

Epizyme, Inc.
Form 10-Q
November 06, 2014
Table of Contents

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

FORM 10-Q

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

For the quarterly period ended September 30, 2014

OR

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

For the transition period from _____ to _____

Commission File Number: 001-35945

EPIZYME, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

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

400 Technology Square, Cambridge, Massachusetts
(Address of principal executive offices)
617-229-5872

02139
(Zip code)

(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, or a smaller reporting company. See definitions of "accelerated filer," "large accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer Accelerated filer

Non-accelerated filer (Do not check if a smaller reporting company) Smaller reporting company

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 October 31, 2014: 34,163,233 shares.

Table of Contents

PART I - FINANCIAL INFORMATION

Item 1. Financial Statements

Consolidated Balance Sheets as of September 30, 2014 and December 31, 2013 2

Consolidated Statements of Operations and Comprehensive Loss for the Three and Nine Months Ended September 30, 2014 and 2013 3

Consolidated Statements of Cash Flows for the Nine Months Ended September 30, 2014 and 2013 4

Notes to Consolidated Financial Statements 5

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations 13

Item 3. Quantitative and Qualitative Disclosures About Market Risk 24

Item 4. Controls and Procedures 24

PART II - OTHER INFORMATION

Item 1A. Risk Factors 25

Item 6. Exhibits 51

Signatures 52

Table of Contents**PART I FINANCIAL INFORMATION****Item 1. Financial Statements**

	September 30, 2014	December 31, 2013
ASSETS		
Current Assets:		
Cash and cash equivalents	\$ 211,669	\$ 123,564
Accounts receivable	2,109	33,667
Prepaid expenses and other current assets	3,273	2,421
Total current assets	217,051	159,652
Property and equipment, net	2,749	2,157
Restricted cash and other assets	953	1,179
Total Assets	\$ 220,753	\$ 162,988
LIABILITIES AND STOCKHOLDERS EQUITY		
Current Liabilities:		
Accounts payable	\$ 5,715	\$ 4,698
Accrued expenses	8,652	6,632
Current portion of deferred revenue	9,415	23,243
Total current liabilities	23,782	34,573
Deferred revenue, net of current portion	23,735	23,629
Other long-term liabilities	482	473
Commitments and contingencies		
Stockholders Equity:		
Preferred stock, \$0.0001 par value; 5,000,000 shares authorized; 0 shares issued and outstanding		
Common stock, \$0.0001 par value; 125,000,000 shares authorized; 34,063,303 shares and 28,494,447 shares issued, respectively; 34,063,303 shares and 28,488,892 shares outstanding, respectively	3	3
Additional paid-in capital	268,801	160,390
Accumulated deficit	(96,050)	(56,080)
Total stockholders equity	172,754	104,313
Total Liabilities and Stockholders Equity	\$ 220,753	\$ 162,988

See notes to consolidated financial statements.

Table of Contents

EPIZYME, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS (UNAUDITED)

(Amounts in thousands except per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2014	2013	2014	2013
Collaboration revenue	\$ 8,177	\$ 8,444	\$ 31,062	\$ 32,165
Operating expenses:				
Research and development	22,244	14,584	55,090	41,882
General and administrative	5,669	3,587	15,931	9,664
Total operating expenses	27,913	18,171	71,021	51,546
Operating loss	(19,736)	(9,727)	(39,959)	(19,381)
Other income (expense):				
Interest income	24	20	66	54
Other income (expense), net	17	3	41	(86)
Other income (expense), net	41	23	107	(32)
Loss before income taxes	(19,695)	(9,704)	(39,852)	(19,413)
Income tax expense	5		118	
Net loss	\$ (19,700)	\$ (9,704)	\$ (39,970)	\$ (19,413)
Less: accretion of redeemable convertible preferred stock to redemption value				264
Loss allocable to common stockholders	\$ (19,700)	\$ (9,704)	\$ (39,970)	\$ (19,677)
Loss per share allocable to common stockholders:				
Basic	\$ (0.58)	\$ (0.34)	\$ (1.23)	\$ (1.49)
Diluted	\$ (0.58)	\$ (0.34)	\$ (1.23)	\$ (1.49)
Weighted average shares outstanding:				
Basic	33,676	28,406	32,607	13,212
Diluted	33,676	28,406	32,607	13,212
Comprehensive loss	\$ (19,700)	\$ (9,704)	\$ (39,970)	\$ (19,413)

See notes to consolidated financial statements.

Table of Contents

EPIZYME, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS (UNAUDITED)

(Amounts in thousands)

	Nine Months Ended September 30,	
	2014	2013
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	\$ (39,970)	\$ (19,413)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	548	534
Stock-based compensation	4,678	1,819
Changes in operating assets and liabilities:		
Accounts receivable	31,558	(326)
Prepaid expenses and other current assets	(852)	(1,315)
Accounts payable	1,107	364
Accrued expenses	2,020	1,052
Deferred revenue	(13,722)	(18,739)
Restricted cash and other assets	226	(716)
Other long-term liabilities	9	(1,289)
Net cash used in operating activities	(14,398)	(38,029)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(1,230)	(230)
Net cash used in investing activities	(1,230)	(230)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from public offering, net of commissions	101,283	82,491
Proceeds from stock options exercised	2,348	171
Excess tax benefit from stock option plan	28	
Issuance of shares under employee stock purchase plan	454	
Payment of public offering costs	(649)	(2,809)
Proceeds from reimbursement of public offering costs	269	
Net cash provided by financing activities	103,733	79,853
Net increase in cash and cash equivalents	88,105	41,594
Cash and cash equivalents, beginning of period	123,564	97,981
Cash and cash equivalents, end of period	\$ 211,669	\$ 139,575
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Conversion of redeemable convertible preferred stock to common stock		76,420

Edgar Filing: Epizyme, Inc. - Form 10-Q

Purchases of property and equipment unpaid at period end	192
Accretion of redeemable convertible preferred stock to redemption value	264
Public offering costs incurred but unpaid at period end	6

See notes to consolidated financial statements.

Table of Contents

EPIZYME, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (UNAUDITED)

1. Overview and Basis of Presentation

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 innovative personalized therapeutics for patients with genetically defined cancers. The Company has built a proprietary product platform that it uses to create small molecule inhibitors of a 96-member class of enzymes known as histone methyltransferases (HMTs). Genetic alterations can result in changes to the activity of HMTs, making them oncogenic. The Company's therapeutic strategy is to inhibit oncogenic HMTs to treat the underlying causes of the associated genetically defined cancers.

The 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 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, 2013 (the Annual Report).

The unaudited consolidated financial statements include the accounts of Epizyme and its subsidiary. 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 financial statements are issued to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The three months ended September 30, 2014 and 2013 are referred to as the third quarter of 2014 and 2013, 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.

In February 2014, the Company completed a public offering of its common stock, which resulted in the sale of 3,673,901 shares, including all additional shares available to cover over-allotments, at a price of \$29.25 per share. The Company received net proceeds before expenses from this offering of \$101.3 million after deducting underwriting discounts and commissions paid by the Company.

2. Summary of Significant Accounting Policies

There have been no material changes to the significant accounting policies previously disclosed in the Company's Annual Report.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 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. ASU 2014-09 will be effective for the Company for interim and annual periods beginning after December 15, 2016. The Company is evaluating the impact that this ASU may have on

its consolidated financial statements, if any.

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern*. ASU 2014-15 amends ASC 205-40, *Presentation of Financial Statements - Going Concern*, by providing guidance on determining when and how reporting entities must disclose going-concern uncertainties in their financial statements, including requiring management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date of issuance of the entity's financial statements and providing certain disclosures if there is substantial doubt about the entity's ability to continue as a going concern. ASU 2014-15 will be effective for the Company for annual periods ending after December 15, 2016 and interim periods within annual periods beginning after December 15, 2016. The Company is still evaluating the impact of this ASU on its condensed consolidated financial statements; however, it is disclosure-only in nature.

Table of Contents**3. Fair Value Measurements**

The Company classifies fair value based measurements using a three-level hierarchy that prioritizes the inputs used to measure fair value. This hierarchy requires entities to maximize the use of observable inputs and minimize the use of unobservable inputs. The three levels of inputs used to measure fair value are as follows: Level 1, quoted market prices in active markets for identical assets or liabilities; Level 2, observable inputs other than quoted market prices included in Level 1 such as quoted market prices for markets that are not active or other inputs that are observable or can be corroborated by observable market data; and Level 3, unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities, including certain pricing models, discounted cash flow methodologies and similar techniques that use significant unobservable inputs.

The Company's financial instruments as of September 30, 2014 and December 31, 2013 consisted primarily of cash and cash equivalents, accounts receivable and accounts payable. As of September 30, 2014 and December 31, 2013, the Company's financial assets recognized at fair value consisted of the following:

	Fair Value as of September 30, 2014			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	\$ 199,532	\$ 199,532	\$	\$
Total	\$ 199,532	\$ 199,532	\$	\$

	Fair Value as of December 31, 2013			
	Total	Level 1	Level 2	Level 3
	(In thousands)			
Cash equivalents	\$ 121,424	\$ 121,424	\$	\$
Total	\$ 121,424	\$ 121,424	\$	\$

4. Accrued Expenses

Accrued expenses consisted of the following:

	September 30, 2014	December 31, 2013
	(In thousands)	
Employee compensation and benefits	\$ 2,870	\$ 2,607
Contract termination obligation	94	355
Research and development and professional expenses	5,688	3,670
Accrued expenses	\$ 8,652	\$ 6,632

Edgar Filing: Epizyme, Inc. - Form 10-Q

Contract termination obligation includes estimated lease exit charges related to the Company's former facility at 325 Vassar Street in Cambridge, Massachusetts. As of December 31, 2013, the Company had a recorded contract termination obligation of \$0.4 million. During the nine months ended September 30, 2014, the Company made cash payments of \$0.7 million and recorded sublease income of \$0.4 million, resulting in total remaining contract termination obligations of \$0.1 million as of September 30, 2014.

Table of Contents**5. Income Taxes**

The Company recorded \$0.1 million of income tax expense in the nine months ended September 30, 2014 due to provision-to-return adjustments identified related to the year ended December 31, 2013. The Company did not record a federal or state income tax provision or benefit for the three or nine months ended September 30, 2014 related to the year ending December 31, 2014, due to the expected loss before income taxes to be incurred for the year ending December 31, 2014, as well as the Company's continued maintenance of a full valuation allowance against its net deferred tax assets.

The Company did not record a federal or state income tax provision or benefit for the three or nine months ended September 30, 2013 due to the expected loss before income taxes to be incurred for the year ended December 31, 2013, as well as the Company's continued maintenance of a full valuation allowance against its net deferred tax assets.

6. Collaborations***Celgene***

In April 2012, the Company entered into a collaboration and license agreement with Celgene Corporation and Celgene International Sàrl (collectively, "Celgene") to discover, develop and commercialize, in all countries other than the United States, small molecule HMT inhibitors targeting the DOT1L HMT, including the Company's product candidate EPZ-5676, and any other HMT targets from the Company's product platform for patients with genetically defined cancers, excluding targets already selected by the Company's two other existing therapeutic collaborations (the "available targets").

Agreement Structure

Under the terms of the agreement, the Company recorded 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 recorded a \$25.0 million clinical development milestone payment and \$4.4 million of global development co-funding through September 30, 2014. The Company is also eligible to receive up to \$35.0 million in additional substantive clinical development milestone payments and up to \$100.0 million in substantive regulatory milestone payments related to DOT1L as well as up to \$65.0 million in payments, including a combination of substantive clinical development milestone payments and an option exercise fee for each selected target, and up to \$100.0 million in substantive regulatory milestone payments for each available target as to which Celgene exercises its option during an initial option period ending in July 2015. Celgene has the right to extend the option period until July 2016 by making a significant option extension payment. As to DOT1L and each available target as to which Celgene exercises its option, the Company retains all product rights in the United States and is 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. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone or royalty payments from Celgene. The next potential milestone payment that the Company might be entitled to receive under this agreement is a \$35.0 million substantive milestone for the initiation of a pivotal clinical trial, as defined in the agreement, for its DOT1L inhibitor.

The Company is obligated to conduct and solely fund research and development costs of the Phase 1 clinical trials for EPZ-5676. For all development costs other than the development costs of the Phase 1 clinical trials for EPZ-5676, Celgene and the Company will equally co-fund global development and each party will solely fund territory-specific

development costs for its territory. The Company is obligated to conduct and solely fund research and development costs through the effectiveness of the first investigational new drug application (IND) for an HMT inhibitor directed to each available target selected by Celgene, after which point Celgene and the Company will equally co-fund global development and each party will solely fund territory-specific development costs for its territory. As of September 30, 2014, the Company had recorded accounts receivable of \$1.1 million related to non-Phase 1 global development costs subject to the co-funding provisions of the agreement. Co-funded amounts received or receivable from Celgene are recorded as a reduction to research and development expense.

Table of Contents*Collaboration Revenue*

Through September 30, 2014, in addition to amounts allocated to Celgene's purchase of shares of the Company's series C redeemable convertible preferred stock, the Company had recorded a total of \$97.4 million in cash and accounts receivable under the Celgene agreement, including the \$3.0 million implied premium on Celgene's purchase of shares of the Company's series C redeemable convertible preferred stock. Through September 30, 2014, the Company has recognized \$65.8 million of collaboration revenue, including \$1.2 million and \$4.1 million in the three and nine months ended September 30, 2014, respectively, and \$3.5 million and \$10.8 million in the three and nine months ended September 30, 2013, respectively, and \$4.4 million of global development co-funding as a reduction to research and development expense, including \$1.2 million and \$2.5 million in the three and nine months ended September 30, 2014, respectively, and \$0.7 million in the three and nine months ended September 30, 2013 in the consolidated statements of operations and comprehensive loss related to this agreement. Revenue recognized in the three and nine months ended September 30, 2014 reflects the Company's current plan to reach IND effectiveness for a licensed compound from the other potential DOT1L product candidates by mid-2016. As a result, the remaining deferred revenue of approximately \$5.3 million attributed to this deliverable as of September 30, 2014 will be recognized ratably through June 30, 2016. As of September 30, 2014 and December 31, 2013, the Company had deferred revenue of \$27.2 million and \$31.3 million, respectively, related to this agreement.

Eisai

In April 2011, the Company entered into a collaboration and license agreement with Eisai Co. Ltd. (Eisai) under which the Company granted Eisai an exclusive worldwide license to its small molecule HMT inhibitors directed to the EZH2 HMT, including the Company's product candidate EPZ-6438, while retaining an opt-in right to co-develop, co-commercialize and share profits with Eisai as to licensed products in the United States. Additionally, as part of the research collaboration, the Company agreed to provide research and development services related to the licensed compounds through December 31, 2014.

Agreement Structure

Under the terms of the agreement, the Company recorded a \$3.0 million upfront payment, \$7.0 million in preclinical research and development milestone payments, a \$6.0 million clinical development milestone payment and \$21.8 million for research and development services through September 30, 2014. The Company is eligible to receive up to \$25.0 million in additional clinical development milestone payments, including substantive milestone payments of up to \$10.0 million, up to \$55.0 million in regulatory milestone payments and up to \$115.0 million in sales-based milestone payments. The Company is also eligible to receive royalties at a percentage in the mid-single digits on any net product sales outside of the United States and at a percentage from the mid-single digits to low double-digits on any product sales in the United States, 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 or profit share payments from Eisai. The next potential milestone payment that the Company might be entitled to receive under this agreement is a \$10.0 million substantive milestone for the initiation of the Phase 2 portion of the ongoing Phase 1/2 clinical trial of EPZ-6438.

Eisai solely funds all research, development and commercialization costs for licensed compounds, except for the cost obligations that the Company will undertake if it exercises its opt-in right to co-develop, co-commercialize and share profits with Eisai as to licensed products in the United States. If the Company exercises its opt-in right to a licensed compound, the licensed compound would become a shared product as to which (i) Eisai's obligation to pay royalties to the Company as to such shared product in the United States will terminate; (ii) Eisai and the Company will share in net profits or losses with respect to such shared product in the United States; (iii) 25.0% of specified past development

costs will become creditable by Eisai against future milestones or royalties due to the Company, subject to certain limitations specified in the agreement; (iv) all subsequent milestone payments that become payable by Eisai after the Company exercises its opt-in right will be decreased by 50.0% in certain circumstances; and (v) Eisai and the Company will share equally in subsequent development costs allocated to the United States.

Table of Contents*Collaboration Revenue*

Through September 30, 2014, the Company recorded a total of \$37.8 million in cash and accounts receivable under the Eisai agreement. Through September 30, 2014, the Company has recognized \$37.4 million of collaboration revenue in the consolidated statements of operations and comprehensive loss related to this agreement, including \$1.4 million and \$5.0 million in the three and nine months ended September 30, 2014, respectively, and \$1.9 million and \$12.4 million in the three and nine months ended September 30, 2013, respectively, with a \$6.0 million clinical development milestone achieved and recognized as collaboration revenue in the nine months ended September 30, 2013. As of September 30, 2014 and December 31, 2013, the Company had deferred revenue of \$0.4 million and \$1.6 million, respectively, related to this agreement.

GSK

In January 2011, the Company entered into a collaboration and license agreement with Glaxo Group Limited, an affiliate of GlaxoSmithKline (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 until the earlier of the achievement of development candidate selection for a target or the end of the research term on January 8, 2015. During 2013, development candidate selection was achieved for the first target under the collaboration and license agreement, and, accordingly, the Company is no longer providing research and development services related to this target.

In March 2014, the Company and GSK amended certain terms of this agreement for the third 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. In connection with the execution of this amendment, the Company recorded a \$3.0 million upfront payment. This \$3.0 million upfront payment has been allocated equally to the remaining two targets for which the Company is actively providing research and development services, as these remaining two targets are at similar stages of development, have equal probabilities of success and the remaining research services are expected to be performed concurrently on a ratable basis over the research term. The \$3.0 million is being recognized as collaboration revenue, on a target-by-target basis, ratably from the execution of the amendment, in March 2014, through the end of the research term, or earlier if a target reaches development candidate selection.

Agreement Structure

Under the agreement, the Company 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, \$15.0 million of preclinical research and development milestone payments and \$9.5 million for research and development services through September 30, 2014. The Company is eligible to receive up to \$18.0 million in additional substantive preclinical research and development milestone payments, up to \$109.0 million in clinical development milestone payments, up to \$275.0 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.

For each selected target in the collaboration, the Company is primarily responsible for research until the selection of the development candidate, and GSK is solely responsible for subsequent development and commercialization. GSK provided a fixed amount of research funding during the second and third years of the research term and is obligated to provide research funding equal to 100.0% of research and development costs, subject to specified limitations, for research activities conducted by the Company in the fourth year of the research term.

Collaboration Revenue

Through September 30, 2014, the Company recorded a total of \$53.5 million in payments under the GSK agreement. Through September 30, 2014, the Company has recognized \$48.1 million of collaboration revenue in the consolidated statements of operations and comprehensive loss related to this agreement, including \$5.6 million and \$22.0 million in the three and nine months ended September 30, 2014, respectively, and \$3.0 million and \$9.0 million in the three and nine months ended September 30, 2013, respectively, with \$3.0 million in preclinical research and development milestones achieved and recognized as collaboration revenue in the nine months ended September 30, 2014. As of September 30, 2014 and December 31, 2013, the Company had deferred revenue of \$5.4 million and \$13.9 million, respectively, related to this agreement.

Table of Contents**Companion Diagnostics***Roche*

In December 2012, Eisai and the Company entered into an agreement with Roche Molecular Systems, Inc. (Roche) under which Eisai and the Company are funding Roche's development of a companion diagnostic to identify patients who possess certain point mutations in EZH2. In October 2013, this agreement was amended to include additional point mutations in EZH2. The development costs under the agreement with Roche are the responsibility of Eisai until such time, if any, as the Company exercises its opt-in right under the collaboration agreement with Eisai. Under the terms of the amended agreement, Eisai agreed to pay Roche defined milestone payments of up to \$21.5 million to develop and to make commercially available the companion diagnostic. As a result, the cost of the companion diagnostic agreement, prior to the Company's potential future exercise of its opt-in right under the Eisai collaboration, will not be reflected in the Company's consolidated statements of operations and comprehensive loss. If the Company exercises its opt-in right to co-develop, co-commercialize and share profits in the United States as to EPZ-6438, Eisai will be entitled to offset up to 25.0% of the funding amount it has previously paid to Roche against future milestone payments and royalties that Eisai may be obligated to pay to the Company under the Eisai collaboration and license agreement, and the Company will become obligated to fund up to half of the defined milestones that remain payable to Roche as of the time the Company opts-in.

Abbott

In February 2013, the Company entered into an agreement with Abbott Molecular Inc. (Abbott) under which the Company agreed to fund Abbott's development of a companion diagnostic to identify patients with the mixed lineage leukemia (MLL-r) genetic alteration targeted by the Company's EPZ-5676 product candidate. Under the terms of the agreement, the Company paid Abbott an upfront payment of \$0.9 million upon the execution of the agreement, and agreed to make aggregate milestone-based development payments of up to \$6.0 million and to reimburse Abbott for specified costs not to exceed \$0.9 million. In October 2014, the Company voluntarily terminated this agreement with Abbott, discontinuing development of this proposed companion diagnostic. The termination of this agreement is not expected to have a material impact on the Company's financial statements.

7. Stock-Based Compensation

Total stock-based compensation expense related to stock options, restricted stock and the employee stock purchase plan was \$1.6 million and \$0.9 million for the three months ended September 30, 2014 and 2013, respectively, and \$4.7 million and \$1.8 million for the nine months ended September 30, 2014 and 2013, respectively.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2014	2013	2014	2013
	(In thousands)			
Research and development	\$ 749	\$ 294	\$ 2,245	\$ 695
General and administrative	834	575	2,433	1,124
Total	\$ 1,583	\$ 869	\$ 4,678	\$ 1,819

Stock Options

The weighted-average fair value of options, estimated as of the grant date using the Black-Scholes option pricing model, was \$21.32 and \$21.81 per option for those options granted during the three months ended September 30, 2014 and 2013, respectively, and \$22.21 and \$7.57 per option for those options granted during the nine months ended September 30, 2014 and 2013, respectively. Key assumptions used to apply this pricing model were as follows:

Table of Contents

	Nine Months Ended September 30, 2014	Nine Months Ended September 30, 2013
Risk-free interest rate	1.6%	0.9%
Expected life of options	6.0 years	6.0 years
Expected volatility of underlying stock	92.4%	94.7%
Expected dividend yield	0.0%	0.0%

The following is a summary of stock option activity for the nine months ended September 30, 2014:

	Number of Options	Weighted Average Exercise Price per Share	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Outstanding at December 31, 2013	4,728,503	\$ 3.13		
Granted	782,619	29.48		
Exercised	(1,876,934)	1.25		
Forfeited or expired	(81,757)	18.24		
Outstanding at September 30, 2014	3,552,431	\$ 9.58	7.7	\$ 64,943
Exercisable at September 30, 2014	1,606,793	\$ 2.04	6.4	\$ 40,379

As of September 30, 2014, there was \$19.6 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 2.6 years.

Restricted Stock

The following is a summary of restricted stock activity for the nine months ended September 30, 2014:

	Number of Shares	Weighted Average Grant Date Fair Value per Share
Outstanding at December 31, 2013	5,555	\$ 0.60
Vested	(5,555)	0.60
Outstanding at September 30, 2014		\$

8. Loss Per Share

Basic (loss) earnings per share is computed by dividing (loss) income allocable to common stockholders by the weighted average number of common shares outstanding. During periods of income, participating securities are allocated a proportional share of income determined by dividing total weighted average participating securities by the sum of the total weighted average common shares and participating securities (the two-class method). The Company's restricted stock and, prior to its automatic conversion, redeemable convertible preferred stock participate in any dividends declared by the Company and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods of loss, no loss is allocated to participating securities since they have no contractual obligation to share in the losses of the Company. Diluted (loss) earnings per share is computed after giving consideration to the dilutive effect of stock options that are outstanding during the period, except where such non-participating securities would be anti-dilutive.

Table of Contents

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

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2014	2013	2014	2013
	(In thousands except per share data)			
Net loss	\$ (19,700)	\$ (9,704)	\$ (39,970)	\$ (19,413)
Less: accretion of redeemable convertible preferred stock to redemption value				264
Loss allocable to common stockholders	\$ (19,700)	\$ (9,704)	\$ (39,970)	\$ (19,677)
Weighted average shares outstanding	33,676	28,406	32,607	13,212
Basic and diluted loss per share allocable to common stockholders	\$ (0.58)	\$ (0.34)	\$ (1.23)	\$ (1.49)

In June 2013, the Company issued 5,913,300 shares of common stock in connection with its initial public offering (IPO) and 20,633,046 shares of common stock in connection with the automatic conversion of its redeemable convertible preferred stock upon the closing of the IPO. In February 2014, the Company issued an additional 3,673,901 shares of common stock in connection with a public offering. The issuance of these shares contributed to a significant increase in the Company's shares outstanding, to 34,063,303 shares as of September 30, 2014, and in the weighted average shares outstanding for the three and nine months ended September 30, 2014 when compared to the comparable prior year periods and is expected to continue to impact the year-over-year comparability of the Company's (loss) earnings per share calculations through 2014.

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		Nine Months Ended	
	September 30,		September 30,	
	2014	2013	2014	2013
	(In thousands)			
Stock options	3,552	4,773	3,552	4,773
Unvested restricted stock		10		10
Shares issuable under employee stock purchase plan	2	2	2	2
	3,554	4,785	3,554	4,785

9. Related Party Transactions

The Company's collaboration partner Celgene has made a series of equity investments in the Company, owning 3,334,640 shares of common stock as of December 31, 2013. In the first quarter of 2014, in connection with the Company's public offering of common stock, Celgene made an additional investment in the Company, acquiring an

additional 340,000 shares of the Company's common stock, maintaining an ownership percentage representing 9.8% of the Company's fully diluted equity and 10.8% of the voting interests of the Company as of September 30, 2014. Refer to Note 6, *Collaborations*, for additional information regarding this collaboration agreement.

Under the Celgene collaboration agreement, the Company recognized \$1.2 million and \$4.1 million of collaboration revenue in the three and nine months ended September 30, 2014 and \$3.5 million and \$10.8 million of collaboration revenue in the three and nine months ended September 30, 2013, respectively, and as of September 30, 2014 and December 31, 2013, had recorded \$27.2 million and \$31.3 million of deferred revenue related to the Celgene collaboration arrangement, respectively. Additionally, in the three and nine months ended September 30, 2014, the Company recorded \$1.2 million and \$2.5 million, respectively, in global development co-funding from Celgene. As of September 30, 2014 and December 31, 2013, the Company had accounts receivable of \$1.1 million and \$26.2 million, respectively, related to this collaboration arrangement.

Table of Contents

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

Forward-looking Information

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

our plans to develop and commercialize personalized therapeutics for patients with genetically defined cancers;

our ongoing and planned clinical trials, including the timing of anticipated results;

our ability to receive research funding and achieve anticipated milestones under our collaborations;

the timing of and our ability to 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;

our ability to identify additional products or product candidates with significant commercial potential that are consistent with our commercial objectives; 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.

Management Overview

We are a clinical stage biopharmaceutical company that discovers, develops and plans to commercialize innovative personalized therapeutics for patients with genetically defined cancers. We have built a proprietary product platform that we use to create small molecule inhibitors of a 96-member class of enzymes known as histone methyltransferases, or HMTs. Genetic alterations can result in changes to the activity of HMTs, making them oncogenic. Our therapeutic strategy is to inhibit oncogenic HMTs to treat the underlying causes of the associated genetically defined cancers. The three months ended September 30, 2014 and 2013 are referred to as the third quarter of 2014 and 2013, respectively. Unless the context indicates otherwise, all references herein to our company include our wholly-owned subsidiary.

Table of Contents

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, 2013, or our Annual Report.

We commenced active operations in early 2008, and since inception, have incurred significant operating losses. As we are a clinical stage company, we expect to continue to incur significant expenses and operating losses over the next several years. Since our inception and through September 30, 2014, we have raised an aggregate of \$446.7 million to fund our operations, of which \$186.9 million was non-equity funding through our collaboration agreements, \$183.8 million was from the sale of common stock in our public offerings and \$76.0 million was from the sale of redeemable convertible preferred stock. In addition, as of September 30, 2014, we were entitled to receive \$2.1 million in non-equity funding through our collaboration agreements. As of September 30, 2014, we had \$211.7 million in cash and cash equivalents.

We are a leader in the translation of the science of epigenetics into first-in-class personalized therapeutics for patients with genetically defined cancers and currently have two HMT inhibitors in clinical development for the treatment of patients with genetically defined cancers. We believe we are the first company to conduct a clinical trial of an HMT inhibitor. We are conducting a Phase 1 clinical trial of our product candidate, EPZ-5676, an inhibitor targeting the DOT1L HMT, being developed for the treatment of acute leukemias in adult patients with genetic alterations of the *MLL* gene, referred to as MLL-r or MLL-PTD, and a Phase 1 study in pediatric patients with MLL-r leukemia. With these studies, we now have ongoing assessments of proof-of-concept in three genetically defined cancer patient groups in the EPZ-5676 clinical program: adult MLL-r, adult MLL-PTD and pediatric MLL-r. We are also conducting a Phase 1/2 clinical trial of our product candidate, EPZ-6438, an inhibitor targeting the EZH2 HMT, being developed for the treatment of non-Hodgkin lymphoma and solid tumors including INI1-deficient tumors such as synovial sarcoma and malignant rhabdoid tumors, or MRT. We plan to initiate three proof-of-concept studies for EPZ-6438: a Phase 2 trial in non-Hodgkin lymphoma patients, a Phase 1 trial in pediatric patients with INI1-deficient tumors and a Phase 2 trial in adult patients with INI1-deficient tumors. In addition to our clinical programs, we also have a pipeline of other HMT inhibitors that are in preclinical development that target our other prioritized HMTs, including the PRMT5 HMT. These programs are directed to a variety of hematological and solid tumors.

The initial clinical development plan for each of our therapeutic product candidates is directed towards patients with a particular genetically defined cancer. For many of our therapeutic product candidates, we intend to develop a companion diagnostic to identify patients that we seek to treat with our therapeutic product candidates unless we believe existing, available technology may be sufficient to identify these patients. We plan to include patients with the particular genetically defined cancer in our clinical trials beginning in Phase 1 with a view to assessing possible early evidence of potential therapeutic effect. As we are tailoring our personalized therapeutics for discrete patient populations with genetically defined cancers, we believe that many of our products may qualify for orphan drug designation in the United States, the European Union and other regions.

We have entered into strategic collaborations for certain of our therapeutic programs and corresponding companion diagnostics. Our three primary collaboration partners for our therapeutic programs are Celgene Corporation and Celgene International Sàrl, collectively, Celgene; Eisai Co., Ltd., or Eisai; and Glaxo Group Limited, an affiliate of GlaxoSmithKline, or GSK. We retain all product rights in the United States under the Celgene collaboration and an opt-in right to co-develop, co-commercialize and share profits as to licensed products in the United States under the Eisai collaboration. In October 2014, we terminated our agreement with Abbott, discontinuing development of a

proposed companion diagnostic for use with EPZ-5676. We terminated the agreement because we believe, based on discussions with the United States Food and Drug Administration, that the existing standard of care molecular testing used at the time of diagnosis will be acceptable to support further enrollment of relapsed/refractory MLL-r leukemia patients in our clinical trial as designed, rather than requiring the companion diagnostic test previously under development with Abbott.

Table of Contents

The following table summarizes key information about our two most advanced product candidates:

Product	Candidate	Clinical Populations	Stage of Development	Commercial Rights	Diagnostic Collaborator
	EPZ-5676 (DOT1L inhibitor)	<p>Acute leukemias with alterations in the <i>MLL</i> gene</p> <p>MLL-r subtype of acute myeloid leukemia, or AML, and acute lymphoblastic leukemia, or ALL, in adult patients (Chromosomal translocation involving the <i>MLL</i> gene)</p> <p>MLL partial tandem duplication, or MLL-PTD, subtype of AML in adult patients (Partial tandem duplication of the <i>MLL</i> gene)</p> <p>MLL-r in pediatric patients (Chromosomal translocation involving the <i>MLL</i> gene)</p>	<p>Phase 1 MLL-r and MLL-PTD adult patient trial ongoing</p> <p>Dose escalation stage fully enrolled in MLL-r adult patient trial</p> <p>MLL-r / MLL-PTD only adult expansion stage enrolling</p> <p>Phase 1 MLL-r pediatric patient trial enrolling</p>	<p>Epizyme: United States Celgene: Rest of world</p>	<p>None existing standard of care molecular testing used at time of diagnosis to be utilized for studies in MLL-r leukemia</p>
	EPZ-6438 (EZH2 inhibitor)	<p>Non-Hodgkin lymphomas, including germinal center diffuse large B-cell lymphoma and follicular lymphoma as well as non-germinal center NHL, including primary mediastinal B-cell lymphoma (EZH2)</p> <p>Other solid tumors such as synovial sarcoma and MRT (INI1-deficient)</p>	<p>Phase 1/2 clinical trial ongoing</p> <p>Phase 1 dose escalation enrolling, with expanded enrollment at the top two tested dose levels</p> <p>Phase 2 trial for expanded population of non-Hodgkin lymphoma patients expected to initiate in the first quarter of 2015</p>	<p>Eisai: Worldwide rights, subject to Epizyme's opt-in on 50.0% of United States rights</p>	<p>Roche (Non-Hodgkin lymphoma with EZH2 point mutations)</p>

Phase 1 trial for pediatric patients with INI1-deficient tumors expected to initiate in the first half of 2015, following a planned investigational new drug application filing in the fourth quarter of 2014

None existing standard of care immunohistochemical testing used at time of diagnosis to be utilized for studies in INI1-deficient tumors

Phase 2 trial for adult patients with INI1-deficient tumors expected to initiate in 2015

Program highlights for the nine months ended September 30, 2014 include:

For EPZ-5676, we continued enrollment in the expansion stage of our Phase 1 trial which is limited to patients with MLL-r and MLL-PTD. In November 2014, in connection with the publication of an abstract for the 2014 American Society of Hematology, or ASH, annual meeting, we released preliminary data from the dose escalation and expansion stages of this Phase 1 study measured as of the abstract cut-off date of July 15, 2014. These data showed that, in 36 patients evaluable for safety, EPZ-5676 was safe and well-tolerated, with adverse events predominantly Grade 1 or Grade 2 in severity and only two patients who discontinued treatment due to possible drug-related adverse events. These data

Table of Contents

additionally reported that, of 28 patients evaluable for efficacy, anti-leukemic activity was observed in two patients with MLL-r receiving treatment who achieved complete responses and additional findings of biological activity, such as resolution of cutaneous leukemia or leukemia cell differentiation effects, were observed in several other patients. We expect to present updated data from this trial in December 2014. In May 2014, we initiated our Phase 1 trial of EPZ-5676 in pediatric MLL-r patients. This Phase 1 study is designed to evaluate the safety, pharmacokinetics and pharmacodynamics of escalating doses of EPZ-5676 in patients between the ages of three months and 18 years and also provide a preliminary assessment of efficacy.

For EPZ-6438, which Eisai refers to as E7438, we continued enrollment in the Phase 1 dose escalation portion of our Phase 1/2 clinical trial. In August 2014, we disclosed early clinical observations from the Phase 1 portion of this Phase 1/2 study as well as findings characterizing the activity of EPZ-6438 in preclinical models of non-Hodgkin lymphoma, both as a single agent and in combination with current standards of care. In October 2014, we presented preclinical data characterizing the activity of EPZ-6438 in models of synovial sarcoma. Collectively, these preliminary data further support our plans to expand our patient population to include B-cell lymphomas with both mutant and wild-type EZH2 and support the expansion of our EPZ-6438 clinical program to pediatric and adult patients with INI1-deficient tumors. We plan to present updated data from the Phase 1 portion of our ongoing Phase 1/2 trial in November 2014. In a report that we commissioned, Clarion Healthcare estimated that the annual incidence rate in the major markets of both mutant and wild-type EZH2 germinal center B-cell lymphomas is approximately 72,000 patients. Many of these patients survive beyond the year in which they are diagnosed. Accordingly, we believe that the prevalence of patients that could potentially be treated with EPZ-6438 is significantly higher than the annual incidence. Additionally, in 2014, the United States Patent and Trademark Office granted to us U.S. Patent Nos. 8,691,507 and 8,765,732 with claims that cover the diagnosis and treatment of cancers associated with EZH2 mutation and claims covering methods of treatment of lymphomas with EZH2 inhibitors, including EPZ-6438, respectively, as well as granted notices of allowance for U.S. Patent Application Nos. 13/230,703 and 14/070,675 with claims that cover the treatment of cancers associated with EZH2 mutations and claims covering methods of treatment of lymphoma with EZH2 inhibitors, respectively.

For our discovery and preclinical stage product programs, we continued to progress the target programs partnered with GSK, collectively earning \$3.0 million in preclinical research and development milestones upon the February 2014 selection of a lead candidate for the second of the three targets under the agreement and the April 2014 selection of a lead candidate for the third of the three targets under the agreement. We also continued to progress a number of other research programs directed to high priority HMTs in our pipeline. In September 2014, the United States Patent and Trademark Office granted Notices of Allowance for two of our U.S. patent applications covering inhibitors of PRMT5 and methods of treating cancers with inhibitors of PRMT5 as well as published 10 of our patent applications covering chemical matter targeting several additional HMTs, including CARM1, PRMT1, PRMT3, PRMT6 and PRMT8.

Collaborations

The key terms of our primary collaboration agreements are as follows:

Celgene

In April 2012, we entered into a collaboration and license agreement with Celgene, to discover, develop and commercialize, in all countries other than the United States, small molecule HMT inhibitors targeting DOT1L, including EPZ-5676, and any other HMT targets from our product platform for patients with genetically defined cancers, excluding targets already selected by our two other existing collaborations, which we refer to as the available targets.

Table of Contents*Agreement Structure*

Under the terms of the agreement, we recorded a \$65.0 million upfront payment and \$25.0 million from the sale of our 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, we have recorded a \$25.0 million clinical development milestone payment and \$4.4 million of global development co-funding through September 30, 2014. We are also eligible to receive up to \$35.0 million in additional clinical development milestone payments 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 selected target, and up to \$100.0 million in regulatory milestone payments for each available target as to which Celgene exercises its option during an initial option period ending in July 2015. Celgene has the right to extend the option period until July 2016 by making a significant option extension payment. As to DOT1L and each available target as to which Celgene exercises its option, we retain all product rights in the United States and are 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 reductions in specified circumstances. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any additional milestone or royalty payments from Celgene. The next potential milestone payment that we might be entitled to receive under this agreement is \$35.0 million for the initiation of a pivotal clinical trial, as defined in the agreement, for our DOT1L inhibitor.

We are obligated to conduct and solely fund research and development costs of the Phase 1 clinical trials for EPZ-5676. For all development costs other than the development costs of the Phase 1 clinical trials for EPZ-5676, Celgene and we will equally co-fund global development and each party will solely fund territory-specific development costs for its territory. We are obligated to conduct and solely fund research and development costs through the effectiveness of the first investigational new drug application for an HMT inhibitor directed to each available target selected by Celgene, after which point Celgene and we will equally co-fund global development and each party will solely fund territory-specific development costs for its territory. In the third quarter of 2014, we recorded accounts receivable of \$1.1 million related to non-Phase 1 global development costs subject to the co-funding provisions of this agreement. Co-funded amounts received or receivable from Celgene are recorded as a reduction to research and development expense.

Collaboration Revenue

Through September 30, 2014, in addition to amounts allocated to Celgene's purchase of shares of our series C redeemable convertible preferred stock, we had recorded a total of \$97.4 million in cash and accounts receivable under the Celgene agreement, including the \$3.0 million implied premium on Celgene's purchase of our series C redeemable convertible preferred stock. Through September 30, 2014, we have recognized \$65.8 million of collaboration revenue, including \$1.2 million and \$4.1 million in the three and nine months ended September 30, 2014, respectively, and \$3.5 million and \$10.8 million in the three and nine months ended September 30, 2013, respectively, and \$4.4 million of global development co-funding as a reduction to research and development expense, including \$1.2 million and \$2.5 million in the three and nine months ended September 30, 2014, respectively, and \$0.7 million in the three and nine months ended September 30, 2013 in the consolidated statements of operations and comprehensive loss related to this agreement. As of September 30, 2014 and December 31, 2013, we had deferred revenue of \$27.2 million and \$31.3 million, respectively, related to this agreement.

Eisai

In April 2011, we entered into a collaboration and license agreement with Eisai under which we granted Eisai an exclusive worldwide license to our small molecule HMT inhibitors directed to EZH2, including EPZ-6438, while retaining an opt-in right to co-develop, co-commercialize and share profits with Eisai as to licensed products in the United States. Additionally, as part of the research collaboration, we agreed to provide research and development services related to the licensed compounds through December 31, 2014.

Agreement Structure

Under the terms of the agreement, we recorded a \$3.0 million upfront payment, \$7.0 million in preclinical research and development milestone payments, a \$6.0 million clinical development milestone payment and \$21.8 million for research and development services through September 30, 2014. We are eligible to receive up to \$25.0 million in additional clinical development milestone payments, up to \$55.0 million in regulatory milestone payments and up to \$115.0 million in sales-based milestone payments. We are also eligible to receive royalties at a percentage in the mid-single digits on any net product sales outside of the United States and at a percentage from the mid-single digits to low double-digits on any net product sales in the United States, subject to reduction in specified circumstances. Due to

Table of Contents

the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any additional milestone payments or royalty or profit share payments from Eisai. The next potential milestone payment that we might be entitled to receive under this agreement is \$10.0 million for the initiation of the Phase 2 portion of the ongoing Phase 1/2 clinical trial of EPZ-6438.

Eisai solely funds all research, development and commercialization costs for licensed compounds, except for the cost obligations that we will undertake if we exercise our opt-in right to co-develop, co-commercialize and share profits with Eisai as to licensed products in the United States. If we exercise our opt-in right as to a licensed compound, the licensed compound would become a shared product as to which (i) Eisai's obligation to pay royalties to us as to such shared product in the United States will terminate; (ii) Eisai and we will share in net profits or losses with respect to such shared product in the United States; (iii) 25.0% of specified past development costs will become creditable by Eisai against future milestones or royalties due to us, subject to certain limitations specified in the agreement; (iv) all subsequent milestone payments that become payable by Eisai to us after we exercise our opt-in right will be decreased by 50.0% in certain circumstances; and (v) Eisai and we will share equally in subsequent development costs allocated to the United States.

Collaboration Revenue

Through September 30, 2014, we recorded a total of \$37.8 million in cash and accounts receivable under the Eisai agreement. Through September 30, 2014, we have recognized \$37.4 million of collaboration revenue in the consolidated statements of operations and comprehensive loss related to this agreement, including \$1.4 million and \$5.0 million in the three and nine months ended September 30, 2014, respectively, and \$1.9 million and \$12.4 million in the three and nine months ended September 30, 2013, respectively, with a \$6.0 million clinical development milestone achieved and recognized as collaboration revenue in the nine months ended September 30, 2013. As of September 30, 2014 and December 31, 2013, we had deferred revenue of \$0.4 million and \$1.6 million, respectively, related to this agreement.

GSK

In January 2011, we entered into a collaboration and license agreement with GSK to discover, develop and commercialize novel small molecule HMT inhibitors directed to available targets from our product platform. Under the terms of the agreement, we granted GSK exclusive worldwide license rights to HMT inhibitors directed to three targets. Additionally, as part of the research collaboration provided for in the agreement, we agreed to provide research and development services related to the licensed targets pursuant to agreed upon research plans until the earlier of the achievement of development candidate selection for a target or the end of the research term on January 8, 2015. During 2013, development candidate selection was achieved for the first target under the collaboration and license agreement, and, accordingly, we are no longer providing research and development services related to this target as of September 30, 2014.

In March 2014, we and GSK amended certain terms of this agreement for the third 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. In connection with the execution of this amendment, we recorded a \$3.0 million upfront payment.

Agreement Structure

Under the agreement, we 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, \$15.0 million of preclinical research and development milestone payments and \$9.5 million for research and development services through September 30, 2014. We are eligible to receive up to \$18.0 million in additional preclinical research and development milestone payments, up to \$109.0 million in clinical development milestone payments, up to \$275.0 million in regulatory milestone payments and up to \$218.0 million in sales-based milestone payments. In addition, GSK is required to pay us 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 reductions in specified circumstances. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any additional milestone payments or royalty payments from GSK. Due to the varying stages of development of each licensed target, we are not able to determine the next milestone that might be achieved, if any.

Table of Contents

For each selected target in the collaboration, we are primarily responsible for research until the selection of the development candidate, and GSK is solely responsible for subsequent development and commercialization. GSK provided a fixed amount of research funding during the second and third years of the research term and is obligated to provide research funding equal to 100.0% of research and development costs, subject to specified limitations, for research activities we conduct in the fourth year of the research term.

Collaboration Revenue

Through September 30, 2014, we recorded a total of \$53.5 million in cash and accounts receivable under the GSK agreement. Through September 30, 2014, we have recognized \$48.1 million of collaboration revenue in the consolidated statements of operations and comprehensive loss related to this agreement, including \$5.6 million and \$22.0 million in the three and nine months ended September 30, 2014, respectively, and \$3.0 million and \$9.0 million in the three and nine months ended September 30, 2013, respectively, with \$3.0 million in preclinical research and development milestones achieved and recognized as collaboration revenue in the nine months ended September 30, 2014. As of September 30, 2014 and December 31, 2013, we had deferred revenue of \$5.4 million and \$13.9 million, respectively, related to this agreement.

Results of Operations*Collaboration Revenue*

The following is a comparison of collaboration revenue for the three and nine months ended September 30, 2014 and 2013:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2014	2013	Decrease	2014	2013	Decrease
	(In millions)					
Collaboration revenue	\$ 8.2	\$ 8.4	\$ (0.2)	\$ 31.1	\$ 32.2	\$ (1.1)

Our revenue consists of collaboration revenue, including amounts recognized from deferred revenue related to upfront payments for licenses or options to obtain licenses in the future, research and development services revenue earned and milestone payments earned under collaboration and license agreements with our collaboration partners.

During the three months ended September 30, 2014, collaboration revenue consisted of \$4.2 million recognized from deferred revenue related to upfront payments for licenses and \$4.0 million in research and development funding. This revenue compares to \$6.3 million recognized from deferred revenue related to upfront payments for licenses and \$2.1 million in research and development funding recognized in the three months ended September 30, 2013.

Collaboration revenue recognized from deferred revenue in the three months ended September 30, 2014 comprised \$1.2 million under our Celgene agreement, \$0.4 million under our Eisai agreement and \$2.6 million under our GSK agreement, as compared to \$3.5 million under our Celgene agreement, \$0.4 million under our Eisai agreement and \$2.4 million under our GSK agreement in the three months ended September 30, 2013. Collaboration revenue recognized for research and development services in the three months ended September 30, 2014 comprised \$1.0 million under our Eisai agreement and \$3.0 million under our GSK agreement, as compared to \$1.5 million under our Eisai agreement and \$0.6 million under our GSK agreement in the three months ended September 30, 2013.

Edgar Filing: Epizyme, Inc. - Form 10-Q

During the nine months ended September 30, 2014, collaboration revenue consisted of \$15.1 million recognized from deferred revenue related to upfront payments for licenses, \$3.0 million in milestone revenue and \$13.0 million in research and development funding. This revenue compares to \$19.2 million recognized from deferred revenue related to upfront payments for licenses, \$6.0 million in milestone revenue and \$7.0 million in research and development funding recognized in the nine months ended September 30, 2013.

Table of Contents

Collaboration revenue recognized from deferred revenue in the nine months ended September 30, 2014 comprised \$4.1 million under our Celgene agreement, \$1.2 million under our Eisai agreement and \$9.8 million under our GSK agreement, as compared to \$10.8 million under our Celgene agreement, \$1.2 million under our Eisai agreement and \$7.2 million under our GSK agreement in the nine months ended September 30, 2013. Milestone revenue in the nine months ended September 30, 2014 consisted of \$3.0 million in preclinical research and development milestones achieved under our GSK agreement, as compared to a \$6.0 million clinical development milestone achieved under our Eisai agreement in the nine months ended September 30, 2013. Collaboration revenue recognized for research and development services in the nine months ended September 30, 2014 comprised \$3.8 million under our Eisai agreement and \$9.2 million under our GSK agreement, as compared to \$5.2 million under our Eisai agreement and \$1.8 million under our GSK agreement in the nine months ended September 30, 2013.

Research and Development

The following is a comparison of research and development expenses for the three and nine months ended September 30, 2014 and 2013:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2014	2013	Increase	2014	2013	Increase
	(In millions)					
Research and development	\$ 22.2	\$ 14.6	\$ 7.6	\$ 55.1	\$ 41.9	\$ 13.2

Research and development expenses consist of expenses incurred in performing research and development activities, including compensation and benefits for full-time research and development employees, facilities expenses, overhead expenses, clinical trial and related clinical manufacturing expenses, fees paid to third party contract research organizations, or CROs, and other outside expenses. As we advance our product platform, we are conducting research on several prioritized HMT targets. Our research and development team is organized such that the strategy, design, management and evaluation of results of all of our research and development plans is accomplished internally while some of our research and development activities are executed using our multinational network of CROs. In the early phases of development, our research and development costs are often devoted to enhancing our product platform and are not necessarily allocable to specific targets. In circumstances, such as our Celgene collaboration, where our collaboration and license agreements provide for equally co-funded global development under joint risk sharing collaborations, amounts received from collaboration partners for such co-funding are recorded as a reduction to research and development expense.

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

Product Program (Phase as of the latest period end)	Three Months Ended September 30,		Nine Months Ended September 30,	
	2014	2013	2014	2013
	(In millions)			
External research and development expenses:				
EPZ-5676 (Phase 1) and related DOT1L programs	\$ 4.3	\$ 3.4	\$ 10.8	\$ 9.4
EPZ-6438 (Phase 1/2) and related EZH2 programs	1.4	0.8	2.9	3.1
Discovery and preclinical stage product programs, collectively	9.9	6.0	22.7	16.0
Internal research and development expenses	6.6	4.4	18.7	13.4

Edgar Filing: Epizyme, Inc. - Form 10-Q

Total research and development expenses	\$ 22.2	\$ 14.6	\$ 55.1	\$ 41.9
---	---------	---------	---------	---------

During the three and nine months ended September 30, 2014, our total research and development expenses increased by \$7.6 million and \$13.2 million, respectively, compared to the same periods of 2013, primarily due to the expansion of our product platform and the advancement of our EPZ-5676 clinical trials and related DOT1L programs. Research and development expenses for EPZ-5676 for the three and nine months ended September 30, 2014 are net of \$1.2 million and \$2.5 million, respectively, of global development co-funding from Celgene.

Most of our research and development costs have been external costs, which we began tracking on a program-by-program basis in the first quarter of 2010. Our internal research and development costs are primarily compensation expenses for our full-time research and development employees. We do not track internal research and development costs on a program-by-program basis. However, by employing a multinational network of CROs, our employees are able to dedicate significant amounts of their time to the expansion and development of our product platform while managing the research performed by our CROs. Our internal research and development expenses increased by \$2.2 million and \$5.3 million in the three and nine months ended September 30, 2014, respectively, including increases of \$0.5 million and \$1.6 million, respectively, in stock-based compensation expense, as compared to the same periods of the prior year as the number of our research and development employees grew from 54 employees as of September 30, 2013 to 65 employees as of September 30, 2014.

Table of Contents

External research and development expenses for EPZ-5676 and related DOT1L programs focused on the ongoing EPZ-5676 Phase 1 clinical trial in adult MLL-r and MLL-PTD patients and the ongoing EPZ-5676 Phase 1 clinical trial in pediatric MLL-r patients, which we initiated in May 2014, with expenses increasing from \$3.4 million in the third quarter of 2013 to \$4.3 million in the third quarter of 2014, including \$1.2 million and \$0.7 million of global development co-funding from Celgene in the third quarters of 2014 and 2013, respectively, which is recorded as a reduction to research and development expense. External research and development expenses for EPZ-6438 and related EZH2 programs focused on the ongoing EPZ-6438 Phase 1/2 clinical trial and additional preclinical screening and combination studies, with expenses increasing from \$0.8 million in the third quarter of 2013 to \$1.4 million in the third quarter of 2014. External research and development expenses for discovery and preclinical stage product programs, including the three target programs partnered with GSK, increased from \$6.0 million in the third quarter of 2013 to \$9.9 million in the third quarter of 2014 as we advanced the research and development of these programs. Research and development expenses in the nine months ended September 30, 2014 reflect similar advancement and expansion of our product programs when compared to the same period of 2013.

External research and development expenses from January 1, 2010 through September 30, 2014 were \$43.3 million for EPZ-5676 and related DOT1L programs and \$15.7 million for EPZ-6438 and related EZH2 programs. We did not maintain program-specific external cost information prior to January 1, 2010.

We expect that research and development expenses will continue to increase in the remainder of 2014, when compared to 2013, as we continue to progress and expand our ongoing clinical trials and as we continue to build our product platform and advance our other discovery and preclinical stage product programs.

General and Administrative

The following is a comparison of general and administrative expenses for the three and nine months ended September 30, 2014 and 2013:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2014	2013	Increase	2014	2013	Increase
	(In millions)					
General and administrative	\$ 5.7	\$ 3.6	\$ 2.1	\$ 15.9	\$ 9.7	\$ 6.2

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, intellectual property, business development and support functions. Other general and administrative expenses include allocated facility-related costs not otherwise included in research and development expenses, travel expenses and professional fees for auditing, tax and legal services, including intellectual property-related legal services.

For the three and nine months ended September 30, 2014, our general and administrative expenses increased compared to the same periods of the prior year, primarily related to additional professional fees, insurance and other costs associated with public company operation as well as increased stock-based compensation expense, intellectual property-related legal services and other costs to support our growing organization.

We expect that general and administrative expenses will continue to increase in the remainder of 2014, when compared to 2013, as we expand our operating activities and incur a full year of costs as a publicly traded company.

Other Income (Expense), net

Other income (expense), net consists of interest income earned on our cash equivalents, offset by interest and other expense. The change to other income, net in the nine months ended September 30, 2014 from other expense, net in the nine months ended September 30, 2013 reflects the recognition of interest expense in the nine months ended September 30, 2013 on a contract termination obligation that we incurred in the second quarter of 2012 and paid in full in the second quarter of 2013.

Table of Contents

Income Tax Expense

We recorded \$0.1 million of income tax expense in the nine months ended September 30, 2014 due to provision-to-return adjustments identified related to the year ended December 31, 2013. We did not record a federal or state income tax provision or benefit for the three or nine months ended September 30, 2014 related to the year ending December 31, 2014, due to the expected loss before income taxes to be incurred for the year ending December 31, 2014, as well as our continued maintenance of a full valuation allowance against our net deferred tax assets.

We did not record a federal or state income tax provision or benefit for the three or nine months ended September 30, 2013 due to the expected loss before income taxes to be incurred for the year ended December 31, 2013, as well as our continued maintenance of a full valuation allowance against our net deferred tax assets.

Accretion of Redeemable Convertible Preferred Stock to Redemption Value

Our redeemable convertible preferred stock automatically converted into common stock upon the closing of our initial public offering in June 2013. Our preferred stock was redeemable beginning in 2017 at its original issue prices per share plus any declared but unpaid dividends upon a specified vote of the preferred stockholders. Accretion of preferred stock reflected the periodic accretion of issuance costs and premiums on each series of preferred stock, where applicable, to their respective redemption values. We recorded \$0.3 million of accretion in the nine months ended September 30, 2013. As a result of the conversion into common stock, as of September 30, 2014 and December 31, 2013, we did not have any preferred stock outstanding and will not record any additional accretion of preferred stock related to the shares of redeemable convertible preferred stock previously issued.

Liquidity and Capital Resources

In February 2014, we completed an offering of 3,673,901 shares of our common stock, at a price of \$29.25 per share. We received net proceeds before expenses from this offering of \$101.3 million after deducting underwriting discounts and commissions paid by us.

Since our inception and through September 30, 2014, we have raised an aggregate of \$446.7 million to fund our operations, of which \$186.9 million was non-equity funding through our collaboration agreements, \$183.8 million was from the sale of common stock in our public offerings and \$76.0 million was from the sale of redeemable convertible preferred stock. In addition, as of September 30, 2014, we were entitled to receive \$2.1 million in non-equity funding through our collaboration agreements. As of September 30, 2014, we had \$211.7 million in cash and cash equivalents.

In addition to our existing cash and cash equivalents, we receive research and development 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. Our rights to payments under our collaboration agreements are our only committed external sources of funds.

Funding Requirements

Our primary uses of capital are, and we expect will continue to be, compensation and related expenses, third party clinical research and development services, laboratory and related supplies, clinical costs, legal and other regulatory expenses and general corporate costs. We believe our multinational network of CROs provides us with flexibility in managing our spending and limits our cost commitments at any point in time.

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 reimburse us for research and development expenses or to make option exercise, 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,

Table of Contents

the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our existing common stockholders. Our ability to enter into collaboration agreements for additional HMT targets is significantly limited until the end of the option period under the Celgene agreement and may continue to be limited after the end of the option period depending on how many other HMT targets Celgene elects to license, if any. If we raise additional funds through collaboration arrangements in the future, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise any additional funds that may be needed through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Outlook

Based on our research and development plans and our timing expectations related to the progress of our programs, we believe that our existing cash and cash equivalents as of September 30, 2014 and research funding that we expect to receive under our existing collaborations will enable us to fund our operating expenses and capital expenditure requirements until at least mid-2016, 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 nine months ended September 30, 2014 and 2013:

	Nine Months Ended September 30,	
	2014	2013
	(In millions)	
Net cash used in operating activities	\$ (14.4)	\$ (38.0)
Net cash used in investing activities	(1.2)	(0.2)
Net cash provided by financing activities	103.7	79.9

Net cash used in operating activities

Net cash used in operating activities was \$14.4 million during the nine months ended September 30, 2014 compared to \$38.0 million during the nine months ended September 30, 2013. The decrease in net cash used in operating activities reflects the receipt of \$51.4 million in non-equity funding, comprising \$32.0 million in milestone payments, \$3.0 million in upfront payments and \$16.4 million in research reimbursements, during the nine months ended September 30, 2014, offset by cash used in operating activities during the nine months ended September 30, 2014.

Net cash used in investing activities

Net cash used in investing activities during each of the nine months ended September 30, 2014 and 2013 relates solely to purchases of property and equipment in both periods presented and represents general maintenance capital.

Net cash provided by financing activities

Edgar Filing: Epizyme, Inc. - Form 10-Q

Net cash provided by financing activities of \$103.7 million during the nine months ended September 30, 2014 primarily reflects net cash received from our February 2014 public offering of our common stock as well as cash received for stock option exercises and the purchase of shares under our employee stock purchase plan. Net cash provided by financing activities of \$79.9 million during the nine months ended September 30, 2013 reflects net cash received from our initial public offering as well as cash received from stock option exercises.

Table of Contents**Critical Accounting Policies**

Our critical accounting policies are those policies which require the most significant judgments and estimates in the preparation of our consolidated financial statements. Management has determined that our most critical accounting policies are those relating to revenue recognition and stock-based compensation. There have been no significant changes to our critical accounting policies discussed in the Annual Report.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 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. ASU 2014-09 will be effective for us for interim and annual periods beginning after December 15, 2016. We are evaluating the impact that this ASU may have on our consolidated financial statements, if any.

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern*. ASU 2014-15 amends ASC 205-40, *Presentation of Financial Statements - Going Concern*, by providing guidance on determining when and how reporting entities must disclose going-concern uncertainties in their financial statements, including requiring management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date of issuance of the entity's financial statements and providing certain disclosures if there is substantial doubt about the entity's ability to continue as a going concern. ASU 2014-15 will be effective for us for annual periods ending after December 15, 2016 and interim periods within annual periods beginning after December 15, 2016. We are still evaluating the impact of this ASU on our condensed consolidated financial statements; however, it is disclosure-only in nature.

Contractual Obligations

There were no material changes to our contractual obligations during the third quarter of 2014. In October 2014, we terminated our agreement to develop a companion diagnostic with Abbott Molecular, Inc. As a result of this termination, as of December 31, 2014, we will have no further obligations under the research and development contract obligation previously disclosed in the Annual Report. For a complete discussion of our contractual obligations, please refer to our *Management's Discussion and Analysis of Financial Condition and Results of Operations* in the Annual Report.

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 September 30, 2014, we had cash equivalents of \$199.5 million consisting of interest-bearing money market accounts and prime money market funds. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term maturities of our cash equivalents and the low risk profile of these investments, an immediate 100 basis point change in interest rates at levels as of September 30, 2014 would not have a material effect on the fair market value of our cash equivalents.

We contract with CROs and manufacturers internationally. 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

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

Table of Contents

Our management, under the supervision and with the participation of our Chief Executive 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 concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of September 30, 2014.

Changes in Internal Control over Financial Reporting

No change in the Company's 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 September 30, 2014 that has materially affected, or is reasonably likely to materially affect, the Company's 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 the 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 the 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 personalized therapeutics for patients with genetically defined cancers, 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 personalized drug therapeutics for patients with genetically defined cancers 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, very few drugs premised on epigenetics have been discovered. Moreover, those drugs based on an epigenetic mechanism that have received marketing approval are in a different target class than HMTs, where our research and development is focused. Although preclinical studies suggest that genetic alterations in HMTs cause them to drive particular human cancers, 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 we are the first company to conduct a clinical trial of an HMT inhibitor. Therefore, we do not know if our approach of inhibiting HMTs to treat patients with genetically defined cancers will be successful.

We are early in our development efforts and have only two product candidates in clinical trials. 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.

We are very early in our development efforts and have only two product candidates in clinical trials. All of our other product candidates are still in preclinical development. We have invested substantially all of our efforts and financial resources in the identification and preclinical development of HMT inhibitors. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, 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:

Table of Contents

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 product platform to build a pipeline of product candidates.

A key element of our strategy is to use and expand our product platform to build a pipeline of small molecule inhibitors of HMT targets and progress these product candidates through clinical development for the treatment of a variety of different types of cancer. Although our research and development efforts to date have resulted in a pipeline of programs directed at specific HMT targets, we may not be able to develop product candidates that are safe and effective HMT 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.

Two of our product candidates are in early clinical development, and our remaining product candidates are in preclinical development. 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. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, the complete responses that were observed in two MLL-r patients in the fourth dose cohort of the dose escalation stage of our Phase 1 clinical trial of EPZ-5676 and that were disclosed in January 2014 were achieved in an open-label setting, are not statistically significant and might not be achieved by any other patient treated with EPZ-5676. 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;

Table of Contents

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;

the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;

our third party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;

regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;

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

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

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

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

be delayed in obtaining marketing approval for our product candidates;

not obtain marketing approval at all;

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

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

be subject to additional post-marketing testing requirements; or

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

Our product development costs will 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 United States Food and Drug Administration, or FDA, or similar regulatory authorities outside of the United States. In particular, because we are focused on patients with genetically defined cancers, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. For example, enrollment in our Phase 1 clinical trial of EPZ-5676 was slower than we expected because of delays in establishing trial sites. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the broader patient populations within which our product candidates are being developed for the treatment of a subset of identifiable patients with genetically defined cancers, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates.

Table of Contents

Patient enrollment is affected by other factors including:

the severity of the disease under investigation;

the eligibility criteria for the trial in question;

the perceived risks and benefits of the product candidate under trial;

the efforts to facilitate timely enrollment in clinical trials;

the patient referral practices of physicians;

the ability to monitor patients adequately during and after treatment; and

the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Following our general product development strategy, we have designed our ongoing clinical trials of EPZ-5676 and EPZ-6438, and expect to design future trials, to include some patients with the applicable genetic alteration that causes the disease with a view to assessing possible early evidence of potential therapeutic effect. If we are unable to include patients with the applicable genetic alteration, this could compromise our ability to seek participation in FDA expedited review and approval programs, including breakthrough therapy and fast track designation, or otherwise to seek to accelerate clinical development and regulatory timelines.

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

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

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

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

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

We intend to develop companion diagnostics for our therapeutic product candidates when existing, available technology may not be sufficient to identify patients for treatment with our therapeutic product candidates. We expect that, at least in some cases, the FDA and similar regulatory authorities outside of the United States may require the development and regulatory

Table of Contents

approval of a companion diagnostic as a condition to approving our therapeutic product candidates. We do not have experience or capabilities in developing or commercializing diagnostics and plan to rely in large part on third parties to perform these functions. For example, in December 2012, Eisai and we entered into an agreement with Roche to develop and commercialize a companion diagnostic for use with EPZ-6438 for non-Hodgkin lymphoma patients with EZH2 point mutations. We may seek to enter into a similar agreement with a third party to create a companion diagnostic for use with EPZ-5676 in MLL-PTD patients. However, the MLL-PTD genetic alteration is not currently identified as part of standard diagnostic care, and as a result, it may be more difficult to enter into an agreement with a diagnostic company to create a companion diagnostic for this potential indication or to obtain comparable diagnostic results from those methods being used by sites enrolling MLL-PTD patients in our ongoing Phase 1 trial of EPZ-5676.

We may seek to enter into similar agreements for our other therapeutic product candidates and possible expansion indications for EPZ-5676 and EPZ-6438. Companion diagnostics are subject to regulation by the FDA and similar regulatory authorities outside of the United States as medical devices and require separate regulatory approval prior to commercialization.

If we, or any third parties that we engage to assist us, are unable to successfully develop companion diagnostics that are needed for our therapeutic product candidates, or experience delays in doing so:

the development of our therapeutic product candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;

our therapeutic product candidates may not receive marketing approval if their safe and effective use depends on a companion diagnostic; and

we may not realize the full commercial potential of any therapeutic product candidates that receive marketing approval if, among other reasons, we are unable to appropriately identify patients with the specific genetic alterations targeted by our therapeutic product candidates.

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

Risks Related to Our Financial Position and Need For Additional Capital

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

Since inception, we have incurred significant operating losses. Our net loss was \$40.0 million for the nine months ended September 30, 2014. As of September 30, 2014, we had an accumulated deficit of \$96.1 million. To date, we have financed our operations primarily through our collaborations, our initial public offering, our follow-on public offering and private placements of our preferred stock. All of our revenue to date has been collaboration revenue. We have devoted substantially all of our financial resources and efforts to research and development, including preclinical studies and, beginning in 2012, clinical trials. We are still in the early stages of development of our product candidates, and we have not completed development of any drugs. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially over the next several years as we:

continue our Phase 1 clinical trial of EPZ-5676 for treatment of patients with MLL-r and patients with MLL-PTD;

continue, together with Eisai, the Phase 1/2 clinical trial of EPZ-6438 for treatment of patients with non-Hodgkin lymphoma;

continue our Phase 1 clinical trial of EPZ-5676 in pediatric patients with MLL-r;

initiate our planned clinical trials of EPZ-6438 in adult and pediatric patients with INI1-deficient tumors;

continue the research and development of our other product candidates;

seek to discover and develop additional product candidates;

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

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

Table of Contents

maintain, expand and protect our intellectual property portfolio;

hire additional clinical, quality control and scientific personnel; and

add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts.

To become and remain profitable, we must succeed in developing, and eventually commercializing, products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing preclinical testing and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the FDA, the European Medicines Agency, or EMA, or other regulatory authorities to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates, our expenses could increase.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. A decline in the value of our company could cause our stockholders to lose all or part of their investment in our company.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the Phase 1 clinical trial of EPZ-5676 in MLL-r and MLL-PTD adult patients, the Phase 1 clinical trial of EPZ-5676 in pediatric patients with MLL-r and the Phase 1/2 clinical trial of EPZ-6438, subject to our opt-in right; initiate our planned clinical trials of EPZ-6438 in adult and pediatric patients with INI1-deficient tumors, subject to our opt-in right; and continue research and development and initiate additional clinical trials of, and seek regulatory approval for, these product candidates and other product candidates. In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on acceptable terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

Based on our research and development plans and our timing expectations related to the progress of our programs, we believe that our existing cash and cash equivalents as of September 30, 2014 and research funding that we expect to receive under our existing collaborations, will enable us to fund our operating expenses and capital expenditure requirements until at least mid-2016, without giving effect to any potential option exercise fees or milestone payments we may receive under our collaboration agreements. Prior to such time, we expect to complete five ongoing and planned proof-of-concept trials in the following six patient groups: MLL-r adult patients, MLL-PTD adult patients,

MLL-r pediatric patients, non-Hodgkin lymphoma patients, pediatric patients with INI1-deficient tumors and adult patients with INI1-deficient tumors. We have based these expectations on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Our future capital requirements will depend on many factors, including:

our collaboration agreements remaining in effect and our ability to obtain research funding and achieve milestones under these agreements;

the progress and results of our ongoing Phase 1 clinical trials of EPZ-5676 and Phase 1/2 clinical trial of EPZ-6438 and our planned trials of EPZ-6438;

Table of Contents

the number and development requirements of additional indications for EPZ-5676 and EPZ-6438 and other product candidates that we may pursue, including the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for such product candidates;

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

the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution for any of our product candidates for which we receive marketing approval;

the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval;

the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and

the extent to which we acquire or in-license other products and technologies.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

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

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

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

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

We commenced active operations in early 2008, and our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, identifying potential product candidates, undertaking preclinical studies and, beginning in 2012, conducting clinical trials. All but two of our product candidates are still in preclinical development. We are conducting Phase 1 clinical trials of EPZ-5676 and a Phase 1/2 clinical trial of EPZ-6438 but have not completed enrollment in any of these trials. We have not yet demonstrated our ability to successfully complete any clinical trials, obtain regulatory approvals, manufacture a commercial scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history.

Table of Contents

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

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

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

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

Risks Related to the Commercialization of Our Product Candidates

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

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third party payors and others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

the efficacy and potential advantages compared to alternative treatments;

our ability to offer our products for sale at competitive prices;

the convenience and ease of administration compared to alternative treatments;

the willingness of the patient population to try new therapies and of physicians to prescribe these therapies;

the strength of marketing and distribution support;

the availability of third party coverage and adequate reimbursement;

the prevalence and severity of any side effects; and

any restrictions on the use of our products together with other medications.

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

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

In the future, we expect to build a focused sales and marketing infrastructure to market or co-promote some of our product candidates in the United States, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Table of Contents

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

our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;

the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;

the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and

unforeseen costs and expenses associated with creating an independent sales and marketing organization.

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

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

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

Specifically, there are a large number of companies developing or marketing treatments for cancer, including many major pharmaceutical and biotechnology companies. In addition, many companies are developing cancer therapeutics that work by targeting epigenetic mechanisms other than HMTs, and some companies, including Celgene and Eisai, are marketing such treatments. There are also a number of companies that we believe are developing new epigenetic treatments for cancer that target HMTs, including GSK, Novartis AG, Pfizer, Inc. and Genentech, Inc.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their

products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third party payors seeking to encourage the use of generic products. Generic products are currently on the market for the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic products.

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

Table of Contents

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

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

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval.

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

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third party payors often rely upon

Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

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

decreased demand for any product candidates or products that we may develop;

Table of Contents

injury to our reputation and significant negative media attention;

withdrawal of clinical trial participants;

significant costs to defend any related litigation;

substantial monetary awards to trial participants or patients;

loss of revenue;

reduced resources of our management to pursue our business strategy; and

the inability to commercialize any products that we may develop.

We currently hold \$5.0 million in product liability insurance coverage in the aggregate, with a per incident limit of \$5.0 million, which may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Risks Related to Our Dependence on Third Parties

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

We have limited capabilities for drug development and do not yet have any capability for sales, marketing or distribution. Accordingly, we have entered into therapeutic collaborations with other companies that we believe can provide such capabilities, including our collaboration and license agreements with Celgene, Eisai and GSK. These collaborations also have provided us with important funding for our development programs and product platform and we expect to receive additional funding under these collaborations in the future. Our existing therapeutic collaborations, and any future collaborations we enter into, may pose a number of risks, including the following:

collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;

collaborators may not perform their obligations as expected;

collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that may divert resources or create competing priorities;

collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;

collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products and product candidates if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;

a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;

a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such product or products;

Table of Contents

disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and

collaborations may be terminated for the convenience of the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

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

Each of our existing three therapeutic collaborations contains a restriction on our engaging in activities that are the subject of the collaboration with third parties for specified periods of time. In addition, under our collaboration agreement with Celgene, during the option period specified in the agreement, which could extend to July 2016, Celgene has the right to exercise its option to acquire a license to additional targets other than DOT1L until the effectiveness of an investigational new drug application, or IND, for an HMT inhibitor directed to such additional target. This option effectively covers all HMT targets that are not currently subject to our Eisai and GSK collaborations. As a result, our ability to enter into collaboration agreements for additional HMT targets is significantly limited until the end of the option period under the Celgene agreement and may continue to be limited after that time depending on how many targets Celgene elects to license, if any. These restrictions may have the effect of preventing us from undertaking development and other efforts that may appear to be attractive to us.

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

For some of our product candidates or for some HMT targets, we may in the future determine to collaborate with pharmaceutical and biotechnology companies for development and potential commercialization of therapeutic products. We face significant competition in seeking appropriate collaborators. Our ability to reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and

expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market or continue to develop our product platform and our business may be materially and adversely affected.

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

Table of Contents

We do not plan to develop companion diagnostics internally and, as a result, we are dependent on the efforts of our third party collaborators to successfully commercialize companion diagnostics when existing, available technology may not be sufficient to identify patients for treatment with our therapeutic product candidates. Our collaborators:

may not perform their obligations as expected;

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

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

may not pursue commercialization of any therapeutic product candidates that achieve regulatory approval;

may elect not to continue or renew commercialization programs based on changes in the collaborators strategic focus or available funding, or external factors such as an acquisition, that divert resources or create competing priorities;

may not commit sufficient resources to the marketing and distribution of such product or products; and

may terminate their relationship with us.

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

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

We currently rely on third party clinical research organizations to conduct our ongoing Phase 1 clinical trials of EPZ-5676 and our ongoing Phase 1/2 clinical trial of EPZ-6438 and do not plan to independently conduct clinical trials of our other product candidates. We expect to continue to rely on third parties, such as clinical research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. These agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities might be delayed.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for

conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

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

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

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

Table of Contents

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

We also expect to rely on third party manufacturers or third party collaborators for the manufacture of commercial supply of any other product candidates for which our collaborators or we obtain marketing approval.

We may be unable to establish any agreements with third party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third party manufacturers, reliance on third party manufacturers entails additional risks, including:

reliance on the third party for regulatory compliance and quality assurance;

the possible breach of the manufacturing agreement by the third party;

the possible misappropriation of our proprietary information, including our trade secrets and know-how; and

the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

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

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

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

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

Risks Related to Our Intellectual Property

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

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

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

Table of Contents

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

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The United States Patent Office recently developed new regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, only became effective on March 16, 2013. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Moreover, we may be subject to a third party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

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

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

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

patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

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

Table of Contents

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

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

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

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including interference or derivation proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future.

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

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

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

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

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

Table of Contents

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

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

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

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

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

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

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

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

Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside of the United States. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third party CROs to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may

Table of Contents

prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product.

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

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

We may not be able to obtain orphan drug exclusivity for our product candidates.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same drug for that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

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

A fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

We intend to seek fast track designation for some of our product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this

condition, the drug sponsor may apply for FDA fast track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot assure that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

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

Table of Contents

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

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

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

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

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

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a risk evaluation and mitigation strategy. New cancer drugs frequently are indicated only for patient populations that have not responded to an existing therapy or have relapsed. If any of our product candidates receives marketing approval,

the accompanying label may limit the approved use of our drug in this way, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure drugs are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use, and if we do not market our products for their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

Table of Contents

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

restrictions on such products, manufacturers or manufacturing processes;

restrictions on the labeling or marketing of a product;

restrictions on product distribution or use;

requirements to conduct post-marketing studies or clinical trials;

warning letters;

withdrawal of the products from the market;

refusal to approve pending applications or supplements to approved applications that we submit;

recall of products;

fines, restitution or disgorgement of profits or revenues;

suspension or withdrawal of marketing approvals;

refusal to permit the import or export of our products;

product seizure; or

injunctions or the imposition of civil or criminal penalties.

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

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

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

the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

the federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

the federal Physician Payments Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals, with data collection beginning in August 2013; and

analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers.

Table of Contents

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

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

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

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

More recently, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the PPACA, a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms.

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

an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;

an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;

expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;

extension of manufacturers' Medicaid rebate liability;

expansion of eligibility criteria for Medicaid programs;

Table of Contents

expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

new requirements to report financial arrangements with physicians and teaching hospitals;

a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and

a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding.

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

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

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

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our

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

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

Table of Contents

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

Risks Related to Employee Matters and Managing Growth

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

We are highly dependent on the research and development, clinical and business development expertise of Robert J. Gould, Ph.D., our President and Chief Executive Officer, Robert A. Copeland, Ph.D., our Executive Vice President and Chief Scientific Officer, and Peter T.C. Ho, M.D., Ph.D., our Chief Development Officer, as well as the other principal members of our management, scientific and clinical team. Although we have entered into employment letter agreements with our executive officers, each of them may terminate their employment with us at any time. We are also actively engaged in a search to identify and hire a new Chief Financial Officer. We do not maintain key person insurance for any of our executives or other employees.

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

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

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

Risks Related to Our Common Stock

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

As of October 31, 2014, our executive officers and directors and their affiliates beneficially own, in the aggregate, shares representing approximately 37.3% of our common stock. As a result, if these stockholders were to choose to act together, they would be able to significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

Table of Contents

This concentration of ownership control may:

delay, defer or prevent a change in control;

entrench our management and board of directors; or

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

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

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

establish a classified board of directors such that only one of three classes of directors is elected each year;

allow the authorized number of our directors to be changed only by resolution of our board of directors;

limit the manner in which stockholders can remove directors from our board of directors;

establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;

require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;

limit who may call stockholder meetings;

authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a poison pill that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and

require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

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

Some provisions in our collaboration agreements with Celgene and Eisai could deter potential buyers of our company from proposing an acquisition and could make us a less attractive target for them. These provisions include the following:

We granted Celgene an exclusive license, for all countries other than the United States, to HMT inhibitors directed to DOT1L and an option, on a target-by-target basis, to exclusively license, for all countries of the world other than the United States, rights to HMT inhibitors directed to any other HMT targets during the option period, excluding targets covered by our two other existing therapeutic collaborations. During the option period specified in the agreement, which could extend until July 2016, Celgene has the right to exercise its option to license non-U.S. rights to additional targets other than DOT1L until the effectiveness of an IND for an HMT inhibitor directed to such additional target. This option effectively covers all HMT targets that are not currently subject to our Eisai and GSK collaborations. The decision to exercise the options for available targets is in Celgene's sole discretion.

Table of Contents

Under our collaboration agreement with Celgene, we granted to Celgene a right of first negotiation with respect to business combination transactions that we may desire to pursue with third parties during the option period, including any extension of this period. During the option period, we are required to notify Celgene if we desire to pursue a specified business combination transaction with a third party prior to negotiating terms with the third party, and after so notifying Celgene, we have agreed not to, directly or indirectly, solicit, initiate or encourage proposals from, discuss or negotiate with, or provide any information to, any third party related to the proposed transaction for a specified period from the date we first notify Celgene of such proposed transaction, or the Celgene negotiation period. If Celgene notifies us that it is interested in entering into the proposed transaction, we have agreed to negotiate in good faith with Celgene during the Celgene negotiation period. Following the Celgene negotiation period, if we have not entered into the proposed transaction with Celgene, or if Celgene does not notify us that it is interested in entering into the proposed transaction, we are free to enter into the proposed transaction with a third party for a period of 225 days following the expiration of the Celgene negotiation period, but we are obligated to re-offer the proposed transaction to Celgene if, during the option term, we propose to enter into the proposed transaction with a third party on terms that, in specified respects, are less favorable to us than the terms last offered by Celgene.

Under our collaboration agreement with Eisai, if we undergo a specified change of control event in which we are acquired by or combine with an entity with a specified competing business, or if following a change of control event we materially breach the agreement, Eisai will have the right to terminate our co-development, co-commercialization and profit sharing option and, if we have previously exercised our option, our co-development, co-commercialization and profit sharing rights.

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

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

The price of our common stock has been and may in the future be volatile and fluctuate substantially.

Our stock price has been and may in the future be volatile. From May 31, 2013 to October 31, 2014, the sale price of our common stock as reported on the NASDAQ Global Market ranged from a high of \$45.72 per share to a low of \$18.10 per share. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

the success of competitive products or technologies;

results of clinical trials of our product candidates or those of our competitors;

regulatory or legal developments in the United States and other countries;

developments or disputes concerning patent applications, issued patents or other proprietary rights;

the recruitment or departure of key personnel;

the level of expenses related to any of our product candidates or clinical development programs;

the results of our efforts to discover, develop, acquire or in-license additional product candidates or products;

actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;

variations in our financial results or the financial results of companies that are perceived to be similar to us;

changes in the structure of healthcare payment systems;

market conditions in the pharmaceutical and biotechnology sectors;

general economic, industry and market conditions; and

the other factors described in this *Risk Factors* section.

Table of Contents

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

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

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

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

reduced disclosure obligations regarding executive compensation; and

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

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

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

As a public company, and particularly after we are no longer an emerging growth company, we will continue to incur significant legal, accounting and other expenses. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and make some activities more time-consuming and costly.

We cannot predict or estimate the amount of additional costs we may incur to continue to operate as a public company, nor can we predict the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve

over time as new guidance is provided by regulatory and governing bodies which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we are not required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

Table of Contents

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

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

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

Item 6. Exhibits

- 10.1 Consulting agreement dated as of September 2, 2014 by and between the Registrant and Jason P. Rhodes (1)
- 10.2 Employment Offer Letter with Peter T.C. Ho, M.D., Ph.D. (2)
- 31.1 Certification of Chief Executive Officer pursuant to Rules 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. (2)
- 32.1 Certifications pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of The Sarbanes-Oxley Act of 2002, by Robert J. Gould, Ph.D., President and Chief Executive Officer of the Company. (2)
- 101.INS XBRL Instance Document.
- 101.SCH XBRL Schema Document.
- 101.CAL XBRL Calculation Linkbase Document.
- 101.LAB XBRL Labels Linkbase Document.
- 101.PRE XBRL Presentation Linkbase Document.
- 101.DEF XBRL Definition Linkbase Document.

- (1) Incorporated by reference to the Registrant's Current Report on Form 8-K (File No. 001-35945) filed with the Securities and Exchange Commission on September 2, 2014.
- (2) Filed with this Form 10-Q.

Table of Contents

SIGNATURES

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

Dated: November 6, 2014

EPIZYME, INC.

By: /s/ Robert J. Gould
Robert J. Gould, Ph.D.
President and Chief Executive Officer
(Principal Executive and Financial
Officer)