Epizyme, Inc.
Form 10-Q
August 07, 2017
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-Q

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

For the quarterly period ended June 30, 2017

OR

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

For the transition period from _____ to _____

Commission File Number: 001-35945

EPIZYME, INC.

(Exact name of registrant as specified in its charter)

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

617-229-5872

(Registrant s telephone number, including area code)

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See definitions of large accelerated filer, accelerated filer, smaller reporting company, and emerging growth company in Rule 12b-2 of the Exchange Act.

Large accelerated filer	Accelerated filer
Non-accelerated filer (Do not check if a smaller reporting company)	Smaller reporting company
	Emerging growth company

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

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

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

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PART I FINANCIAL INFORMATION

PART II OTHER INFORMATION

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

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

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

estimates or projections or other circumstances affecting such forward-looking statements occurring after the date of this Quarterly Report on Form 10-Q, even if such results, changes or circumstances make it clear that any forward-looking information will not be realized. Any public statements or disclosures by us following this Quarterly Report on Form 10-Q which modify or impact any of the forward-looking statements contained in this Quarterly Report on Form 10-Q will be deemed to modify or supersede such statements in this Quarterly Report on Form 10-Q.

Our management s discussion and analysis of our financial condition and results of operations are based upon our unaudited consolidated financial statements included in this Quarterly Report on Form 10-Q, which have been prepared by us in accordance with accounting principles generally accepted in the United States of America, or GAAP, for interim periods and with Regulation S-X promulgated under the Securities Exchange Act of 1934, as amended, or the Exchange Act. This discussion and analysis should be read in conjunction with these unaudited consolidated financial statements and the notes thereto as well as in conjunction with our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, or our Annual Report. The three months ended June 30, 2017 and 2016 are referred to as the second quarter of 2017 and 2016, respectively. Unless the context indicates otherwise, all references herein to our company include our wholly-owned subsidiary.

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PART I FINANCIAL INFORMATION

Item 1. Financial Statements

EPIZYME, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS (UNAUDITED)

(Amounts in thousands except per share data)

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

Total Liabilities and Stockholders	Equity	$ 205,310	$ 252,441

See notes to consolidated financial statements.

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EPIZYME, INC.

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(UNAUDITED)

(Amounts in thousands except per share data)

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

See notes to consolidated financial statements.

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EPIZYME, INC.

CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS (UNAUDITED)

(Amounts in thousands)

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

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

See notes to consolidated financial statements.

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EPIZYME, INC.

NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS (UNAUDITED)

1. Overview

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

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

Through June 30, 2017, the Company has raised an aggregate of $740.3 million to fund its operations, of which $217.8 million was non-equity funding through its collaboration agreements, $446.5 million was from the sale of common stock in the Company s public offerings, which includes $1.6 million during the six months ended June 30, 2017 and $76.0 million from the sale of redeemable convertible preferred stock in private financings prior to the Company s initial public offering in May 2013. As of June 30, 2017, the Company had $193.0 million in cash, cash equivalents, and marketable securities.

The Company commenced active operations in early 2008. Since its inception, the Company has generated an accumulated deficit of $414.3 million through June 30, 2017, and will require substantial additional capital to fund its research and development. The Company is subject to risks common to companies in the biotechnology industry, including, but not limited to, risks of failure of clinical trials and preclinical studies, the need to obtain additional financing to fund the future development of tazemetostat and the rest of its pipeline, the need to obtain marketing approval for its product candidates, the need to successfully commercialize and gain market acceptance of its product candidates, dependence on key personnel, protection of proprietary technology, compliance with government regulations, development by competitors of technological innovations and ability to transition from clinical-stage manufacturing to commercial-stage production of products.

2. Summary of Significant Accounting Policies

Basis of Presentation

The condensed consolidated financial statements of the Company included herein have been prepared, without audit, pursuant to the rules and regulations of the Securities and Exchange Commission (SEC). Certain information and footnote disclosures normally included in financial statements prepared in accordance with accounting principles generally accepted in the United States of America have been condensed or omitted from this report, as is permitted by such rules and regulations. Accordingly, these condensed consolidated financial statements should be read in

conjunction with the financial statements and notes thereto included in the Company s Annual Report on Form 10-K for the fiscal year ended December 31, 2016 (the Annual Report).

The unaudited condensed consolidated financial statements include the accounts of Epizyme, Inc. and its wholly owned, controlled subsidiary, Epizyme Securities Corporation. All intercompany transactions and balances of subsidiaries have been eliminated in consolidation. In the opinion of management, the information furnished reflects all adjustments, all of which are of a normal and recurring nature, necessary for a fair presentation of the results for the reported interim periods. The Company considers events or transactions that occur after the balance sheet date but before the consolidated financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The three months ended June 30, 2017 and 2016 are referred to as the second quarter of 2017 and 2016, respectively. The results of operations for interim periods are not necessarily indicative of results to be expected for the full year or any other interim period.

Significant Accounting Policies

There have been no material changes to the Company s significant accounting policies during the six months ended June 30, 2017, as compared to the significant accounting policies disclosed in Note 2, *Summary of Significant Accounting Policies*, of the Company s financial statements included in the Annual Report.

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Recent Accounting Pronouncements

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

In February 2016, the FASB issued ASU 2016-02, *Leases (Topic 842)*, which requires lessees to recognize a right-of-use asset and lease liability for most lease arrangements. The new standard is effective for annual reporting periods beginning after December 15, 2018 with early adoption permitted. The Company is currently evaluating the potential changes to the Company s future financial reporting and disclosures that may result from adopting this ASU.

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

In November 2016, the FASB issued ASU 2016-18, *Restricted Cash*, or ASU 2016-18, which requires an entity to reconcile and explain the period-over-period change in total cash, cash equivalents and restricted cash within its statements of cash flows. ASU 2018-18 is effective for fiscal years, and interim periods within, beginning after December 15, 2017. Early adoption is permitted. A reporting entity must apply the amendments in ASU 2016-18 using a full retrospective approach. The Company is currently evaluating the impact the adoption of the ASU will have on its consolidated financial statements.

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

Going Concern

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

The Company s evaluation entails analyzing prospective operating budgets and forecasts for expectations of the Company s cash needs, and comparing those needs to the current cash, cash equivalent and marketable security balances. After considering the Company s current research and development plans and the timing expectations related to the progress of its programs, and after considering its existing cash, cash equivalents and marketable securities as of June 30, 2017, the Company did not identify conditions or events that raise substantial doubt about the Company s ability to continue as a going concern within one year from the date these financial statements were issued.

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Share-Based Payment

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

3. Marketable Securities

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

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

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

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

The amortized cost of available for sale securities is adjusted for amortization of premiums and accretion of discounts to maturity. At June 30, 2017, the balance in the Company s accumulated other comprehensive loss was composed solely of activity related to the Company s available for sale marketable securities. There were no realized gains or losses recognized on the sale or maturity of available-for-sale securities during the three and six months ended June 30, 2017, and as a result, the Company did not reclassify any amounts out of accumulated other comprehensive loss for the same period.

The aggregate fair value of available for sale securities held by the Company in an unrealized loss position for less than twelve months as of June 30, 2017 was $88.4 million. The aggregate unrealized loss for those securities in an unrealized loss position for less than twelve months as of June 30, 2017 was $0.1 million. The Company determined that there was no material change in the credit risk of any of its investments. As a result, the Company determined it did not hold any investments with any other-than-temporary impairment as of June 30, 2017. The weighted average maturity of the Company s portfolio was approximately two months at June 30, 2017.

4. Fair Value Measurements

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

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

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

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

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

5. Supplemental Balance Sheet Information

Accrued expenses consisted of the following:

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

Accrued expenses	$ 16,143	$ 16,007

6. Income Taxes

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

7. Commitments and Contingencies

There have been no significant changes to the Company s commitments and contingencies in the three and six months ended June 30, 2017, as compared to those disclosed in Note 7, *Commitments and Contingencies*, included in its Annual Report, except as summarized below.

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

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Lease

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

In May 2017, the Company entered into a Third Amendment to Lease (the Third Amendment) with the Landlord, and a Fourth Amendment to Lease with the Landlord (the Fourth Amendment, and, together with the Third Amendment, the Amendments). The Amendments each amend the Lease.

Under the Amendments, the Company extended the term of the Lease at the Company s headquarters in Cambridge, Massachusetts to November 30, 2022, subject to the Company s right to terminate the Lease effective as of December 31, 2018, by giving written notice to the Landlord by December 31, 2017 and paying an early termination fee. Under the Lease, the Company has agreed to pay a monthly base rent of approximately $0.2 million for the period commencing December 1, 2017 through May 31, 2018, with an increase on June 1, 2018 and annual increases December 1 of each subsequent year until December 1, 2021.

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

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

8. Collaborations

Celgene

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

Original Agreement Structure

Under the original agreement, the Company granted Celgene an exclusive license, for all countries other than the United States, to small molecule HMT inhibitors targeting the DOT1L HMT, including pinometostat, and an option, on a target-by-target basis, to exclusively license, for all countries other than the United States, rights to small molecule HMT inhibitors targeting any HMT targets, other than the EZH2 HMT, including tazemetostat, and targets covered by the Company s collaboration and license agreement dated January 8, 2011 with GSK. Under the original

agreement, Celgene s option was exercisable during an option period that would have expired on July 9, 2015.

Under the original agreement, the Company received a $65.0 million upfront payment and $25.0 million from the sale of its series C redeemable convertible preferred stock to an affiliate of Celgene, of which $3.0 million was considered a premium and included as collaboration arrangement consideration for a total upfront payment of $68.0 million. In addition, the Company has received a $25.0 million clinical development milestone payment and $7.0 million of global development co-funding through June 30, 2017. The Company was also eligible to receive $35.0 million in an additional clinical development milestone payment and up to $100.0 million in regulatory milestone payments related to DOT1L as well as up to $65.0 million in payments, including a combination of clinical development milestone payments and an option exercise fee for each available target to which Celgene had the right to exercise its option during an initial option period that would have ended in July 2015 (each a selected target), and up to $100.0 million in regulatory milestone payments for each selected target. As to DOT1L and each selected target, the Company retained all product rights in the United States and was eligible to receive royalties for each target at defined percentages ranging from the mid-single digits to the mid-teens on net product sales outside of the United States subject to reduction in specified circumstances.

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

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Amended and Restated Agreement Structure

Under the amended and restated collaboration and license agreement:

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

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

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

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

Collaboration Revenue

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

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GSK

In January 2011, the Company entered into a collaboration and license agreement with GSK, to discover, develop and commercialize novel small molecule HMT inhibitors directed to available targets from the Company s platform. Under the terms of the agreement, the Company granted GSK exclusive worldwide license rights to HMT inhibitors directed to three targets. Additionally, as part of the research collaboration, the Company agreed to provide research and development services related to the licensed targets pursuant to agreed upon research plans during a research term that ended January 8, 2015. In March 2014, the Company and GSK amended certain terms of this agreement for the third licensed target, revising the license terms with respect to candidate compounds and amending the corresponding financial terms, including reallocating milestone payments and increasing royalty rates as to the third target. The Company substantially completed all research obligations under this agreement by the end of the first quarter of 2015 and completed the transfer of the remaining data and materials for these programs to GSK in the second quarter of 2015.

Agreement Structure

Under the agreement, the Company has recorded a $20.0 million upfront payment, a $3.0 million payment upon the execution of the March 2014 agreement amendment, $6.0 million of fixed research funding, $9.0 million for research and development services and $31.0 million of preclinical research and development milestone payments, which includes a $10.0 million milestone payment earned in May 2017 upon GSK s initiation of good laboratory practices toxicology studies for a first-in-class methyltransferase inhibitor discovered by the Company and licensed to GSK and paid in the three months ended June 30, 2017. As of June 30, 2017, the Company was eligible to receive up to $8.0 million in additional preclinical research and development milestone payments, up to $103.0 million in clinical development milestone payments, up to $278.0 million in regulatory milestone payments and up to $218.0 million in sales-based milestone payments. In addition, GSK is required to pay the Company royalties, at percentages from the mid-single digits to the low double-digits, on a licensed product-by-licensed product basis, on worldwide net product sales, subject to reduction in specified circumstances. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or royalty payments from GSK. Due to the varying stages of development of each licensed target, the Company is not able to determine the next milestone that might be achieved under this agreement, if any. GSK became solely responsible for development and commercialization for each licensed target in the collaboration when the research term ended on January 8, 2015.

Collaboration Revenue

Through June 30, 2017, the Company has earned a total of $69.0 million under the GSK agreement, which the Company recognized as collaboration revenue in the condensed consolidated statements of operations and comprehensive loss. The Company recognized $10.0 million of collaboration revenue in the three months ended June 30, 2017 related to achievement of the milestone described in the preceding paragraph. The Company did not have any deferred revenue related to this agreement as of June 30, 2017 or December 31, 2016 and any future revenues will relate to any milestone payments and royalties received under the agreement, if any.

Roche Molecular

In December 2012, Eisai and the Company entered into an agreement with Roche Molecular under which Eisai and the Company engaged Roche Molecular to develop a companion diagnostic to identify patients who possess certain activating mutations of EZH2. In October 2013, this agreement was amended to include additional mutations in EZH2. The development costs due under the amended agreement with Roche Molecular were the responsibility of

Eisai until the execution of the amended and restated collaboration and license agreement with Eisai in March 2015, at which time the Company assumed responsibility for the remaining development costs due under the agreement. In December 2015, the Company entered into a second amendment to the companion diagnostic agreement with Roche Molecular. As of June 30, 2017, the Company is responsible for the remaining development costs of $10.5 million due under the agreement. The Company expects the remaining development costs under the agreement to be incurred and paid through 2019.

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

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

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9. Stock-Based Compensation

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

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

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

Stock Options

The weighted-average grant date fair value of options, estimated as of the grant date using the Black-Scholes option pricing model, was $10.13 and $7.27 per option for those options granted during the three months ended June 30, 2017 and 2016, respectively, and $8.54 and $6.43 per option for those options granted during the six months ended June 30, 2017 and 2016, respectively. Key assumptions used to apply this pricing model were as follows:

	Three Months Ended June 30		Six Months Ended June 30	
	2017	2016	2017	2016
Risk-free interest rate	1.8%	1.3%	1.8%	1.2%
Expected life of options	6 years	6 years	6 years	6 years
Expected volatility of underlying stock	74.4%	79.0%	74.5%	78.9%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%

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

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

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

As of June 30, 2017, there was $27.7 million of unrecognized compensation cost related to stock options that are expected to vest. These costs are expected to be recognized over a weighted average remaining vesting period of 2.9 years.

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Restricted Stock Units

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

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

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

10. Loss Per Share

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
	(In thousands except per share data)			
Net loss	$ (28,024)	$ (27,981)	$ (60,546)	$ (50,860)
Weighted average shares outstanding	58,377	57,352	58,298	56,250
Basic and diluted loss per share allocable to common stockholders	$ (0.48)	$ (0.49)	$ (1.04)	$ (0.90)

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2017	2016	2017	2016
	(In thousands)			
Stock options	5,107	3,927	5,107	3,927
Unvested restricted stock units	49	79	49	79
Shares issuable under employee stock purchase plan	32	24	32	24

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

11. Related Party Transactions

Celgene has made a series of equity investments in the Company, owning 3,674,640 shares of common stock representing 6.3% of the Company s outstanding common stock as of June 30, 2017. Refer to Note 8, *Collaborations,* for additional information regarding the Company s original agreement with Celgene entered into in April 2012 and the amended and restated agreement with Celgene entered into in July 2015.

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

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

Management Overview

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

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

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

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

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

We own the global development and commercialization rights to tazemetostat outside of Japan. Eisai Co. Ltd, or Eisai, holds the rights to develop and commercialize tazemetostat in Japan, and holds a limited right of first negotiation for the rest of Asia. Tazemetostat is covered by claims of U.S. composition of matter patents, which are expected to expire in 2032. Tazemetostat has been granted Fast Track designation by the FDA in patients with DLBCL with EZH2 activating mutations and relapsed or refractory FL patients, with or without activating EZH2 mutations, and orphan drug designation by the FDA for the treatment of malignant rhabdoid tumors, or MRT, and soft tissue sarcoma, or STS. The orphan drug designation for the treatment of MRT applies to INI1-negative MRT as well as SMARCA4-negative malignant rhabdoid tumor of ovary, or MRTO.

We have collaboration agreements with Celgene Corporation and Celgene RIVOT Ltd., an affiliate of Celgene Corporation, which we collectively refer to as Celgene, Glaxo Group Limited (an affiliate of GlaxoSmithKline), or GSK, and Eisai. We also have a collaboration with Roche Molecular Systems, Inc., or Roche Molecular, to develop a companion diagnostic for use with tazemetostat to identify NHL patients with EZH2 activating mutations. These collaborations provide us with access to considerable scientific, development, regulatory and commercial capabilities. As of June 30, 2017, we had received $217.8 million in non-equity funding under these collaborations.

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

We commenced active operations in early 2008, and since inception, have incurred significant operating losses. As of June 30, 2017, our accumulated deficit totaled $414.3 million. As a clinical stage company, we expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We expect our expenses to increase in connection with our ongoing activities, including as we execute on our clinical development plans for tazemetostat.

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Development Program Update

The following table summarizes our current pipeline:

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

Tazemetostat Clinical Program

Tazemetostat NHL Clinical Program

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

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Tazemetostat Monotherapy Clinical Trials for NHL

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

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

DLBCL with GCB subtype and wild-type EZH2;

DLBCL with non-GCB subtype;

FL with EZH2 mutations; and

FL with wild-type EZH2.

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

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

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

Follicular Lymphoma Efficacy Data

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

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

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

Diffuse Large B-Cell Lymphoma Efficacy Data

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

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

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

Tazemetostat NHL Safety Data

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

Tazemetostat Combination Clinical Trials for NHL

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

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

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

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

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

Tazemetostat Clinical Program in Molecularly Defined Solid Tumors

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

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

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

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

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

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

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

Tazemetostat Mesothelioma Clinical Program

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

Tazemetostat Clinical Program in Non-Small Cell Lung Cancer

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

Tazemetostat Clinical Program in Other Tumor Types

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

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

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Pinometostat DOT1L Inhibitor

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

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

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

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

Corporate Strategy

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

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

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

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

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

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

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

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

Collaborations

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

Results of Operations

Collaboration Revenue

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

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

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

Research and Development

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

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

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

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

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

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

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

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

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

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

General and Administrative

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

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

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

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

Other Income, Net

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

Income Tax Expense

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

Liquidity and Capital Resources

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

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

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

Funding Requirements

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

Because our product candidates are in various stages of clinical and preclinical development and the outcome of these efforts is uncertain, we cannot estimate the actual amounts necessary to successfully complete the development and

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

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Outlook

Based on our research and development plans and our timing expectations related to the progress of our programs, we expect that our existing cash, cash equivalents and marketable securities as of June 30, 2017, will be sufficient to fund our planned operating expenses and capital expenditure requirements into at least the third quarter of 2018, without giving effect to any potential option exercise fees or milestone payments we may receive under our collaboration agreements. We have based this estimate on assumptions that may prove to be wrong, particularly as the process of testing drug candidates in clinical trials is costly and the timing of progress in these trials is uncertain. As a result, we could use our capital resources sooner than we expect.

Cash Flows

The following is a summary of cash flows for the six months ended June 30, 2017 and 2016:

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

Net Cash Used in Operating Activities

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

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

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

Net Cash Provided by (Used in) Investing Activities

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

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

Net Cash Provided by Financing Activities

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

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

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Contractual Obligations

There were no material changes to our contractual obligations and commitments described under Management s Discussion and Analysis and Results of Operations in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, except for the following:

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

In May 2017, we entered into a Third Amendment to Lease with the Landlord, and a Fourth Amendment to Lease with the Landlord, which we refer to collectively as the Amendments. The Amendments each amend the Lease.

Under the Amendments, we extended the term of the Lease at our headquarters in Cambridge, Massachusetts to November 30, 2022, subject to our right to terminate the Lease effective as of December 31, 2018, by giving written notice to the Landlord by December 31, 2017 and paying an early termination fee. Under the Lease, we have agreed to pay a monthly base rent of approximately $0.2 million for the period commencing December 1, 2017 through May 31, 2018, with an increase on June 1, 2018 and annual increases December 1 of each subsequent year until December 1, 2021.

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

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

Critical Accounting Policies and Use of Estimates

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

We define our critical accounting policies as those accounting principles generally accepted in the United States of America that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations as well as the specific manner in which we

apply those principles. Management has determined that our most critical accounting policies are those relating to revenue recognition, stock-based compensation and research and development expenses, including our accounting for clinical trial expense and accruals. As our clinical development plan for tazemetostat progresses, we expect research and development expenses and, in particular, our accounting for clinical trial accruals to be an increasingly important critical accounting policy. There have been no material changes or other required disclosures to our critical accounting policies disclosed in our Annual Report on Form 10-K for our fiscal year ended December 31, 2016.

Recent Accounting Pronouncements

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

Item 3. Quantitative and Qualitative Disclosures About Market Risk

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of June 30, 2017, we had cash equivalents and available for sale securities of $193.0 million consisting of money market funds, corporate bonds, commercial paper and government-related obligations. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. We estimate that a hypothetical 100-basis point change in market interest rates would impact the fair value of our investment portfolio as of June 30, 2017 by $0.3 million.

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

Item 4. Controls and Procedures

Disclosure Controls and Procedures

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

Our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of the end of the period covered by this Quarterly Report on Form 10-Q. Management recognizes that any disclosure controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on such evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of June 30, 2017.

Changes in Internal Control over Financial Reporting

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

PART II OTHER INFORMATION

Item 1A. Risk Factors

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

Risks Related to the Discovery and Development of Our Product Candidates

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

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

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

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

- successful completion of preclinical studies and clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- making arrangements with third party manufacturers for, or establishing, commercial manufacturing capabilities;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others;
- acceptance of the products, if and when approved, by patients, the medical community and third party payors;
- effectively competing with other therapies;
- obtaining and maintaining healthcare coverage and adequate reimbursement;
- protecting our rights in our intellectual property portfolio; and
- maintaining a continued acceptable safety profile of the products following approval.

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

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

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

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

Three of our product candidates are in clinical development, and our remaining product candidates are in preclinical development. Two of our product candidates in clinical development are being developed by us and the third product candidate is being developed by GSK. The risk of failure for each of our product candidates is high. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans.

Product candidates are subject to continued preclinical safety studies, which may be conducted concurrent with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future clinical studies. For example, in the course of our preclinical safety studies of tazemetostat, we observed the development of lymphoma in Sprague Dawley rats. As a result of these findings, coupled with our limited clinical experience in FL at the time of the IND submission in December 2015, we were unable to conduct our Phase 2 trial of tazemetostat in FL patients in the United States until the beginning of 2017. If we are unable to adequately address matters such as this when they arise, we may be unable to conduct clinical trials of our product candidates in the United States or in other countries, our trials may be limited to certain patient populations or our ability to conduct other trials in the United States or in other countries may be delayed.

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Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, the CRs that were observed in two patients with MLL-r in the fourth dose cohort of the dose escalation portion of our Phase 1 clinical trial of pinometostat in adults were not achieved by any other patient treated with pinometostat in the Phase 1 clinical trial. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

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

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

finding that the participants are being exposed to unacceptable health risks;

the cost of clinical trials of our product candidates may be greater than we anticipate;

the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; and

our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the trials.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

be delayed in obtaining marketing approval for our product candidates;

not obtain marketing approval at all;

obtain approval for indications or patient populations that are not as broad as intended or desired;

obtain approval with labeling or a risk evaluation mitigation strategy that includes significant use or distribution restrictions or safety warnings;

be subject to additional post-marketing testing requirements; or

have the product removed from the market after obtaining marketing approval.

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

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

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. In particular, because certain of our products may be focused on specific patient populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. In addition, some of our competitors have ongoing clinical trials for product candidates that may treat the broader patient populations within which our product candidates are being developed for the treatment of a subset of identifiable patients with cancer and other diseases, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors product candidates. For instance, our ongoing clinical trials of tazemetostat in adult and pediatric patients with INI1-negative tumors are targeting rare patient populations. In addition, our Phase 2 clinical trial of tazemetostat in patients with NHL has two arms targeting patients with EZH2 activating mutations in their tumors, one in GCB DLBCL and one in FL. Based on the aggregate scientific literature, we believe that patients wit