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Epizyme, Inc.  
Form 10-Q  
August 02, 2018

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, 2018

OR

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

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission File Number: 001-35945

EPIZYME, INC.

(Exact name of registrant as specified in its charter)

Delaware 26-1349956  
(State or other jurisdiction of (I.R.S. Employer

incorporation or organization) Identification No.)

400 Technology Square, Cambridge, Massachusetts 02139  
(Address of principal executive offices) (Zip code)

617-229-5872

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(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 July 30, 2018: 69,503,076 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,” “should,” “statements or variations of such terms. Our forward-looking statements are based on a series of expectations, assumptions, estimates and projections about our company, are not guarantees of future results or performance and involve substantial risks and uncertainty. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. Our business and our forward-looking statements involve substantial known and unknown risks and uncertainties, including the risks and uncertainties inherent in our statements regarding:

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

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

Our management’s discussion and analysis of our financial condition and results of operations are based upon our unaudited condensed consolidated financial statements included in this Quarterly Report on Form 10-Q, which have been prepared by us in accordance with accounting principles generally accepted in the United States of America, or GAAP, for interim periods and with Regulation S-X promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act. This discussion and analysis should be read in conjunction with these unaudited condensed consolidated financial statements and the notes thereto as well as in conjunction with our Annual Report on Form 10-K for the fiscal year ended December 31, 2017, or our Annual Report. The three months ended June 30, 2018 and 2017 are referred to as the second quarter of 2018 and 2017, respectively. Unless the context indicates otherwise, all references herein to our company include our wholly owned subsidiary.

## PART I – FINANCIAL INFORMATION

## Item 1. Financial Statements

## EPIZYME, INC.

## CONDENSED CONSOLIDATED BALANCE SHEETS (UNAUDITED)

(Amounts in thousands except per share data)

	June 30, 2018	December 31, 2017
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$67,906	\$ 226,664
Marketable securities	147,718	49,775
Accounts receivable	—	382
Contract asset	12,000	—
Prepaid expenses and other current assets	8,514	8,983
Total current assets	236,138	285,804
Property and equipment, net	2,141	2,527
Restricted cash and other assets	1,046	1,028
Total assets	\$239,325	\$ 289,359
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
Current liabilities:		
Accounts payable	\$10,989	\$ 7,001
Accrued expenses	18,168	17,549
Current portion of capital lease obligation	16	110
Other current liabilities	5	4
Total current liabilities	29,178	24,664
Capital lease obligation, net of current portion	52	—
Deferred revenue	3,806	28,809
Other long-term liabilities	711	515
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, \$0.0001 par value; 5,000 shares authorized;		
no shares issued and outstanding	—	—
Common stock, \$0.0001 par value; 125,000 shares		
authorized; 69,495 shares and 69,302 shares		
issued and outstanding, respectively	7	7
Additional paid-in capital	731,884	723,510
Accumulated other comprehensive loss	(26 )	(49 )
Accumulated deficit	(526,287)	(488,097 )
Total stockholders' equity	205,578	235,371
Total liabilities and stockholders' equity	\$239,325	\$ 289,359

See notes to condensed consolidated financial statements.

EPIZYME, INC.

## CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(UNAUDITED)

(Amounts in thousands except per share data)

	Three Months Ended		Six Months Ended	
	June 30,		June 30,	
	2018	2017	2018	2017
Collaboration revenue	\$ 12,000	\$ 10,000	\$ 12,000	\$ 10,000
Operating expenses:				
Research and development	31,346	27,292	56,968	51,987
General and administrative	10,914	11,170	20,274	19,439
Total operating expenses	42,260	38,462	77,242	71,426
Operating loss	(30,260)	(28,462)	(65,242)	(61,426)
Other income, net:				
Interest income, net	1,143	428	2,042	866
Other (expense) income, net	(11)	10	7	14
Other income, net	1,132	438	2,049	880
Net loss	\$(29,128)	\$(28,024)	\$(63,193)	\$(60,546)
Other comprehensive income (loss):				
Unrealized gain on available-for-sale securities	46	34	23	46
Comprehensive loss	\$(29,082)	\$(27,990)	\$(63,170)	\$(60,500)
Loss per share allocable to common stockholders:				
Basic	\$(0.42)	\$(0.48)	\$(0.91)	\$(1.04)
Diluted	\$(0.42)	\$(0.48)	\$(0.91)	\$(1.04)
Weighted average shares outstanding:				
Basic	69,490	58,377	69,438	58,298
Diluted	69,490	58,377	69,438	58,298

See notes to condensed consolidated financial statements.

EPIZYME, INC.

## CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS (UNAUDITED)

(Amounts in thousands)

	Six Months Ended,	
	June 30, 2018	2017 (as revised)*
<b>CASH FLOWS FROM OPERATING ACTIVITIES:</b>		
Net loss	\$(63,193 )	\$(60,546 )
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	582	824
Stock-based compensation	6,311	5,778
Amortization of discount on investments	(565 )	(69 )
Changes in operating assets and liabilities:		
Accounts receivable	382	(2 )
Contract asset	(12,000 )	—
Prepaid expenses and other current assets	469	(1,947 )
Accounts payable	3,988	4,600
Accrued expenses	619	138
Other assets	(18 )	(20 )
Other liabilities	196	96
Net cash used in operating activities	(63,229 )	(51,148 )
<b>CASH FLOWS FROM INVESTING ACTIVITIES:</b>		
Purchases of available-for-sale securities	(165,688)	(80,846 )
Maturities of available-for-sale securities	68,334	140,552
Purchases of property and equipment	(109 )	(683 )
Net cash (used in) provided by investing activities	(97,463 )	59,023
<b>CASH FLOWS FROM FINANCING ACTIVITIES:</b>		
Payments under capital lease obligation	(129 )	(303 )
Proceeds from public offering, net of commissions	—	1,587
Proceeds from stock options exercised	1,604	1,128
Issuance of shares under employee stock purchase plan	459	347
Net cash provided by financing activities	1,934	2,759
Net (decrease) increase in cash, cash equivalents and restricted cash	(158,758)	10,634
Cash, cash equivalents and restricted cash, beginning of period	227,126	78,357
Cash, cash equivalents and restricted cash, end of period	\$68,368	\$88,991
<b>SUPPLEMENTAL CASH FLOW INFORMATION:</b>		
Cash paid for income taxes	\$38	\$—
Unrealized gain on investments	\$23	\$46
Cumulative catch up related to the adoption of ASU 2016-09	\$—	\$115

\* Revised as a result of the adoption of ASU 2016-18



See notes to condensed consolidated financial statements.

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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 is committed to rewriting treatment for cancer and other serious diseases through discovering, developing, and commercializing novel epigenetic medicines. By focusing on the genetic drivers of disease, the Company’s science seeks to match targeted medicines with the patients who need them. The Company is developing its lead product candidate, tazemetostat, an oral, first-in-class selective inhibitor of the EZH2 histone methyltransferase, or HMT, in a range of cancer types and settings, and developing the lead development candidate in the Company’s novel G9a program, EZM8266, for the treatment of sickle cell disease.

Through June 30, 2018, the Company has raised, including amounts received under collaboration agreements, an aggregate of \$891.6 million to fund its operations, of which \$217.8 million was non-equity funding through its collaboration agreements, \$597.8 million was from the sale of common stock in the Company’s public offerings and \$76.0 million was from the sale of redeemable convertible preferred stock in private financings prior to the Company’s initial public offering in May 2013. As of June 30, 2018, the Company had \$215.6 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 \$526.3 million through June 30, 2018, 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 and commercialization of tazemetostat and the rest of its pipeline, the need to obtain marketing approval for its product candidates, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and ability to transition from clinical-stage manufacturing to commercial-stage production of products.

2. Summary of Significant Accounting Policies

Basis of Presentation

The condensed consolidated financial statements of the Company included herein have been prepared, without audit, pursuant to the rules and regulations of the Securities and Exchange Commission, or the SEC. Certain information and footnote disclosures normally included in financial statements prepared in accordance with accounting principles generally accepted in the United States of America have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these condensed consolidated financial statements should be read in conjunction with the financial statements and notes thereto included in the Company’s Annual Report on Form 10-K for the fiscal year ended December 31, 2017, or the Annual Report.

The unaudited condensed consolidated financial statements include the accounts of Epizyme, Inc. and its wholly owned, controlled subsidiary, Epizyme Securities Corporation. All intercompany transactions and balances of subsidiaries have been eliminated in consolidation. In the opinion of management, the information furnished reflects all adjustments, all of which are of a normal and recurring nature, necessary for a fair presentation of the results for the reported interim periods. The Company considers events or transactions that occur after the balance sheet date but before the condensed consolidated financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The three months ended June 30, 2018 and 2017 are

referred to as the second quarter of 2018 and 2017, 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

During the quarter ended March 31, 2018, the Company adopted Accounting Standards Codification, or ASC, Topic 606, Revenue from Contracts with Customers, or ASC 606, using the modified retrospective transition method, resulting in a significant change in the Company's revenue recognition policy, as referenced below in this Note 2 under Recently Adopted Accounting Pronouncements. In addition, the Company adopted ASC 2016-18, Restricted Cash, resulting in a change to the beginning and ending cash balances for the periods presented in the condensed consolidated statements of cash flows, also referenced below in this Note 2. There have been no other material changes to the Company's significant accounting policies during the three months ended June 30, 2018, as compared to the significant accounting policies disclosed in Note 2, Summary of Significant Accounting Policies, of the Company's financial statements included in the Annual Report.

## Going Concern

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

The Company's evaluation entails analyzing prospective operating budgets and forecasts for expectations of the Company's cash needs, and comparing those needs to the current cash, cash equivalent and marketable securities balances. After considering the Company's current research and development plans 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, 2018, 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.

## Revenue Recognition

Effective January 1, 2018, the Company adopted Accounting Standards Codification, or ASC, Topic 606, Revenue from Contracts with Customers, or ASC 606, using the modified retrospective transition method. Under this method, results for reporting periods beginning after January 1, 2018 are presented pursuant to ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with ASC 605. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company has entered into collaboration and license agreements, which are within the scope of ASC 606, to discover, develop, manufacture and commercialize product candidates. The terms of these agreements typically contain multiple promises or obligations, which may include: (i) licenses, or options to obtain licenses, to compounds directed to specific HMT targets (referred to as "exclusive licenses") and (ii) research and development activities to be performed on behalf of the collaboration partner related to the licensed HMT targets. Payments to the Company under these agreements may include non-refundable license fees, customer option exercise fees, payments for research activities, reimbursement of certain costs, payments based upon the achievement of certain milestones and royalties on any resulting net product sales.

The Company first evaluates license and/or collaboration arrangements to determine whether the arrangement (or part of the arrangement) represents a collaborative arrangement pursuant to ASC Topic 808, Collaborative Arrangements, based on the risks and rewards and activities of the parties pursuant to the contractual arrangement. The Company accounts for collaborative arrangements (or elements within the contract that are deemed part of a collaborative arrangement), which represent a collaborative relationship and not a customer relationship, outside the scope of ASC 606. The Company's collaborations primarily represent revenue arrangements. For the arrangements or arrangement components that are subject to revenue accounting guidance, in determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must use significant judgment to determine: a) the number of performance obligations based on the determination under step (ii) above and whether those performance obligations are distinct from other performance obligations in the contract; b) the transaction price under step (iii) above; and c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above. The Company uses judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price as described further below. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. In determining the stand-alone selling

price of a license to the Company's proprietary technology or a material right provided by a customer option, the Company considers market conditions as well as entity-specific factors, including those factors contemplated in negotiating the agreements as well as internally developed estimates that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating its estimated stand-alone selling price, the Company evaluates whether changes in the key assumptions used to determine its estimated stand-alone selling price will have a significant effect on the allocation of arrangement consideration between performance obligations.

Amounts received prior to revenue recognition are recorded as deferred revenue. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current portion of deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion. Amounts recognized as revenue, but not yet received or invoiced are generally recognized as contract assets.

**Exclusive Licenses** – If the license to the Company's intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, which generally include research and development services, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a license is distinct from the other promises, the Company considers relevant facts and circumstances of each arrangement, including the research and development capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can benefit from the license for its intended purpose without the receipt of the remaining promise, whether the value of the license is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise, and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. The measure of progress, and thereby periods over which revenue should be recognized, are subject to estimates by management and may change over the course of the research and development and licensing agreement.

**Research and Development Services** – The promises under the Company's collaboration and license agreements generally include research and development services to be performed by the Company on behalf of the collaboration partner. For performance obligations that include research and development services, the Company generally recognizes revenue allocated to such performance obligations based on an appropriate measure of progress. The Company utilizes judgment to determine the appropriate method of measuring progress for purposes of recognizing revenue, which is generally an input measure such as costs incurred. The Company evaluates the measure of progress each reporting period as described under Exclusive Licenses above. Reimbursements from the partner that are the result of a collaborative relationship with the partner, instead of a customer relationship, such as co-development activities, are recorded as a reduction to research and development expense.

**Customer Options** – The Company's arrangements may provide a collaborator with the right to select a target for licensing either at the inception of the arrangement or within an initial pre-defined selection period, which may, in certain cases, include the right of the collaborator to extend the selection period. Under these agreements, fees may be due to the Company (i) at the inception of the arrangement as an upfront fee or payment, (ii) upon the exercise of an option to acquire a license or (iii) upon extending the selection period as an extension fee or payment. If an

arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights, or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the inception of the arrangement. The Company allocates the transaction price to material rights based on the relative stand-alone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised or expires.

Milestone Payments – At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial, and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such

adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. If a milestone or other variable consideration relates specifically to the Company's efforts to satisfy a single performance obligation or to a specific outcome from satisfying the performance obligation, the Company generally allocates the milestone amount entirely to that performance obligation once it is probable that a significant revenue reversal would not occur.

Royalties – For arrangements that include sales-based royalties, including milestone payments based on a level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from any of its licensing arrangements.

For a complete discussion of accounting for collaboration revenues, see Note 8, Collaborations.

#### Pending Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or 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. Although early adoption is permitted, the Company does not plan to early adopt the new standard. The Company is currently evaluating the potential changes to the Company's future financial reporting and disclosures that may result from adopting this ASU, but expects that all of its lease commitments will be subject to the new standard.

#### Recently Adopted Accounting Pronouncements

##### Revenue Recognition

In May 2014, the FASB, issued ASU, 2014-09, Revenue From Contracts With Customers. ASU 2014-09 amends Accounting Standards Codification, or ASC, 605, Revenue Recognition ("ASC 605"), by outlining a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers. In addition, the FASB 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 new standards are codified under ASC 606, Revenue From Contracts with Customers ("ASC 606"). The Company adopted this new standard on January 1, 2018 using the modified retrospective approach. The Company has elected to use the following practical expedient that is permitted under the rules of the adoption, which has been applied consistently to all contracts: the Company has not retrospectively restated its contracts that have been amended at each amendment date as is generally required under ASC 606. Instead, upon adoption, an entity may reflect the aggregate effect of all modifications that occurred before the beginning of the earliest period presented when identifying the satisfied and unsatisfied performance obligations; determining the transaction price; and allocating the transaction price to the satisfied and unsatisfied performance obligations.



As a result of adopting ASC 606 on January 1, 2018, the Company recorded a cumulative-effect credit to opening accumulated deficit of \$25.0 million as of January 1, 2018 and a corresponding decrease to deferred revenue, net of current portion. For the three and six months ended June 30, 2018, it became probable that a significant reversal of cumulative revenue would not occur for a development milestone for \$12.0 million and this milestone was recognized in accordance with ASC 606 as well as a related contract asset. No revenue would have been recognized pursuant to ASC 605 for three and six months ended June 30, 2018. Deferred revenue as of June 30, 2018 was \$3.8 million under ASC 606, as compared to a balance of \$28.9 million, which would have resulted under ASC 605.

The cumulative-effect change relates principally to the Company's treatment of option rights under its agreement with Celgene Corporation, or Celgene, and the identification of more performance obligations under ASC 606 in comparison with identified units of accounting under ASC 605. The adoption did not impact the previous accounting for the Company's agreements with Glaxo Group Limited, or GSK and Eisai Co. Ltd., or Eisai. Pursuant to ASC 605, the Company had deemed Celgene's options to license the three small molecule HMT inhibitors targeting three predefined targets, or the Option Targets, as non-substantive and therefore included the services that it would be required to perform upon option exercise as deliverables. ASC 606 provides that only options that are deemed to be material rights are a performance obligation and that any goods or services required upon exercise of the option be excluded from the evaluation of performance obligations until the option is exercised. As a result of this change to the guidance, (1) the pre-IND research services performed by the Company for each of the three Option Targets were deemed to be distinct performance obligations whereas each had previously been combined into one unit of accounting with the respective license that is subject to the exercise of the option and (2) a lesser amount of transaction price was allocated to the options. For further discussion of the change and the adoption of this standard, see Note 8, Collaborations.

## Cash

As of January 1, 2018, the Company adopted 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 adoption of this standard did not have a material impact on the Company's condensed consolidated statements of cash flows.

As of January 1, 2018, the Company adopted 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. The Company adopted the standard using the retrospective approach. The adoption of the standard did not have a material impact on the Company's condensed consolidated financial statements or disclosures; however, prior period restricted cash was added to beginning and ending cash and cash equivalents in the condensed consolidated statements of cash flows to conform to the current period presentation.

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

	As of June 30,	
	2018	2017
	(In thousands)	
Cash and cash equivalents	\$67,906	\$88,529
Restricted cash, as part of other assets	462	462
Total cash, cash equivalents, and restricted cash		
shown in the consolidated statements of cash flows	\$68,368	\$88,991

The \$0.5 million relates to a letter of credit as a security deposit for the office and laboratory lease at Technology Square in Cambridge, Massachusetts. The Company has recorded cash held to secure this letter of credit as restricted cash in restricted cash and other assets on the condensed consolidated balance sheet. There were no other material changes to the Company's consolidated financial statements or disclosures.

## Share-Based Payment

As of January 1, 2018, the Company adopted 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 adoption of this standard did not materially impact the Company's stock-based compensation expense as no awards were modified during the three and six months ended June 30, 2018.

## 3. Marketable Securities

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The following table summarizes the available-for-sale securities held at June 30, 2018 (in thousands):

Description	Amortized Unrealized Unrealized			Fair Value
	Cost	Gains	Losses	
Commercial paper	\$ 89,445	\$ 3	\$ —	\$ 89,448
Corporate notes	58,299	—	(29 )	58,270
Total	\$ 147,744	\$ 3	\$ (29 )	\$ 147,718

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The following table summarizes the available-for-sale securities held at December 31, 2017 (in thousands):

Description	Amortized		Unrealized		Fair Value
	Cost	Gains	Losses		
Commercial paper	\$ 16,964	\$ —	\$ (6	)	\$ 16,958
Corporate notes	31,610	—	(43	)	31,567
U.S. government agency securities and U.S. Treasuries	1,250	—	—		1,250
Total	\$ 49,824	\$ —	\$ (49	)	\$ 49,775

The amortized cost of available-for-sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At June 30, 2018, 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, 2018, 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, 2018 was \$91.0 million, which consisted of 10 commercial paper securities and 18 corporate notes securities. The aggregate unrealized loss for those securities in an unrealized loss position for less than twelve months as of June 30, 2018 was less than \$0.1 million. The aggregate fair value of available-for-sale securities held by the Company in an unrealized gain position for less than twelve months as of June 30, 2018 was \$56.8 million, which consisted of 11 commercial paper securities and 2 corporate notes securities. The aggregate unrealized gain for those securities in an unrealized gain position for less than twelve months as of June 30, 2018 was less than \$0.1 million.

The Company does not intend to sell and it is unlikely that the Company will be required to sell the above investments before recovery of their amortized cost bases, which may be maturity. The Company determined that there was no material change in the credit risk of any of its investments. As a result, the Company determined it did not hold any investments with any other-than-temporary impairment as of June 30, 2018. The weighted-average maturity of the Company's portfolio was approximately three months at June 30, 2018.

#### 4. Fair Value Measurements

The Company's financial instruments as of June 30, 2018 and December 31, 2017 consisted primarily of cash and cash equivalents, marketable securities and accounts receivable and accounts payable. As of June 30, 2018 and December 31, 2017, the Company's financial assets recognized at fair value consisted of the following:

	Fair Value as of June 30, 2018			Level 3
	Total	Level 1	Level 2	
	(In thousands)			
Cash equivalents	\$56,030	\$20,577	\$35,453	\$ —
Marketable securities:				
Commercial paper	89,448	—	89,448	—
Corporate notes	58,270	—	58,270	—

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Total	\$203,748	\$20,577	\$183,171	\$ —
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	Fair Value as of December 31, 2017			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	\$207,251	\$207,251	\$—	\$ —
Marketable securities:				
Commercial paper	16,958	—	16,958	—
Corporate notes	31,567	—	31,567	—
U.S. government agency securities and treasuries	1,250	—	1,250	—
Total	\$257,026	\$207,251	\$49,775	\$ —

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

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

## 5. Supplemental Balance Sheet Information

Accrued expenses consisted of the following:

	December	
	June 30,	31,
	2018	2017
	(In thousands)	
Employee compensation and benefits	\$3,826	\$ 4,628
Research and development expenses	12,197	11,658
Professional services and other	2,145	1,263
Accrued expenses	\$18,168	\$ 17,549

## 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, 2018 and 2017 due to the expected and known loss before income taxes to be incurred, or incurred, as applicable, for the years ended December 31, 2018 and 2017, as well as the Company's continued maintenance of a full valuation allowance against its net deferred tax assets, with the exception of the deferred tax asset related to alternative minimum tax credit.

In accordance with SAB 118, the Company's preliminary estimate of the effects of the Tax Cuts and Jobs Act, or the TCJA, including the remeasurement of deferred tax assets and liabilities, is subject to the finalization of management's analysis related to certain matters, such as developing interpretations of the provisions of the TCJA and the filing of its tax returns. U.S. Treasury regulations, administrative interpretations or court decisions interpreting the TCJA may require further adjustments and changes in its estimates. The final determination of the effects of the TCJA will be completed as additional information becomes available, but no later than one year from the enactment of the TCJA. In all cases, the Company will continue to make and refine its calculations as additional analysis is completed. In addition, the Company's estimates may also be affected as it gains a more thorough understanding of the tax law. The Company notes that as of June 30, 2018, no adjustments were made to the provisional amounts.

## 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, 2018, as compared to those disclosed in Note 7, Commitments and Contingencies, included in its Annual Report.

## 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, 2018. The Company was also eligible to receive \$35.0 million in an additional clinical development milestone payment and up to \$100.0 million in regulatory milestone payments related to DOT1L as well as up to \$65.0 million in payments, including a combination of clinical development milestone payments and an option exercise fee for each available target to which Celgene had the right to exercise its option during an initial option period that would have ended in July 2015 but was extended pursuant to the amended and restated agreement as discussed below under “Amended and Restated Agreement Structure” (each a “selected target”), and up to \$100.0 million in regulatory milestone payments for each selected target. As to DOT1L and each selected target, the Company retained all product rights in the United States and was eligible to receive royalties for each target at defined percentages ranging from the mid-single digits to the mid-teens on net product sales outside of the United States subject to reduction in specified circumstances.

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

#### Amended and Restated Agreement Structure

Under the amended and restated collaboration and license agreement:

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

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



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

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

and the Company will equally co-fund global development and each party will solely fund territory-specific development costs for its respective territory; and, as to the other two Option Targets, after the completion of Phase 1 development, Celgene will solely fund all development costs on a worldwide basis.

#### Accounting Considerations of the Amended and Restated Agreement

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

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

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

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

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

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

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

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

The transaction price was allocated to the performance obligations based on the estimated stand-alone selling prices at the time of the amendment. For the DOT1L performance obligation that includes the license and pre-IND research services, the stand-alone selling price was determined considering the stage and status of the program and the technology involved and the level of development expected, as well as the expected cost and margin for the research services. For the post-IND research and development services for DOT1L and the pre-IND research services for each Option Target, the stand-alone selling price was determined considering the expected cost and a reasonable margin for the respective services. The material rights from the option rights at the time of an IND filing for each Option Target were valued based on the estimated discount at which the option is priced and the Company's estimated

probability of the options' exercise as of the time of the amendment. The Company believes that a change in the assumptions used to determine its stand-alone selling price for the performance obligations most likely would not have a significant effect on the allocation of consideration received (or receivable) to the performance obligations that were not satisfied as of the adoption of ASC 606.

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

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

All performance obligations, except for the three material rights were substantially satisfied as of the adoption of ASC 606 and therefore all of the transaction price allocated to those performance obligations has been recognized as revenue under ASC 606. Through June 30, 2018, the Company has recognized revenue of \$99.2 million under the agreement as collaboration revenue in the Company's consolidated statements of operations and comprehensive loss and in accumulated deficit as a result of the cumulative-effect recognition upon adoption of ASC 606. The amounts received that have not yet been recognized as revenue, related to the material rights, are recorded in deferred revenue on the Company's condensed consolidated balance sheet. Deferred revenue related to the agreement amounted to \$3.8 million as of June 30, 2018, all of which is included in noncurrent liabilities.

## GSK

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

## Agreement Structure

Under the agreement, the Company has received and recognized as collaboration revenue a \$20.0 million upfront payment, a \$3.0 million payment upon the execution of the March 2014 agreement amendment, \$6.0 million of fixed research funding, \$9.0 million for research and development services and \$43.0 million of preclinical and research and

development milestone payments.

During the three months ended June 30, 2018, it became probable that a significant reversal of cumulative revenue would not occur for a development milestone for \$12.0 million for the first dosing of a patient in a Phase 2 clinical trial of the PRMT5 inhibitor licensed under the agreement. During the three months ended June 30, 2018, the associated consideration was added to the estimated transaction price and recognized as revenue and a contract asset on the Company's condensed consolidated balance sheet.

As of June 30, 2018, for the PRMT5 and PRMT1 targets, the Company is eligible to receive up to \$58.0 million in clinical development milestone payments, up to \$197.0 million in regulatory milestone payments and up to \$128.0 million in sales-based milestone payments. As a result of the termination of the agreement as it relates to the third target, the Company will receive no additional payments related to that target. In addition, GSK is required to pay the Company royalties, at percentages from the mid-single digits to the low double-digits, on a licensed product-by-licensed product basis, on worldwide net product sales, subject to reduction in specified circumstances.

The Company determined the next milestone that might be achieved under this agreement is an \$8.0 million milestone due at the first dosing of a patient for a PRMT1 inhibitor under a Phase 1 study. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or royalty payments from GSK. GSK became solely responsible for development and commercialization for each licensed target in the collaboration when the research term ended on January 8, 2015.

## Collaboration Revenue

Through June 30, 2018, the Company has earned a total of \$81.0 million under the GSK agreement, which the Company recognized as collaboration revenue in the condensed consolidated statements of operations and comprehensive loss, including \$12.0 million of milestone revenue in the three and six months ended June 30, 2018 and \$10.0 million of milestone revenue in the three and six months ended June 30, 2017. The Company did not have any deferred revenue related to this agreement as of June 30, 2018 or December 31, 2017 and any future revenues will relate to milestone payments and royalties received under the agreement with respect to the two remaining targets, if any.

The Company will reevaluate the likelihood of achieving future milestones at the end of each reporting period. The remaining future milestone payments are related to performance obligations that have been satisfied. Therefore, if the risk of significant reversal is resolved, any future milestone revenue from the arrangement will be recognized as revenue in the period the risk is relieved.

## Eisai

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

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

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

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

The Company recorded the reacquisition of worldwide rights, excluding Japan, to the EZH2 program, including tazemetostat, under the amended and restated agreement with Eisai as an acquisition of an in-process research and development asset. As this asset was acquired without corresponding processes or activities that would constitute a business, had not achieved regulatory approval for marketing and, absent obtaining such approval, had no alternative future use, the Company recorded the \$40.0 million upfront payment made to Eisai in March 2015 as research and development expense in the consolidated statements of operations and comprehensive loss. The Company has also agreed to pay Eisai up to \$20.0 million in clinical development milestone payments, including a \$10.0 million milestone upon the earlier of initiation of a first phase 3 clinical trial of any EZH2 product or the first submission of an NDA or MAA, up to \$50.0 million in regulatory milestone payments, including a \$25.0 million milestone payment upon regulatory approval of the first NDA or MAA, and royalties at a percentage in the mid-teens on worldwide net

sales of any EZH2 product, excluding net sales in Japan. The Company is eligible to receive from Eisai royalties at a percentage in the mid-teens on net sales of any EZH2 product in Japan.

#### Companion Diagnostics

##### Roche Molecular

In December 2012, Eisai and the Company entered into an agreement with Roche Molecular under which Eisai and the Company engaged Roche Molecular to develop a companion diagnostic to identify patients who possess certain activating mutations of EZH2. In October 2013, this agreement was amended to include additional mutations in EZH2. The development costs due under the amended agreement with Roche Molecular were the responsibility of Eisai until the execution of the amended and restated collaboration and license agreement with Eisai in March 2015, at which time the Company assumed responsibility for the remaining development costs due under the agreement. In December 2015, the Company entered into a second amendment to the companion diagnostic agreement with Roche Molecular. The agreement was further amended in March 2018. Before the additional amendment, the Company was responsible for the remaining development costs of \$10.5 million due under the agreement. Under the amended agreement, the Company is responsible for remaining development costs of \$10.4 million due under the agreement and Eisai has agreed to reimburse the Company \$0.9 million of this amount related to a regulatory milestone for Japan. The Company expects the remaining development costs under the amended agreement to be incurred and paid through 2020.

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

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

## 9. Stock-Based Compensation

Total stock-based compensation expense related to stock options, restricted stock units and shares issued under the employee stock purchase plan was \$3.4 million and \$3.0 million for the three months ended June 30, 2018 and 2017, respectively, and \$6.3 and \$5.8 million for the six months ended June 30, 2018 and 2017, respectively.

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

	Three Months Ended		Six Months Ended	
	June 30, 2018	2017	June 30, 2018	2017
	(In thousands)		(In thousands)	
Research and development	\$1,222	\$1,509	\$2,346	\$2,901
General and administrative	2,202	1,512	3,965	2,877
<b>Total</b>	<b>\$3,424</b>	<b>\$3,021</b>	<b>\$6,311</b>	<b>\$5,778</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 \$10.08 and \$10.13 per option for those options granted during the three months ended June 30, 2018 and 2017, respectively, and \$10.34 and \$8.54 per option for those options granted during the six months ended June 30, 2018 and 2017, respectively. Key assumptions used to apply this pricing model were as follows:

	Three Months Ended		Six Months Ended	
	June 30 2018	2017	June 30 2018	2017
Risk-free interest rate	2.8 %	1.8 %	2.6 %	1.8 %
Expected life of options	6.0 years	6.0 years	6.0 years	6.0 years
Expected volatility of underlying	71.9 %	74.4 %	71.5 %	74.5 %



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stock

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, 2018:

	Number of Options (In thousands)	Price per Share	Weighted Average Exercise Term (In years)	Weighted Average Remaining Aggregate Contractual Term (In years)	Intrinsic Value (In thousands)
Outstanding at December 31,					
2017	4,576	\$ 14.57			
Granted	1,874	15.98			
Exercised	(163 )	9.89			
Forfeited or expired	(469 )	18.14			
Outstanding at June 30, 2018	5,818	\$ 14.87	8.27		\$ 7,591
Exercisable at June 30, 2018	2,062	\$ 15.35	7.00		\$ 4,571

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As of June 30, 2018, there was \$33.1 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 2.82 years.

Restricted Stock Units

As of June 30, 2018, there were no restricted stock units outstanding.

10. Loss Per Share

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

	Three Months Ended		Six Months Ended	
	June 30, 2018	2017	June 30, 2018	2017
	(In thousands except per share data)		(In thousands except per share data)	
Net loss	\$(29,128)	\$(28,024)	\$(63,193)	\$(60,546)
Weighted average shares outstanding	69,490	58,377	69,438	58,298
Basic and diluted loss per share				
allocable to common stockholders	\$(0.42 )	\$(0.48 )	\$(0.91 )	\$(1.04 )

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		Six Months Ended	
	June 30, 2018	2017	June 30, 2018	2017
	(In thousands)		(In thousands)	
Stock options	5,818	5,107	5,818	5,107
Unvested restricted stock units	—	49	—	49
Shares issuable under employee				
stock purchase plan	20	32	20	32
	5,838	5,188	5,838	5,188

11. Related Party Transactions

Celgene has made a series of equity investments in the Company, owning 3,674,640 shares of common stock representing 5.3% of the Company's outstanding common stock as of June 30, 2018. 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.

The Company has received consulting and advisory services from a director. The Company paid this director approximately \$137,000 and \$0 for these services during the three months ended June 30, 2018 and 2017, respectively, and \$327,000 and \$0 during the six months ended June 30, 2018 and 2017, respectively. Of these amounts, \$60,000 and \$48,000 of amounts due to the director were included in accrued expenses at June 30, 2018 and December 31, 2017, respectively.

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

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

### Overview

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

We have taken a "pipeline in a product" approach to developing tazemetostat with a broad clinical development program through company-sponsored studies and collaborations that are evaluating tazemetostat as both a monotherapy and combination treatment in both hematological malignancies and solid tumors. Tazemetostat has shown meaningful clinical activity as a monotherapy in indications in both disease areas and has been generally well tolerated across clinical trials to date.

In April 2018, following a safety report of a pediatric patient who developed a secondary T-cell lymphoblastic lymphoma, or T-LBL, in our ongoing Phase 1 clinical trial of tazemetostat in pediatric patients, the U.S. Food and Drug Administration, or FDA, issued a partial clinical hold on new enrollment of patients with genetically defined solid tumors and hematologic malignancies in our ongoing clinical trials of tazemetostat. In the second quarter of 2018, the French National Agency for Medicines and Health Products Safety and Germany's Federal Institute for Drugs and Medical Devices each took similar actions. Under these regulatory actions, patients on study who have not experienced disease progression may be able to continue to receive tazemetostat.

To resolve the partial clinical hold, we have re-consented all patients in our clinical trials and updated our informed consent form based on this safety report. We have also reviewed the single T-cell lymphoblastic lymphoma, or T-LBL, case in detail, completed a comprehensive assessment of tazemetostat safety data and clinical activity observed to date across clinical trials, and convened a panel of external experts to review and validate the assessment. This information will be included in a formal response to regulatory authorities. We plan to continue to engage with the FDA regarding the partial clinical hold and then finalize our response to regulatory authorities, which may include proposed amendments to our study protocols, which could include changes to the patient populations we are investigating for treatment and how any potential future secondary malignancies in our trials may be handled. Once we have gained alignment with regulators in the United States, France and Germany, we anticipate that the partial clinical hold would be lifted and that enrollment activities would be able to proceed in those countries. In light of the partial clinical hold, we are assessing our timelines for completing patient enrollment in trials not fully enrolled at the time of the partial clinical hold.

In our hematological program, we are conducting a global Phase 2 study evaluating tazemetostat's treatment potential in patients with relapsed or refractory follicular lymphoma, or FL, or diffuse large B-cell lymphoma, or DLBCL, the

two most prevalent forms of non-Hodgkin lymphoma, or NHL, both with and without EZH2 activating mutations. FL patients in this trial are receiving tazemetostat as a monotherapy. DLBCL patients in this trial are receiving tazemetostat as a monotherapy or in combination with the steroid prednisolone.

At the 23rd Congress of the European Hematology Association in June 2018, positive interim data were reported from the FL cohorts in this Phase 2 study. The interim data as of May 1, 2018 showed that tazemetostat had meaningful clinical activity and had been generally well tolerated in adult patients with relapsed or refractory FL in the trial. An objective response rate, or ORR, of 71 percent was observed in the cohort of FL patients with EZH2 activating mutations (n=28) with an interim median progression-free survival of approximately 49 weeks and a median duration of response of 32 weeks. An ORR of 33 percent was observed in the fully-enrolled cohort of FL patients with wild-type EZH2 (n=54) with an interim median progression-free survival of 30 weeks and a median duration of response of approximately 76 weeks. The median duration of response in both cohorts continue to mature, with more than half of the responders still on treatment. Interim safety results at the time of this analysis showed that six percent of FL patients discontinued treatment due to treatment-related adverse events. Adverse events of Grade 3 or higher were reported across 17 percent

of patients, the most frequent of which included thrombocytopenia, anemia, asthenia and fatigue. We are continuing to enroll FL patients with EZH2 mutations outside of the United States, France and Germany in our ongoing global Phase 2 study. Based on our initial engagement with the FDA in late 2017, we believe we have the opportunity to submit for accelerated approval for tazemetostat as a monotherapy in FL, subject to the results of the FL cohorts of our Phase 2 study and additional regulatory engagement. We plan to continue to engage with the FDA throughout 2018 in regard to the partial clinical hold and to further refine our registration strategy for FL, and are assessing our timeline for submitting to the FDA a New Drug Application, or NDA, for tazemetostat for FL. We also plan to commence a combination study of tazemetostat in FL.

We have conducted an interim assessment of data from this same Phase 2 trial in the DLBCL patients, including the patients receiving tazemetostat monotherapy and the patients receiving the tazemetostat combination with prednisolone. This assessment has shown that tazemetostat was clinically active and generally well-tolerated in the monotherapy cohorts. In the combination cohort, prednisolone was not found to augment tazemetostat clinical activity. After taking into consideration the level of clinical activity in these cohorts, input from key opinion leaders and our clinical investigators and the evolving DLBCL treatment landscape, we have determined that further development of tazemetostat for DLBCL as a monotherapy and in combination with prednisolone is not warranted. While patients with ongoing responses in these cohorts are able to remain on tazemetostat, we do not plan to enroll any additional DLBCL patients. We plan to report the findings from these cohorts at a medical meeting in the second half of 2018. We also plan to evaluate other potential combinations in DLBCL and have two Phase 1b combination studies ongoing.

The first is being conducted with the Lymphoma Study Association, or LYSA, and is evaluating tazemetostat in combination with R-CHOP as a front-line treatment regimen for high-risk DLBCL patients. We plan to engage further with LYSA to assess the potential of advancing this combination into Phase 2. The other is a combination study with Genentech, Inc., or Genentech, that is investigating tazemetostat in combination with Genentech's checkpoint inhibitor atezolizumab in relapsed or refractory DLBCL.

In our solid tumor program, we are evaluating tazemetostat's treatment potential in adults and children with molecularly defined solid tumors, including INI1- and SMARCA4-negative tumors, which we collectively refer to as INI1-negative tumors. We are conducting a global Phase 2 trial of tazemetostat in adults with INI1-negative tumors, including epithelioid sarcoma, malignant rhabdoid tumors, or MRT, other INI1-negative tumors, and chordoma. Based on positive data that we observed in the epithelioid sarcoma cohort in the ongoing study, we engaged with the FDA in May 2017. Based on this FDA interaction, we have identified a potential path to submission for accelerated approval in this indication and are targeting submission of our first NDA to the FDA for tazemetostat for epithelioid sarcoma in the first half of 2019. We are targeting a 2019 submission in order to include more mature durability data in our submission package and provide time to resolve the partial clinical hold prior to participating in a pre-NDA meeting. In connection with this planned submission, we plan to commence a clinical trial of tazemetostat for epithelioid sarcoma that could serve as the confirmatory trial required in connection with any accelerated approval.

We are also evaluating tazemetostat in the dose-expansion portion of a Phase 1 study in pediatric patients with INI1-negative tumors and in a Phase 2 clinical trial in pediatric patients with solid tumors and lymphoma, called the Pediatric MATCH trial, under a Cooperative Research and Development Agreement, or CRADA, with the NCI.

In April 2018, we voluntarily paused enrollment worldwide in our Phase 1 pediatric trial following the receipt of the safety report regarding the patient who developed a secondary T-cell lymphoma. At the time of the safety report, the patient, who had advanced poorly differentiated chordoma, had been on study for approximately 15 months and had achieved a confirmed partial response. This patient has now discontinued tazemetostat and is being treated for T-cell lymphoma. We are assessing appropriate next steps for this pediatric study.

In addition, we are evaluating tazemetostat in adults with mesothelioma characterized by BRCA1-associated protein 1 (BAP1) loss-of-function. At the American Society of Clinical Oncology Annual Meeting in June 2018, encouraging

clinical data were reported from our Phase 2 study of tazemetostat as a monotherapy in relapsed/refractory malignant mesothelioma patients with BAP1 loss-of-function. The primary endpoint in this trial was met with 51% of patients (31/61) having achieved disease control at 12 weeks, exceeding the pre-specified disease control rate (DCR) threshold of  $\geq 35$  percent. Tazemetostat was generally well tolerated in this study.

Subject to the resolution of the holds on enrollment, Genentech has agreed that, as a part of its MORPHEUS study, it will evaluate tazemetostat in combination with atezolizumab (TECENTRIQ®), a PD-L1 inhibitor, in patients with non-small cell lung cancer. We also plan to evaluate tazemetostat in a Phase 2 clinical trial in adult patients with ovarian cancer under a Cooperative Research and Development Agreement, or CRADA, with the NCI.

We have announced that the FDA has granted tazemetostat:

• Fast Track designations for the treatment of patients with relapsed or refractory FL, with or without activating EZH2 mutations, relapsed or refractory DLBCL with EZH2 activating mutations and metastatic or locally advanced epithelioid sarcoma who have progressed on or following an anthracycline-based treatment regimen; and  
• Orphan drug designation for the treatment of patients with FL, chordoma, malignant rhabdoid tumors, or MRT, soft tissue sarcoma and mesothelioma. The orphan drug designation for the treatment of MRT applies to INI1-negative MRT as well as SMARCA4-negative malignant rhabdoid tumor of ovary, or MRTO.

In addition, the European Commission has granted orphan drug designation to tazemetostat for the treatment of patients with FL, DLBCL and malignant mesothelioma.

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. Tazemetostat is covered by claims of U.S. and European composition of matter patents, which are expected to expire in 2032, exclusive of any extensions. We own global rights to EZM8266.

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, 2018, we had received \$217.8 million in non-equity funding under these collaborations.

We have retained commercialization rights in the United States to all of our other programs, except two programs that are the subject of our collaboration with GSK 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 in select 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 capabilities to lead global commercial strategy. We have recently begun building the infrastructure necessary to support the successful launch and marketing of tazemetostat and other product candidates that may receive marketing approval.

Through June 30, 2018, we have raised an aggregate of \$891.6 million to fund our operations, of which \$217.8 million was non-equity funding through our collaboration agreements, \$597.8 million was from the sale of common stock in our public offerings and \$76.0 million was from the sale of redeemable convertible preferred stock. As of June 30, 2018, we had \$215.6 million in cash, cash equivalents and marketable securities.

We commenced active operations in early 2008, and since inception, have incurred significant operating losses. As of June 30, 2018, our accumulated deficit totaled \$526.3 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 our continued execution on our clinical development and commercialization plans for tazemetostat.

#### Collaborations

Refer to Note 8, Collaborations, of the notes to our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q for a description of the key terms of our arrangements with Celgene, GSK, Eisai and Roche Molecular.

As of June 30, 2018, we had recognized revenue of \$99.2 million under the Celgene agreement as collaboration revenue in our condensed consolidated statements of operations and comprehensive loss and in accumulated deficit as



a result of the cumulative-effect recognition upon adoption of Accounting Standards Codification Topic 606, Revenue from Contracts with Customers, or ASC 606. Deferred revenue related to the Celgene agreement amounted to \$3.8 million as of June 30, 2018, all of which is included in noncurrent liabilities.

There have been no updates to the accounting for our GSK and Eisai collaboration agreements as a result of the adoption of ASC 606.

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## Results of Operations

## Collaboration Revenue

The following is a comparison of collaboration revenue for the three and six months ended June 30, 2018 and 2017:

	Three Months Ended			Six Months Ended		
	June 30, 2018	2017	Change	June 30, 2018	2017	Change
	(In millions)			(In millions)		
Collaboration revenue	\$ 12.0	\$ 10.0	\$ 2.0	\$ 12.0	\$ 10.0	\$ 2.0

We recognized \$12.0 million of collaboration revenue in the three and six months ended June 30, 2018. Collaboration revenue in the three and six months ended June 30, 2018 reflects a \$12.0 million milestone payment from GSK, for which it became probable of achievement. This milestone relates to the first dosing of a patient in a Phase 2 clinical trial of GSK3326595, a PRMT5 inhibitor discovered by us and licensed to GSK under the collaboration agreement.

We recognized \$10.0 million of collaboration revenue in the three and six months ended June 30, 2017. 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 targeting PRMT1 that we discovered and licensed to GSK.

## Research and Development

The following is a comparison of research and development expenses for the three and six months ended June 30, 2018 and 2017:

	Three Months Ended			Six Months Ended		
	June 30, 2018	2017	Change	June 30, 2018	2017	Change
	(In millions)			(In millions)		
Research and development	\$ 31.3	\$ 27.3	\$ 4.0	\$ 57.0	\$ 52.0	\$ 5.0

During the three months ended June 30, 2018, total research and development expenses increased by \$4.0 million compared to the three months ended June 30, 2017. During the six months ended June 30, 2018, total research and development expenses increased by \$5.0 million compared to the six months ended June 30, 2017. The increases in the three and six months ended June 30, 2018 are primarily due to greater tazemetostat manufacturing costs, increased clinical and regulatory activities associated with the development of tazemetostat, and preclinical studies related to our preclinical G9a inhibitor program, EZM8266, offset by decreases in our discovery research activities due to a greater focus on our most promising programs.

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

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Product Program	Three Months Ended		Six Months Ended	
	June 30, 2018 (In millions)	2017	June 30, 2018 (In millions)	2017
External research and development expenses:				
Tazemetostat and related EZH2 programs	\$ 16.6	\$ 11.7	\$ 27.8	\$ 23.0
Pinometostat and related DOT1L programs	0.0	0.2	0.0	0.5
Discovery and preclinical stage product programs, collectively	4.3	6.0	8.3	9.4
Unallocated personnel and other expenses	10.4	9.4	20.9	19.1
Total research and development expenses	\$ 31.3	\$ 27.3	\$ 57.0	\$ 52.0

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External research and development expenses for tazemetostat and related EZH2 programs increased \$4.9 million and \$4.8 million during the three and six months ended June 30, 2018, respectively, compared to the three and six months ended June 30, 2017. External research and development costs include external manufacturing costs related to the acquisition of active pharmaceutical ingredient and manufacturing of clinical drug supply, ongoing clinical trial costs, discovery and preclinical research in support of the tazemetostat program and expenses associated with our companion diagnostic program.

External research and development expenses for pinometostat and related DOT1L programs decreased \$0.2 million and \$0.5 million for the three and six months ended June 30, 2018, respectively, compared to the three and six months ended June 30, 2017. The decline in program spending reflects our completion of the pinometostat Phase 1 clinical trials during the fourth quarter of 2016 and the associated reduction in costs. The costs incurred related to pinometostat in the three and six months ended June 30, 2018 are primarily associated with costs attributed to the CRADA with the NCI.

External research and development expenses for discovery and preclinical stage product programs decreased \$1.7 million and \$1.1 million for the three and six months ended June 30, 2018, respectively, compared to the three and six months ended June 30, 2017, primarily related to decreased spending for discovery research activities, offset by increased development activities related to our novel G9a program, EZM8266, for the potential treatment of sickle cell disease.

Unallocated personnel and other expenses are comprised of compensation expenses for our full-time research and development employees and other general research and development expenses. Unallocated personnel and other expenses increased \$1.0 million and \$1.8 million for the three and six months ended June 30, 2018, respectively, compared to the three and six months ended June 30, 2017. The increase in unallocated personnel and other expenses in the three and six months ended June 30, 2018 was primarily due to growth in our clinical, regulatory, and manufacturing functions to support continued development of tazemetostat.

We expect research and development expenses to increase during the remainder of 2018, as we progress our development program for tazemetostat, expand our regulatory activities, and advance our preclinical G9a program, EZM8266, 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, 2018 and 2017:

	Three Months Ended			Six Months Ended		
	June 30, 2018	2017	Change	June 30, 2018	2017	Change
	(In millions)			(In millions)		
General and administrative	\$10.9	\$11.2	\$ (0.3 )	\$20.3	\$19.4	\$ 0.9

For the three months ended June 30, 2018, our general and administrative expenses decreased \$0.3 million compared to the three months ended June 30, 2017. For the six months ended June 30, 2018, our general and administrative expenses increased \$0.9 million, compared to the six months ended June 30, 2017. The decrease for the three months ended June 30, 2018 compared to the three months ended June 30, 2017 is due to decreased consulting costs, offset by an increase in pre-commercial activities. The increase for the six months ended June 30, 2018 compared to the six

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months ended June 30, 2017 is due to increased headcount and pre-commercial activities, including the build out of our medical affairs and commercial organizations.

We expect that general and administrative expenses will increase during the remainder of 2018, as we increase our pre-commercial activities for tazemetostat.

Other Income, Net

The following is a comparison of other income, net for the three and six months ended June 30, 2018 and 2017:

	Three Months Ended			Six Months Ended		
	June 30, 2018 (In thousands)	2017	Change	June 30, 2018 (In thousands)	2017	Change
Other income, net						
Interest income, net	\$1,143	\$428	\$ 715	\$2,042	\$866	\$1,176
Other (expense) income, net	(11 )	10	(21 )	7	14	(7 )
Other income, net	\$1,132	\$438	\$ 694	\$2,049	\$880	\$1,169

Other income, net consists of interest income earned on our cash equivalents and marketable securities, net of imputed interest expense paid under our capital lease obligation. The increase in other income is principally due to net interest income, which increased \$0.7 million and \$1.2 million for the three and six months ended June 30, 2018, respectively, compared to the three and six months ended June 30, 2017. The increased net interest income is primarily due to active management of the Company's investment portfolio, an increase in investment yields, and an increased cash balance as a result of the September 2017 follow-on offering.

#### Income Tax Expense

We did not record a federal or state income tax provision or benefit for the three and six months ended June 30, 2018 and 2017 due to the expected and known loss before income taxes to be incurred, or incurred, as applicable, for the years ended December 31, 2018 and 2017, as well as our continued maintenance of a full valuation allowance against our net deferred tax assets, with the exception of the deferred tax asset related to alternative minimum tax credit.

#### Liquidity and Capital Resources

In September 2017, we raised \$151.3 million, net of underwriting discounts and commissions, but before direct and incremental costs of the offering, from the sale of 10,557,000 shares of our common stock in a public offering at a price of \$15.25 per share. Through June 30, 2018, we have raised an aggregate of \$891.6 million to fund our operations, of which \$217.8 million was non-equity funding through our collaboration agreements, \$597.8 million was from the sale of common stock in our public offerings and \$76.0 million from the sale of redeemable convertible preferred stock. As of June 30, 2018, we had \$215.6 million in cash, cash equivalents, and marketable securities.

In April 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. 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, including \$1.6 million in net proceeds relating to the ATM Offering in the three months ended March 31, 2017. 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 clinical trial costs, third party research and development services, expenses related to preparation for commercialization, compensation and related expenses, laboratory and related supplies, our potential future milestone payment obligations to Eisai and Roche Molecular under the amended Eisai collaboration agreement and Roche Molecular companion diagnostic agreement, legal and other regulatory expenses and general overhead costs.

Because our product candidates are in various stages of clinical and preclinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates or whether, or when, we may achieve profitability. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity or debt financings and collaboration arrangements. Except for any obligations of our collaborators to make license, milestone or royalty payments under our agreements with them, we do not have any committed external sources of liquidity. To the extent that we raise additional capital through the future sale of equity or debt, the

ownership interest of our stockholders may be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise any additional funds that may be needed through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

## Outlook

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that our existing cash, cash equivalents and marketable securities as of June 30, 2018, will be sufficient to fund our planned operating expenses and capital expenditure requirements into the fourth quarter of 2019, 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, 2018 and 2017:

	Six months ended June 30,		
	2018	2017	Change
	(In millions)		
Net cash used in operating activities	\$(63.2)	\$(51.1)	\$(12.1)
Net cash (used in) provided by investing activities	(97.5)	59.0	(156.5)
Net cash provided by financing activities	1.9	2.8	(0.9)

### Net Cash Used in Operating Activities

Net cash used in operating activities was \$63.2 million during the six months ended June 30, 2018 compared to \$51.1 million during the six months ended June 30, 2017. The increase in net cash used in operating activities primarily relates to the increase in net loss in the period ended June 30, 2018 compared to the period ended June 30, 2017, offset by changes in working capital. The most significant items affecting working capital in the six months ended June 30, 2018 include a contract asset related to the milestone revenue recognized with GSK and accounts payable and accrued expenses due to the timing of invoices and payments.

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

Net cash used in operating activities for the 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) Provided by Investing Activities

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



Net cash provided by 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 \$0.7 million of purchases of property and equipment.

#### Net Cash Provided by Financing Activities

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

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.

## 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, 2017.

## Critical Accounting Policies and Use of Estimates

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

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

During the quarter ended March 31, 2018, we adopted ASC 606 using the modified retrospective transition method, resulting in a change in our revenue recognition policy, as described in Note 2, Summary of Significant Accounting Policies—Recently Adopted Accounting Pronouncements, in the accompanying Notes to Condensed Consolidated Financial Statements included in Item 1 of this Quarterly Report on Form 10-Q. During the six months ended June 30, 2018, there have been no other material changes to our critical accounting policies disclosed in our Annual Report on Form 10-K for our fiscal year ended December 31, 2017.

## Recently Adopted Accounting Pronouncements

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

## Item 3. Quantitative and Qualitative Disclosures About Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of June 30, 2018, we had cash and cash equivalents and available-for-sale securities of \$215.6 million consisting of money market funds, corporate bonds, and commercial paper. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. We estimate that a hypothetical 100-basis point change in market interest rates would impact the fair value of

our investment portfolio as of June 30, 2018 by \$0.5 million.

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

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Item 4. Controls and Procedures  
Disclosure Controls and Procedures

We have established disclosure controls and procedures designed to ensure that information required to be disclosed in the reports that we file or submit under the Securities Exchange Act of 1934, as amended, 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 Business Officer), to allow timely decisions regarding required disclosure.

Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Business Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Quarterly Report on Form 10-Q. Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on such evaluation, our Chief Executive Officer and Chief Business Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of June 30, 2018.

Changes in Internal Control over Financial Reporting

We implemented the new revenue recognition standard as of January 1, 2018. As a result, we made the following significant modifications to our internal control over financial reporting, including changes to accounting policies and procedures, operational processes, and documentation practices:

- updated our policies and procedures related to revenue recognition and added documentation processes related to meeting the new criteria for revenue recognition;
- modified our contract review controls to take into account the new criteria for recognizing revenue, specifically the identification of implied promises and the evaluation of whether performance obligations are distinct in the context of the contract; and
- added controls to address related required disclosures regarding revenue, including the disclosure of performance obligations and our significant judgment and estimates for determining the transaction prices and when to recognize revenue.

Other than the items described above, there were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended June 30, 2018 that materially affected, or are 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

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

We currently have no products approved for sale and are investing a significant portion of our efforts and financial resources to fund the development of our lead product candidate, tazemetostat. We have another product candidate in clinical trials that we are developing, pinometostat, and GlaxoSmithKline, or GSK has initiated a Phase 2 clinical trial for a PRMT5 inhibitor that it has licensed from us. However, these development programs are early stage, and all of our other product candidates are still in preclinical development. As a result, our prospects are substantially dependent on our ability, or the ability of any future collaborator, to develop, obtain marketing approval for and successfully commercialize tazemetostat in one or more disease indications. The success of tazemetostat and any other product candidate will depend on several factors, including the following:

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

Many of these factors are beyond our control, including clinical development, the regulatory review process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any collaborator. If any of these factors adversely affect the development or commercialization of tazemetostat or any other product candidate, our business could be harmed.

In April 2018, following a safety report of a pediatric patient who developed a secondary T-cell lymphoma in our ongoing Phase 1 clinical trial of tazemetostat in pediatric patients, the FDA issued a partial clinical hold on new enrollment of patients with genetically defined solid tumors and hematologic malignancies in our ongoing clinical

trials of tazemetostat. In the second quarter of 2018 the French National Agency for Medicines and Health Products Safety and Germany's Federal Institute for Drugs and Medical Devices each took similar actions. Under these regulatory actions, patients on study who have not experienced disease progression may be able to continue to receive tazemetostat. To resolve the partial clinical hold, we have reconsented all patients in our clinical trials and updated our informed consent form based on this safety report. We have also reviewed the single T-cell lymphoblastic lymphoma, or T-LBL, case in detail, completed a comprehensive assessment of tazemetostat safety data and clinical activity observed to date across clinical trials, and convened a panel of external experts to review and validate the assessment. This information will be included in a

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formal response to regulatory authorities. We plan to continue to engage with the FDA regarding the partial clinical hold and then finalize our response to regulatory authorities, which may include proposed amendments to our study protocols, which could include changes to the patient populations we are investigating for treatment and how any potential future secondary malignancies in our trials may be handled. Once we have gained alignment with regulators in the United States, France and Germany, we anticipate that the partial clinical hold would be lifted and that enrollment activities would be able to proceed in those countries. We submitted the safety report to regulatory authorities in countries in which we are conducting our trials of tazemetostat. Additional regulatory authorities may determine to issue clinical holds on new enrollment of patients in our ongoing clinical trials of tazemetostat similar to the clinical holds issued in the United States, France and Germany or take other regulatory actions with respect to the trials of tazemetostat. If we are unable to address the partial clinical hold to the satisfaction of these regulatory authorities on a timely basis or at all, or other regulatory authorities, including in other jurisdictions, impose clinical holds on enrollment or other conditions on our clinical trials of tazemetostat, we may be unable to continue or conduct clinical trials of tazemetostat on a timely basis or at all, and our business could be harmed.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

We are conducting multiple clinical trials of tazemetostat and pinometostat, and GSK's PRMT5 inhibitor is in clinical development. The risk of failure for each of these product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans.

Product candidates are subject to preclinical safety studies, which are required prior to clinical testing, as well as continued clinical safety assessment throughout clinical testing. The outcomes of these safety studies or assessments may delay the launch of or enrollment in clinical studies. For example, in the course of our preclinical safety studies of tazemetostat, we observed the development of lymphoma in Sprague Dawley rats. As a result of these findings, coupled with our limited clinical experience in FL at the time of the IND submission in December 2015, we were unable to conduct our Phase 2 trial of tazemetostat in FL patients in the United States until the beginning of 2017. In addition, in April 2018, following a safety report of a pediatric patient who developed a secondary T-cell lymphoma in our ongoing Phase 1 clinical trial of tazemetostat in pediatric patients, the FDA issued a partial clinical hold on new enrollment of patients in our ongoing clinical trials of tazemetostat. In the second quarter of 2018, the French National Agency for Medicines and Health Products Safety and Germany's Federal Institute for Drugs and Medical Devices each took similar actions. We are working diligently to address the hold on new patient enrollment, including updating the patient informed consent form, investigator's brochure and study protocols, and will need to confirm alignment with regulatory authorities in the United States, France and Germany in order to resume enrollment. If we are unable to adequately address the partial clinical hold to the satisfaction of these regulatory authorities, or any other regulatory authorities that impose a hold on enrollment, and other matters such as these when they arise, we may be unable to continue or conduct clinical trials of our product candidates in the United States, France, Germany 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.

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 complete responses 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;

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- 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, limit the scope of our clinical trials, halt ongoing 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.

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 continue or begin as planned, will need to be restructured or will be completed on schedule, or at all. Specifically, we do not know if or when we will be able to resume U.S., French or German enrollment in our trials of tazemetostat in patients in our hematological and solid tumor programs. Significant preclinical or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. In particular, because certain of our product candidates may be focused on specific patient populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. In addition, some of our competitors have ongoing clinical trials for product candidates that may treat the broader patient populations within which our product candidates are being developed for the treatment of a

subset of identifiable patients with cancer and other diseases, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates. For instance, our ongoing clinical trials of tazemetostat in adult and pediatric patients with INI1-negative tumors are targeting rare patient populations. In

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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 diffuse large B-cell lymphoma, or DLBCL, originating from the germinal center of the lymph node, or GCB DLBCL, and one in follicular lymphoma, or 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. As a result, these arms of the Phase 2 NHL clinical trial have been, and are likely to continue to be, slower to enroll than the other arms of the Phase 2 NHL clinical trial.

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).

In April 2018, following a safety report of a pediatric patient who developed a secondary T-cell lymphoma, the FDA issued a partial clinical hold on new enrollment of patients in our ongoing clinical trials of tazemetostat. In the second quarter of 2018, the French National Agency for Medicines and Health Products Safety and Germany's Federal Institute for Drugs and Medical Devices each took similar actions. Even if we resume enrollment, the safety event could adversely affect enrollment in trials of tazemetostat.

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 preclinical testing or clinical trials or have characteristics that are unexpected in preclinical testing or clinical trials, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. In pharmaceutical development, many compounds that initially show promise in early-stage testing for treating cancer are later found to cause side effects that prevent further development of the compound.

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

The discovery of novel epigenetic therapies for patients with cancer and other serious diseases is an emerging field, and the scientific discoveries that form the basis for our efforts to discover and develop product candidates are relatively new. Although epigenetic regulation of gene expression plays an essential role in biological function, few drugs premised on epigenetics have been discovered. Moreover, those drugs based on an epigenetic mechanism that have received marketing approval are in different target classes than the chromatin modifying protein, or CMP, inhibitors where our research and development is principally focused. Although preclinical studies suggest that genetic alterations can result in changes to the activity of CMPs making them oncogenic, to date no company has

translated these biological observations into systematic drug discovery that has yielded a drug that has received marketing approval. We believe that our first three inhibitors of histone methyltransferases, or HMTs, in the clinic are all the first molecules against these targets to enter clinical development. Therefore, we do not know if our approach of inhibiting HMTs or other CMPs to treat patients with cancer and other serious diseases will be successful.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

If we or our collaborators 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, or we may work with collaborators, to 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.

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

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



## Risks Related to Our Financial Position and Need For Additional Capital

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

Since inception, we have incurred significant operating losses. Our net loss was \$63.2 million for the six months ended June 30, 2018, \$134.3 million for the year ended December 31, 2017, \$110.2 million for the year ended December 31, 2016, and \$132.4 million for the year ended December 31, 2015. As of June 30, 2018, we had an accumulated deficit of \$526.3 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 product candidates. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will continue to increase over the next several years if and as we:

- continue our Phase 2 clinical trial of tazemetostat for the treatment of patients with FL;
- continue our Phase 2 clinical trial of tazemetostat for the treatment of adult patients with certain molecularly defined solid tumors;
- continue our Phase 1 clinical trial of tazemetostat for the treatment of pediatric patients with certain molecularly-defined solid tumors;
- continue our clinical trials of tazemetostat in combination with R-CHOP in first line elderly patients with DLBCL and in combination with Genentech Inc.'s anti-PD-L1 cancer immunotherapy, atezolizumab, in patients with relapsed or refractory DLBCL being conducted by our collaborators;
- continue our clinical trial of tazemetostat in combination with Genentech's anti-PD-L1 cancer immunotherapy, atezolizumab, in patients with relapsed or refractory non-small cell lung cancer being conducted by our collaborator, 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 Co. Ltd, or Eisai;
- complete IND-enabling studies for EZM8266, a G9a inhibitor designed to treat patients with sickle cell disease, and prepare for a Phase 1 study;
- continue the research and development of our additional proprietary product candidates, as well as for Celgene Corporation, or Celgene, under our amended and restated collaboration and license agreement;
- 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, manufacturing and scientific personnel; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

To become and remain profitable, we must succeed in developing, and eventually commercializing, a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We 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 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 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, 2018, will be sufficient to fund our planned operating expenses and capital expenditure requirements into the fourth quarter of 2019, without giving effect to milestone payments we may receive under our collaboration agreements. We have based these expectations on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Our future capital requirements will depend on many factors, including:

- the progress and results of our ongoing and planned clinical trials of tazemetostat;
- the number and development requirements of additional indications for tazemetostat and other product candidates that we may pursue, including the scope, progress, results and costs of discovery research, preclinical development, laboratory testing and clinical trials for such product candidates;
- 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;
- 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

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

Based on interactions with the FDA, we have identified a potential path for accelerated approval in epithelioid sarcoma and we are targeting submission of our first new drug application, or NDA, to the FDA for tazemetostat for this indication in the first half of 2019. In addition, based on initial engagement with the FDA, we believe we have the opportunity to submit for accelerated approval for tazemetostat as a monotherapy in FL, subject to the results of the FL cohorts in our ongoing global Phase 2 study of tazemetostat in NHL and additional regulatory engagement. We plan to continue to engage with the FDA throughout 2018 in regard to the partial clinical hold and to further refine our registration strategy for FL, and are assessing our timeline for submitting to the FDA an NDA for tazemetostat as a monotherapy in FL. It is possible that the FDA or any other regulatory authority may refuse to accept our applications for substantive review, or that the FDA or other regulatory authority may conclude after review of our data that our application is insufficient to obtain marketing approval of tazemetostat on an accelerated basis or at all. If the FDA does not agree that we have sufficient data to seek accelerated approval or does not accept or approve one or more of our planned NDAs for tazemetostat, we may be required to study tazemetostat in additional patients or conduct additional clinical trials, preclinical studies or manufacturing validation studies and submit that data to regulators before our application can be resubmitted or will be reconsidered. Depending on the extent of these or any other required trials or studies, submission of our planned NDAs or acceptance or approval of these NDAs for tazemetostat may be delayed by several years, or may require us to expend more resources than we have available. It is also

possible that additional trials or studies, if performed and completed, may not be considered sufficient by the FDA to accept or approve the planned NDAs for tazemetostat. Any delay in obtaining, or an inability to obtain, marketing approvals would prevent us from commercializing tazemetostat in the United States and/or abroad, generating revenue and achieving and sustaining profitability. If any of these outcomes occurs, either to tazemetostat or to any future product candidate for which we may seek marketing approval, we may be forced to abandon our development efforts for tazemetostat or such future product candidates, which could significantly harm our business.

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

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

- the efficacy and potential advantages compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;

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- the convenience and ease of administration compared to alternative treatments;
- the willingness of the patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the availability of third party coverage and adequate reimbursement;
- the prevalence and severity of any side effects;
- any safety events that may have occurred in connection with the development of the product candidate; and
- any restrictions on the use of our products together with other medications.

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

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 have recently begun building the infrastructure necessary to support the successful commercial launch and marketing of tazemetostat and other product candidates that may receive marketing approval. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute our product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

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

The development and commercialization of new drug products is highly competitive. We face competition with respect to our current product candidates, and will likely face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of many of the disease indications for which we are developing our product candidates. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection

and establish collaborative arrangements for research, development, manufacturing and commercialization.

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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, Johnson & Johnson, Novartis AG, Pfizer, Inc., Merck & Co., Inc., Daiichi Sankyo Company Limited, Takeda Pharmaceutical Company Limited, AbbVie Inc., AstraZeneca Plc, Bayer Schering Pharma AG and Constellation Pharmaceuticals. Specifically, companies which are known to have EZH2 inhibitor programs or related programs include: Constellation Pharmaceuticals, developing EZH2 inhibitors (CPI-1205 in Phase 1/2 castration-resistant prostate cancer; CPI-0209 in preclinical development), Novartis AG, developing an EED inhibitor which indirectly blocks EZH2 (MAK683, Phase 1/2, advanced malignancies), Daiichi Sankyo, developing a EZH1/EZH2 dual inhibitor (DS-3201, Phase 1, relapsed or refractory non-Hodgkin lymphomas), and Pfizer, which declared a development candidate (PF-06821497) in April 2017. In July 2017, GSK discontinued their EZH2 inhibitor program, GSK2816126, which had been in Phase 1 development in solid tumors and hematological malignancies. In addition, many companies are developing cancer therapeutics that work by targeting epigenetic mechanisms other than HMTs, and some including Celgene, Merck & Co., Inc., Novartis AG, Spectrum Pharmaceuticals, 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 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 trial of tazemetostat and atezolizumab in relapsed or refractory DLBCL and relapsed or refractory non-small cell lung cancer, and on the Lymphoma Study Association to manage our combination study of tazemetostat and R-CHOP in newly diagnosed, elderly, high risk patients with DLBCL. With our reacquisition of tazemetostat rights under our amended and restated collaboration and license agreement with Eisai, we do not have access to Eisai's capabilities for tazemetostat except with Eisai in Japan. Our collaborations have

provided us with important funding for our development programs and product platform and we expect to receive additional funding under these collaborations in the future. Our existing therapeutic collaborations, and any future collaborations we enter into, may pose a number of risks, including the following:

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

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

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

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

We do not plan to develop 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 may rely on Roche Molecular to develop a companion diagnostic for detecting activating mutations in EZH2 in the tazemetostat in NHL program. Our collaborators:

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

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

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

ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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

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

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

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

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

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

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

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

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

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

#### Risks Related to Our Intellectual Property

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

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary technology and products. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates.



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

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

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

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

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

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

Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

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

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

Competitors may infringe our issued patents or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly.

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

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

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

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, 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.

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

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

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

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

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

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

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

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

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

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

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

However, we plan to submit an NDA to the FDA for tazemetostat for the treatment of epithelioid sarcoma in the first half of 2019 and are assessing our timeline for submitting an NDA to the FDA for tazemetostat for FL. Failure to obtain marketing approval for tazemetostat or any other product candidate will prevent us from commercializing the product candidate. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third party clinical research organizations to assist us in this process.

Securing marketing approval requires the submission of extensive preclinical 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. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed.

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

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 patients with FL, malignant rhabdoid tumors, or MRT, soft tissue sarcoma and mesothelioma. The orphan drug designation for the treatment of MRT applies to INI1-negative MRT as well as SMARCA4-negative MRT of the ovary. We have also obtained orphan drug designations 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 the same indication for that time period. The applicable period is seven years in the United States and ten years in Europe. The exclusivity period in Europe can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug

exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

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

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



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

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

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

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

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

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

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

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

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

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. 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;

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

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

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

Healthcare providers, physicians and third party payors will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with healthcare providers, physicians and third party payors may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at \$5,500 to \$11,000 per false claim;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws and transparency statutes, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers.

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



Efforts to ensure that our business with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. We do not have a fully developed compliance program and will need to establish a more robust compliance infrastructure to address our needs in this area. We may fail to establish appropriate compliance measures, and even with a stronger program in place, it is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

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

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

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

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

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

Further, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. In January 2013, the American Taxpayer Relief Act of 2012 became law, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.



We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

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

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

The costs of prescription pharmaceuticals in the United States have also been the subject of considerable discussion in the United States, and members of Congress and the Trump administration have stated that they will address such costs through new legislative and administrative measures. To date, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

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.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

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

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

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

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

While we have not experienced any such material system failure, accident, cyber-attack or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

## Risks Related to Employee Matters and Managing Growth

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

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

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

We expect to expand our development and regulatory capabilities and 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

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;

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limit who may call stockholder meetings;  
authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and  
require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

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

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

Although our common stock is listed on The Nasdaq Global 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, 2017 until July 30, 2018, the sale price of our common stock as reported on the Nasdaq Global Market ranged from a high of \$21.40 to a low of \$9.30. 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 will 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
- 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.

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

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

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

As a public company, and particularly commencing with 2019 when 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.

Item 6. Exhibits

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

Exhibit

Number Description of the Exhibit

- 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.(1)
- 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.(1)
- 32.1 Certifications pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002, by Robert B. Bazemore, President and Chief Executive Officer of the Company, and Susan E. Graf, Chief Business Officer of the Company. (1)

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) Filed with this Form 10-Q.

SIGNATURES

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

Dated: August 2, 2018

EPIZYME, INC.

By: /s/ Susan E. Graf  
Susan E. Graf  
Chief Business Officer  
(Principal Financial Officer)