 patients with relapsed or refractory mesothelioma. The first stage of the trial will evaluate safety and pharmacokinetics in 12 patients with mesothelioma, regardless of BAP1 status. The second stage of the trial will evaluate disease control rate in 55 patients with mesothelioma characterized by BAP1 loss-of-function. The first patient in the study was dosed in August 2016 and enrollment in the first and second stages of the study is complete. Patients are dosed at 800 mg twice daily with tablets taken orally. The primary endpoint of the trial is disease control rate, defined as CR, PR, or SD, at 12 weeks.

***Tazemetostat Clinical Program in Non-Small Cell Lung Cancer***

In June 2017, we expanded our clinical collaboration with Genentech. Under the collaboration, tazemetostat administered in combination with atezolizumab will be evaluated in a Phase 1b/2 clinical study for the treatment of patients with relapsed/refractory metastatic non-small cell lung cancer, or NSCLC. The study will be part of MORPHEUS, Genentech's open-label, multi-center, randomized umbrella study evaluating the efficacy and safety of multiple immunotherapy-based treatment combinations for metastatic NSCLC. Genentech will sponsor the Phase 1b/2 clinical trial. It is anticipated that the study will enroll up to 40 patients who have experienced disease progression during or following treatment with a platinum-containing chemotherapy regimen and a PD-L1/PD-1 checkpoint inhibitor.

***Tazemetostat Clinical Program in Other Tumor Types***

In October 2016, we announced a CRADA with the NCI to evaluate tazemetostat in clinical trials in a variety of hematologic malignancies and solid tumors. Under the CRADA, we plan to evaluate tazemetostat in a Phase 2 clinical trial in adult patients with ovarian cancer and in a Phase 2 study in pediatric patients with solid tumors and lymphoma. As part of the agreement, additional clinical trials will be considered. NCI will predominantly fund the studies and manage study operations. In preclinical studies conducted by us and third parties, inhibition of EZH2 reduced ovarian tumor cell growth.



In July 2017, we announced that the NCI's Pediatric MATCH study will include a phase 2 evaluation of tazemetostat as one of its treatment arms. Conducted under our CRADA executed with NCI in 2016, this multi-institutional study will evaluate tazemetostat as a monotherapy for pediatric patients with advanced solid tumors, including CNS tumors, non-Hodgkin lymphoma or histiocytic disorders that harbor EZH2 activating mutations, or loss of function mutations in the SWI/SNF complex subunits SMARCB1 or SMARCA4. The Pediatric MATCH study, which will be operationalized by the Children's Oncology Group, aims to match targeted agents, such as tazemetostat, with specific molecular changes identified through genomic sequencing of refractory or recurrent tumors from children and adolescents with cancer.

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***Pinometostat DOT1L Inhibitor***

We are developing pinometostat as an intravenously administered small molecule inhibitor of DOT1L for the treatment of acute leukemias with alterations in the mixed lineage leukemia, or MLL, gene, specifically rearrangements of MLL as a consequence of chromosomal translocation, referred to as MLL-r, which includes partial tandem duplications of the MLL gene, referred to as MLL-PTD. We invented pinometostat using our proprietary product platform.

Under the CRADA that we entered with the NCI in October 2016 for pinometostat, the NCI has agreed to evaluate the safety and efficacy of pinometostat in patients with acute leukemias. Initial studies will evaluate the combination of pinometostat with standard-of-care therapies or targeted agents in acute myeloid leukemia, acute lymphoid leukemia, or MLL-r. As part of the agreement, additional clinical trials will be considered. NCI will predominantly fund the studies and manage study operations.

Through external collaborators, we are exploring in preclinical studies combinations of pinometostat with other anti-cancer agents to enhance pinometostat's efficacy in leukemia. We retain all U.S. rights to pinometostat and have granted Celgene an exclusive license to pinometostat outside of the United States. Pinometostat has been granted orphan drug designation by the FDA and the European Commission for the treatment of acute myeloid leukemia and acute lymphoblastic leukemia.

Previously, we conducted a Phase 1 study in 51 adults with MLL-r and a Phase 1 study in 18 children with MLL-r. Although two patients in the adult study experienced CRs, we did not see sufficient activity to justify continuing development of pinometostat as a monotherapy in this indication.

**Corporate Strategy**

Our goal is to become a fully integrated development and commercial biopharmaceutical company developing novel epigenetic therapies for patients with cancer and other diseases. We have a robust proprietary drug discovery platform and the demonstrated ability to move candidates into clinical development. We have recently begun building the infrastructure necessary to support the successful launch and marketing of tazemetostat or any other product candidate that receives marketing approval. The key elements of our strategy to achieve this goal are to:

**Rapidly Advance the Clinical Development of Tazemetostat.** We are executing a broad clinical development program of tazemetostat for molecularly defined solid tumors, NHL and mesothelioma. Due to a lack of treatment options and the severity of disease associated with INI1-negative tumors, we believe that this molecularly defined patient population may represent the fastest potential path to NDA submission and commercial launch for tazemetostat. We met with the FDA in May 2017 to discuss our epithelioid sarcoma data and identify a path to submission for accelerated approval in this indication, and in the second half of 2017, we plan to meet with the FDA to seek to identify the paths to registration for tazemetostat as a monotherapy in NHL.

**Seek to Expand the Range of Potential Indications for Tazemetostat.** We are conducting a broad development program for tazemetostat as a monotherapy and in combination with other therapies. These efforts include our two ongoing combination trials in DLBCL evaluating tazemetostat with atezolizumab and tazemetostat with R-CHOP, as well as our combination arm with prednisolone in

DLBCL, our planned combination study in FL, and our planned combination study with atezolizumab in NSCLC. We also have over two dozen academic collaborations which are investigating the role of tazemetostat in other cancer types in preclinical models. If we see strong preclinical evidence of sensitivity of specific tumors to EZH2 inhibition, and if a medical need exists, we will consider initiating proof of concept human clinical trials.

**Establish Commercialization and Marketing Capabilities in the United States.** We have retained commercialization rights in the United States for all of our programs, other than the three programs that are the subject of our GSK collaboration and two of the preclinical programs that are the subject of our collaboration with Celgene. We plan to retain commercialization rights in the United States and possibly selected foreign jurisdictions in connection with any future collaborations. We intend to build a focused field presence and marketing capabilities to commercialize any of our product candidates that receive regulatory approval in the United States, as well as the capability of leading global commercial strategy.

**Use Our Drug Discovery Platform to Build a Pipeline of Proprietary CMP Inhibitors.** Using our proprietary drug discovery platform, we are developing additional novel, small molecule inhibitors of CMPs. We currently hold U.S. development and commercialization rights to one of our three preclinical programs subject to Celgene's option under our collaboration. In addition, we have identified multiple novel CMP targets against which we are developing small molecule inhibitors in preclinical drug discovery, for which we own global development and commercialization rights. We expect to declare our next development candidate in 2017 with the goal of commencing clinical trials of three new product candidates by 2020.

**Leverage Collaborations.** Our strategic collaborations with Celgene, GSK, Eisai, Genentech, LYSA, Roche Molecular, NCI and numerous external academic researchers provide us with access to the scientific, development, regulatory and commercial capabilities of our collaborators. We believe that collaborations like these can contribute to our ability to rapidly advance our product candidates, build our product platform and concurrently progress a wide range of discovery and development programs. We may seek to enter into additional strategic collaborations in the future.

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**Develop Companion Diagnostics for Use with Our Therapeutic Product Candidates.** We plan to seek to develop companion diagnostics for use in connection with our therapeutic product candidates where appropriate. We believe that this approach may enable us to accelerate the clinical development and regulatory timelines for our therapeutic product candidates and, for any of our therapeutic product candidates that receive marketing approval, improve patient care by identifying patients who are more likely to benefit from the therapy. We intend to develop diagnostics based on currently available diagnostic technologies to the extent possible in order to minimize development and regulatory risk of our diagnostic programs. We are working with Roche Molecular to develop a companion diagnostic, based on currently available technology, for use with tazemetostat to identify NHL patients with EZH2 activating mutations. We also plan to develop a companion diagnostic to identify patients with BAP1 loss-of-function for our mesothelioma program.

**Collaborations**

Refer to Note 8, *Collaborations*, of the notes to our consolidated financial statements included in this Quarterly Report on Form 10-Q for a description of the key terms of our arrangements with Eisai, Celgene and GSK. In May 2017, we earned a \$10.0 million milestone payment from GSK, following GSK's initiation of good laboratory practices toxicology studies for a first-in-class methyltransferase inhibitor discovered by us and licensed to GSK. There have been no updates to our arrangements with LYSA and Genentech since December 31, 2016.

**Results of Operations***Collaboration Revenue*

The following is a comparison of collaboration revenue for the three and six months ended June 30, 2017 and 2016:

	Three Months Ended June 30,			Six Months Ended June 30,		
	2017	2016	Change	2017	2016	Change
	(In millions)					
Collaboration revenue	\$ 10.0	\$ 0.5	\$ 9.5	\$ 10.0	\$ 0.9	\$ 9.1

We recognized \$10.0 million of collaboration revenue in the three and six months ended June 30, 2017, compared to \$0.5 million and \$0.9 million in the three and six months ended June 30, 2016, respectively. Collaboration revenue in the three and six months ended June 30, 2017 reflects a \$10.0 million milestone payment from GSK, which we earned in May 2017 upon GSK's initiation of good laboratory practice, or GLP, toxicology studies for a first-in-class methyltransferase inhibitor that we discovered and licensed to GSK. We had no milestone revenue in the three and six months ended June 30, 2016. There was no collaboration revenue recognized from deferred revenue from upfront payments in the three and six months ended June 30, 2017, as compared to \$0.5 million and \$0.9 million recognized entirely from deferred revenue related to our Celgene agreement in the three and six months ended June 30, 2016, respectively. We did not recognize any collaboration revenue for research and development services in the three and six months ended June 30, 2017 and 2016.

*Research and Development*

The following is a comparison of research and development expenses for the three and six months ended June 30, 2017 and 2016:

	Three Months Ended			Six Months Ended		
	June 30, 2017	2016	Change	2017	2016	Change
Research and development	\$ 27.3	\$ 21.5	\$ 5.8	\$ 52.0	\$ 39.2	\$ 12.8

(In millions)

During the three months ended June 30, 2017, total research and development expenses increased by \$5.8 million compared to the three months ended June 30, 2016. During the six months ended June 30, 2017, total research and development expenses increased by \$12.8 million compared to the six months ended June 30, 2016. The increases in the three and six months ended June 30, 2017 are primarily due to increased research activities related to our next potential development candidate, expansion of activities related to our platform and new target families, increased spending on tazemetostat manufacturing and growth in clinical operations.

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

<b>Product Program</b>	<b>Three Months Ended</b>		<b>Six Months Ended</b>	
	<b>June 30,</b>	<b>June 30,</b>	<b>June 30,</b>	<b>June 30,</b>
	<b>2017</b>	<b>2016</b>	<b>2017</b>	<b>2016</b>
	<b>(In millions)</b>			
External research and development expenses:				
Tazemetostat and related EZH2 programs	\$ 11.7	\$ 9.7	\$ 23.0	\$ 16.2
Pinometostat and related DOT1L programs	0.2	0.2	0.5	1.1
Discovery and preclinical stage product programs, collectively	6.0	3.8	9.4	7.0
Unallocated personnel and other expenses	9.4	7.8	19.1	14.9
Total research and development expenses	\$ 27.3	\$ 21.5	\$ 52.0	\$ 39.2

External research and development expenses for tazemetostat and related EZH2 programs increased \$2.0 million and \$6.8 million during the three and six months ended June 30, 2017, respectively, compared to the three and six months ended June 30, 2016. The increase in tazemetostat related spending in the three and six months ended June 30, 2017 is primarily a result of a significant increase in tazemetostat clinical trial activities in the three and six months ended June 30, 2017 as compared to the three and six months ended June 30, 2016. External research and development costs include the ongoing clinical trial costs, discovery and preclinical research in support of the tazemetostat program, expenses associated with our companion diagnostic program, and external manufacturing costs related to the acquisition of active pharmaceutical ingredient and manufacturing of clinical drug supply.

External research and development expenses for pinometostat and other DOT1L programs for the three months ended June 30, 2017 remained consistent with the three months ended June 30, 2016. External research and development expenses for pinometostat and other DOT1L programs for the six months ended June 30, 2017 decreased \$0.6 million as compared to the six months ended June 30, 2016. The decline in program spending reflects our completion of enrollment in the pinometostat pediatric clinical trial and the associated reduction in costs. We completed enrollment in our pinometostat pediatric Phase 1 clinical trial in the first quarter of 2016. The costs incurred related to pinometostat in the three and six months ended June 30, 2017 are primarily associated with costs attributed to the CRADA with the NCI.

External research and development expenses for discovery and preclinical stage product programs increased \$2.2 million and \$2.4 million for the three and six months ended June 30, 2017, respectively, compared to the three and six months ended June 30, 2016, primarily related to increased research activities related to our next potential development candidate and expansion of activities related to our platform and new target families.

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 for the three and six months ended June 30, 2017 increased \$1.6 million and \$4.2 million, respectively, compared to the three and six months ended June 30, 2016. The increase in unallocated personnel and other expenses in the three and six months ended June 30, 2017 was primarily due to the expansion of our development organization to support expanded tazemetostat clinical trials, chemistry, manufacturing and controls, translational medicine, data analytics and regulatory activities.

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We expect research and development expenses to continue to increase during 2017, as we progress and expand our clinical development program for tazemetostat, expand our regulatory activities, increase tazemetostat manufacturing activities and potentially advance a preclinical program into later stage preclinical testing.

*General and Administrative*

The following is a comparison of general and administrative expenses for the three and six months ended June 30, 2017 and 2016:

	<b>Three Months Ended June 30,</b>			<b>Six Months Ended June 30,</b>		
	<b>2017</b>	<b>2016</b>	<b>Change</b>	<b>2017</b>	<b>2016</b>	<b>Change</b>
	<b>(In millions)</b>					
General and administrative	\$ 11.2	\$ 7.4	\$ 3.8	\$ 19.4	\$ 13.3	\$ 6.1

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For the three and six months ended June 30, 2017, our general and administrative expenses increased \$3.8 million and \$6.1 million, respectively, compared to the three and six months ended June 30, 2016, primarily due to increased headcount, expanded business development and pre-commercial activities, and expanded human resources and finance activities to support our growth.



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We expect that general and administrative expenses will be relatively constant in the second half of 2017 as compared to the first six months of 2017.

### *Other Income, Net*

Other income, net primarily consists of interest income earned on our cash equivalents and marketable securities, net of imputed interest expense paid under our capital lease obligation. Interest income, net remained consistent at \$0.4 million for the three months ended June 30, 2017, compared to the three months ended June 30, 2016. Interest income, net increased \$0.2 million for the six months ended June 30, 2017, compared to the six months ended June 30, 2016, primarily due to interest associated with short-term interest bearing securities that were purchased in May 2016.

### *Income Tax Expense*

We maintain a full valuation allowance against our deferred tax assets and therefore did not recognize an income tax benefit for the three and six months ended June 30, 2017 or June 30, 2016.

## **Liquidity and Capital Resources**

Through June 30, 2017, we have raised an aggregate of \$740.3 million to fund our operations, of which \$217.8 million was non-equity funding through our collaboration agreements, \$446.5 million was from the sale of common stock in our public offerings, which includes \$1.6 million during the six months ended June 30, 2017, and \$76.0 million was from the sale of redeemable convertible preferred stock. As of June 30, 2017, we had \$193.0 million in cash, cash equivalents and marketable securities.

On April 15, 2016, we entered into a Sales Agreement with Cowen and Company, LLC, or Cowen, to sell, from time to time, shares of our common stock having an aggregate sales price of up to \$50.0 million through an at the market offering as defined in Rule 415 under the Securities Act of 1933, as amended, under which Cowen would act as sales agent, which we refer to as the ATM Offering. The shares that may be sold under the Sales Agreement, if any, would be issued and sold pursuant to our \$250.0 million universal shelf registration statement on Form S-3 that was declared effective by the SEC on April 29, 2016. Through March 10, 2017, we sold 155,834 shares of Common Stock under the Sales Agreement, resulting in net proceeds of \$1.9 million related to the ATM Offering. We terminated the Sales Agreement with Cowen, effective March 10, 2017.

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, and we expect will continue to be, clinical trial costs, third party research and development services, 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.

**Table of Contents*****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, 2017, will be sufficient to fund our planned operating expenses and capital expenditure requirements into at least the third quarter of 2018, 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, 2017 and 2016:

	<b>Six months ended June 30,</b>		
	<b>2017</b>	<b>2016</b>	<b>Change</b>
	<b>(In millions)</b>		
Net cash used in operating activities	\$ (51.1)	\$ (50.2)	\$ (0.9)
Net cash provided by (used in) investing activities	59.0	(199.8)	258.8
Net cash provided by financing activities	2.8	131.1	(128.3)

***Net Cash Used in Operating Activities***

Net cash used in operating activities was \$51.1 million during the six months ended June 30, 2017 compared to \$50.2 million during the six months ended June 30, 2016. The increase in net cash used in operating activities primarily relates to the net loss in the period, which includes \$10.0 million of revenue recognized and payment received from GSK, partially offset by changes in working capital.

Net cash used in operating activities for six months ended June 30, 2017 primarily relates to our net loss of \$60.5 million, partially offset by non-cash stock-based compensation of \$5.8 million, depreciation of \$0.8 million and a change in working capital of \$2.8 million. The most significant items affecting working capital in the six months ended June 30, 2017 include increased prepaid expenses associated with the expansion of our clinical activities and increased accounts payable and accrued expenses associated with increased research activities related to our next potential development candidate, expansion of activities related to our platform and new target families.

Net cash used in operating activities for the six months ended June 30, 2016 primarily relates to our net loss of \$50.9 million and a net \$4.3 million use of cash from changes in working capital, partially offset by non-cash stock based compensation of \$5.1 million and depreciation of \$0.8 million. The most significant items affecting working capital in the six months ended June 30, 2016 included a \$3.0 million development milestone paid to Roche Molecular, a \$2.0 million reduction of compensation related accruals, reduced accounts payable of \$1.0 million and the collection of a \$0.7 million tax receivable.

***Net Cash Provided by (Used in) Investing Activities***

Net cash provided by investing activities during the six months ended June 30, 2017 reflects \$80.8 million of purchases of available for sale securities, maturities or sales of available for sale securities of \$140.5 million and purchases of property and equipment of \$0.7 million.

Net cash used in investing activities during the six months ended June 30, 2016 reflects \$199.4 million of purchases of available for sale securities and \$0.3 million of purchases of property and equipment during the period.

***Net Cash Provided by Financing Activities***

Net cash provided by financing activities of \$2.8 million during the six months ended June 30, 2017 primarily reflects net cash received from sales under the ATM Offering of \$1.6 million, cash received from stock option exercises of \$1.1 million, and the purchases of shares under our employee stock purchase plan of \$0.3 million, partially offset by the payments under our capital lease obligation of \$0.3 million.

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Net cash provided by financing activities of \$131.1 million during the six months ended June 30, 2016 primarily reflects net cash received from our January 2016 public offering of our common stock of \$129.7 million as well as cash received from stock option exercises and the purchase of shares under our employee stock purchase plan. This amount was offset in part by the payment of \$0.3 million of principal on our capital lease obligation.

**Table of Contents****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, 2016, except for the following:

We lease 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 the Landlord, with a term that originally continued through May 31, 2018, which included an 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, we entered into a Third Amendment to Lease with the Landlord, and a Fourth Amendment to Lease with the Landlord, which we refer to collectively as the Amendments. The Amendments each amend the Lease.

Under the Amendments, we extended the term of the Lease at our headquarters in Cambridge, Massachusetts to November 30, 2022, subject to our 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. Under the Lease, we have 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 and annual increases December 1 of each subsequent year until December 1, 2021.

Under the Lease as amended by the Amendments, we are responsible for aggregate minimum rent payments of \$18.6 million, of which approximately \$0.5 million was paid prior to June 30, 2017. The remaining future minimum rent payments from July 1, 2017 through November 30, 2022 are as follows:

	<b>Total</b>	<b>Less than 1 Year</b>	<b>1 to 3 Years (In thousands)</b>	<b>3 to 5 Years</b>	<b>More than 5 Years</b>
Real estate leases	\$ 18,098	\$ 2,835	\$ 6,671	\$ 7,078	\$ 1,514

**Critical Accounting Policies and Use of Estimates**

Our management's discussion and analysis of financial condition and results of operations is based upon our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. The preparation of these 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 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. There have been no material changes or other required disclosures to our critical accounting policies disclosed in our Annual Report on Form 10-K for our fiscal year ended December 31, 2016.

### ***Recent Accounting Pronouncements***

For detailed information regarding recently issued accounting pronouncements and the expected impact on our consolidated financial statements, see Note 2, *Summary of Significant Accounting Policies Recent Accounting Pronouncements*, in the accompanying Notes to 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, 2017, we had cash equivalents and available for sale securities of \$193.0 million consisting of money market funds, corporate bonds, commercial paper and government-related obligations. 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, 2017 by \$0.3 million.

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We contract with CROs 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 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 (our Chief Executive Officer) and principal financial officer (our Chief Financial Officer), to allow timely decisions regarding required disclosure.

Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial 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 Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of June 30, 2017.

***Changes in Internal Control over Financial Reporting***

No change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended June 30, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**PART II OTHER INFORMATION**

**Item 1A. Risk Factors**

Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Quarterly Report on Form 10-Q 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**

***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 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. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. 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 CMPs 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 HMT inhibitors in the clinic are each 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 diseases will be successful.

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***Our development efforts are ongoing and we have only two product candidates in clinical trials that we are developing, and one product candidate in clinical trials that has been licensed to GSK. All of our other product candidates are still in preclinical development. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.***

Our development efforts are ongoing and we have only two product candidates in clinical trials that we are developing, tazemetostat and pinometostat. In addition, GSK has initiated a Phase 1 clinical trial for a PRMT5 inhibitor that it has licensed from us. All of our other product candidates are still in preclinical development. We have invested substantially all our efforts and financial resources in the identification and preclinical and clinical development of inhibitors of HMTs and other CMPs. Our ability to generate product revenues when anticipated or at all will depend heavily on the successful development and eventual commercialization of our product candidates. The success of our product candidates will depend on several factors, including the following:

successful completion of preclinical studies and clinical trials;

receipt of marketing approvals from applicable regulatory authorities;

obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;

making arrangements with third party manufacturers for, or establishing, 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;

protecting our rights in our intellectual property portfolio; and

maintaining a continued acceptable safety profile of the products following approval.

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

***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.

***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.***

Three of our product candidates are in clinical development, and our remaining product candidates are in preclinical development. Two of our product candidates in clinical development are being developed by us and the third product candidate is being developed by GSK. The risk of failure for each of our 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 continued preclinical safety studies, which may be conducted concurrent with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future 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 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. If we are unable to adequately address matters such as this when they arise, we may be unable to conduct clinical trials of our product candidates in the United States or in other countries, 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.

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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. For example, the CRs that were observed in two patients with MLL-r in the fourth dose cohort of the dose escalation portion of our Phase 1 clinical trial of pinometostat in adults were not achieved by any other patient treated with pinometostat in the Phase 1 clinical trial. 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.

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 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.

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Our product development costs may also increase if we experience delays in clinical testing or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will 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 products 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. In addition, our Phase 2 clinical trial of tazemetostat in patients with NHL has two arms targeting patients with EZH2 activating mutations in their tumors, one in GCB DLBCL and one in FL. Based on the aggregate scientific literature, we believe that patients with these mutations represent approximately 20% of the total GCB DLBCL and FL population in the United States and other major reimbursable markets. In any clinical study, the actual percentage of patients enrolled with these EZH2 mutations may vary from the range suggested by the literature.

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).

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, 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 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.

***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.

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***If we are unable to successfully develop companion 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 companion 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 companion 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.

## **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 \$60.5 million for the six months ended June 30, 2017. As of June 30, 2017, we had an accumulated deficit of \$414.3 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 drug 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 as we:



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continue our Phase 2 clinical trial of tazemetostat for the treatment of patients with NHL, our Phase 2 clinical trial of tazemetostat for the treatment of adult patients with certain molecularly defined solid tumors and our Phase 1 clinical trial of tazemetostat for the treatment of pediatric patients with certain molecularly-defined solid tumors;

continue our Phase 2 clinical trial of tazemetostat in relapsed or refractory patients with mesothelioma characterized by BAP1 loss-of-function;

continue our clinical trials of tazemetostat in combination with R-CHOP in front line elderly patients with DLBCL and in combination with Genentech's anti-PD-L1 cancer immunotherapy, atezolizumab, in patients with relapsed or refractory DLBCL and in patients with NSCLC being conducted by our collaborators;

continue our rollover study of tazemetostat in certain patients that have completed prior clinical trial protocols;

continue the newest arm of our ongoing Phase 2 NHL trial of tazemetostat in combination with prednisolone in relapsed or refractory patients with DLBCL;

initiate the study of tazemetostat in combination with atezolizumab in patients with relapsed or refractory NSCLC being conducted by Genentech;

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;

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conduct research and development for Celgene under our amended and restated collaboration and license agreement;

continue the research and development of our other product candidates;

seek to discover and develop additional product candidates;

seek regulatory approvals for any product candidates that successfully complete clinical trials;

ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we may obtain regulatory approval;

maintain, expand and protect our intellectual property portfolio;

hire additional clinical, quality control 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 are only in the preliminary stages of most of these activities. 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 European Medicines Agency, or 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; continue research for Celgene under our amended and restated collaboration and license agreement; and continue research and development and initiate additional 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, 2017, will be sufficient to fund our planned operating expenses and capital expenditure requirements into at least the third quarter of 2018. 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;

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;

our ongoing research for Celgene under our amended and restated collaboration and license agreement;

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

milestones, option exercise fees, license fees, and other collaboration-based revenues, if any;

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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 three 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**

*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:

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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; 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.***

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales and marketing organization.

We are in the process of building a focused sales and marketing infrastructure to market some of our product candidates in the United States, and potentially in global markets, if and when they are approved. 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.

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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 HMTs include GSK, Novartis AG, Pfizer, Inc., Merck & Co., Inc., Daiichi Sankyo Company Limited, Takeda Pharmaceutical Company Limited, AbbVie Inc., Bayer Schering Pharma AG and Constellation Pharmaceuticals. In addition, many companies are developing cancer therapeutics that work by targeting epigenetic mechanisms other than HMTs, and some including Celgene and Eisai, are now marketing cancer treatments that work by targeting epigenetic mechanisms other than HMTs.

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

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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 do not yet have any capability for sales, marketing or distribution. 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 and GSK. We also rely on Genentech to manage our combination study of tazemetostat and atezolizumab in patients with relapsed or refractory DLBCL and in patients with relapsed/refractory metastatic NSCLC, and on LYSA to manage our combination study of tazemetostat and R-CHOP in newly diagnosed, elderly, high risk patients with DLBCL. We also rely on the National Cancer Institute to conduct the planned studies of tazemetostat in ovarian cancer and in the pediatric MATCH study. With our reacquisition of tazemetostat rights under our amended and restated collaboration and license agreement with Eisai, we no longer have access to such 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;

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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 this Quarterly Report on Form 10-Q 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.

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***Failure of our third party collaborators to successfully commercialize companion diagnostics developed for use with our therapeutic product candidates could harm our ability to commercialize these product candidates.***

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

may not perform their obligations as expected or have difficulty responding to accelerated approval time lines;

may encounter production difficulties that could constrain the supply of the companion diagnostics;

may encounter delays or have difficulty obtaining regulatory approval for the companion diagnostic in target markets;

may have difficulties gaining acceptance of the use of the companion diagnostics in the clinical community;

may not pursue commercialization of any companion 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 companion 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 companion 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 collaboratives 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, 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, or GCPs, 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. 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.

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*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.

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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 drug 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 our European Patent, 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.



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***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, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our 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.

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***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. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not submitted an application for or received marketing approval for any of our product candidates in the United States or in any other jurisdiction.

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We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third party CROs to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Any pathway to regulatory approval that we have identified is subject to change and may not ultimately be successful. 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 to address the safety, efficacy or clinical or non-clinical pharmacology of our product candidates. 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.

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 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 INI1-negative malignant rhabdoid tumors, or MRT, as well as MRTO, and soft tissue sarcoma, in the United States and for pinometostat for the treatment of acute lymphoblastic leukemia and acute myeloid leukemia in the United States and 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 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.

*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 received Fast Track designation from the FDA for tazemetostat for relapsed or refractory patients with DLBCL with mutated EZH2, and for relapsed or refractory FL patients with or without mutated EZH2 and 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. The FDA has broad discretion whether or not to grant this designation, so



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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. 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 that jurisdiction.***

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.

***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.

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***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. 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 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 requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

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

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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.

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

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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 laws may result in additional reductions in Medicare and

other healthcare funding. In addition, there have been recent actions by members of the U.S. Congress and the new presidential administration regarding the potential repeal and replacement of the PPACA. However, it remains unclear how a repeal or replacement of current healthcare programs might affect our ability to sell our products and the prices we may obtain for any of our approved products.

We expect that the PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

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 business could be harmed, possibly materially.



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***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.

## **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. 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.

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***We expect to expand our development and regulatory capabilities and potentially 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**

***Our executive officers and directors and their affiliates, if they choose to act together, may have the ability to significantly influence all matters submitted to stockholders for approval.***

As of August 1, 2017, our executive officers and directors and their affiliates beneficially own, in the aggregate, shares representing approximately 25% of our common stock. As a result, if these stockholders were to choose to act together, they may be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, could significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of ownership control may:

delay, defer or prevent a change in control;

entrench our management and board of directors; or

impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

***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.

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

Although our common stock is listed on The NASDAQ Global 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, 2015 until August 1, 2017, the sale price of our common stock as reported on the NASDAQ Global Market ranged from a high of \$28.48 to a low of \$7.02. 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.

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

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company through 2018. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;

not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;

reduced disclosure obligations regarding executive compensation; and

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exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive, as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

***We will 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 after we are no longer an emerging growth company, 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 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. However, while we remain an emerging growth company, we are not 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 will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. If we 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.

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**Item 6. Exhibits**

The exhibits listed in the Exhibit Index to this Quarterly Report on Form 10-Q are incorporated herein by reference.

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**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 7, 2017

EPIZYME, INC.

By: /s/ Andrew E. Singer  
Andrew E. Singer  
Executive Vice President, Finance and  
Accounting,

Chief Financial Officer and Treasurer  
(Principal Financial and Accounting  
Officer and Authorized Officer)

**Table of Contents****EXHIBITS INDEX**

<b>Exhibit Number</b>	<b>Description of the Exhibit</b>
10.1	Third Amendment to Lease, entered into May 25, 2017 and effective May 18, 2017, by and between the Company and ARE-TECH Square, LLC.(1)
10.2	Fourth Amendment to Lease, entered into May 25, 2017 and effective May 18, 2017, by and between the Company and ARE-TECH Square, LLC.(1)
31.1	Certification of Chief 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. (2)
31.2	Certification of Chief 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. (2)
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 Andrew E. Singer, Executive Vice President, Finance and Administration, Chief Financial Officer and Treasurer of the Company. (2)
101.INS	XBRL Instance 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) Incorporated by reference to the Current Report on Form 8-K (File No. 001-35945) filed with the Securities and Exchange Commission on May 30, 2017.

(2) Filed with this Form 10-Q.