November 3, 2016

Epizyme Provides Update on Execution of Clinical Program and Reports Third Quarter 2016 Financial Results

Robust Clinical Program Underway for Tazemetostat in Multiple Cancer Indications and Treatment Settings as Both Monotherapy and Combination Agent

Conference Call to Be Held Today at 8:30 a.m. Eastern Time

CAMBRIDGE, Mass., Nov. 03, 2016 (GLOBE NEWSWIRE) -- Epizyme, Inc. (NASDAQ:EPZM), a clinical-stage biopharmaceutical company creating novel epigenetic therapies, today recapped recent progress of the Company's clinical-stage programs and reported financial results for the third quarter of 2016.

"Throughout 2016, we have made substantial progress toward achieving our vision, which includes advancing the clinical development of tazemetostat and expanding its therapeutic benefit into new indications and treatment settings," said Robert Bazemore, President and Chief Executive Officer, Epizyme. "We are executing on a broad clinical program for tazemetostat based on its early clinical activity and safety profile, and guided by strong scientific rationale. We expect 2017 to be an important year for Epizyme, led by data from the Phase 2 studies in non-Hodgkin lymphoma and genetically defined solid tumors in the first half of the year, and determination of our potential registration pathways beginning mid-year."

Execution of Clinical Programs

- **Enrollment in Phase 2 Programs in NHL and Solid Tumors Progressing:** The Company's Phase 2 studies of tazemetostat in non-Hodgkin lymphoma (NHL) and genetically defined solid tumors are progressing and continue to enroll patients. Epizyme plans to report efficacy, safety and biomarker data from both studies in the first half of 2017. The Company is also preparing for intended regulatory engagement, beginning first with the United States Food and Drug Administration (FDA) in mid-2017 to determine potential registration paths for its genetically defined solid tumor program in adult patients. In addition, Epizyme is preparing for FDA engagement on its NHL program, also in 2017, to determine potential registration paths in various subtypes of NHL.
- **Immuno-oncology Combination Study Initiated:** The Phase 1b study is evaluating tazemetostat in combination with Tecentriq™ (atezolizumab), in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). Tecentriq is the first and only anti-PD-L1 cancer immunotherapy approved by FDA. This study is being conducted by Genentech, a member of the Roche Group, under Epizyme's collaboration agreement with Roche.
- **Front-line Combination Study Initiated:** The first study of tazemetostat in the front-line treatment setting has been initiated. The Phase 1b/2 study is evaluating tazemetostat in combination with R-CHOP, a chemotherapy regimen, as a first-line treatment for newly diagnosed elderly, high-risk patients with DLBCL. This study is being conducted under the Company's collaboration with the Lymphoma Study Association.
- **Mesothelioma Study Initiated:** Patient enrollment is underway in Epizyme's global Phase 2 study evaluating tazemetostat for the treatment of adults with mesothelioma characterized by BAP1 loss-of-function. This study marks the expansion of tazemetostat development as a monotherapy into a new cancer indication.
- **CRADAs Established with NCI on Tazemetostat and Pinometostat:** Epizyme recently entered into separate Cooperative Research and Development Agreements (CRADAs) with the National Cancer Institute (NCI) to evaluate tazemetostat in clinical trials in multiple cancer indications and to evaluate Epizyme's novel DOT1L inhibitor, pinometostat, in multiple combination regimens. These CRADAs further expand the clinical evaluation of tazemetostat in both adults and children, while also exploring the potential for pinometostat as a combination therapy for certain kinds of acute leukemia.
- **Collaboration Established with Foundation Medicine:** Epizyme entered into a collaboration agreement with Foundation Medicine, Inc. to support patient identification and enrollment for Epizyme's ongoing Phase 2 clinical trial of tazemetostat in patients with NHL. Foundation Medicine's SmartTrials™ Precision Enrollment Program and FoundationOne® Heme panel will assist in identifying a population of individuals with NHL who harbor EZH2 mutations, which constitute specific cohorts in the Epizyme trial.

Strengthening of Epizyme Team

- The Company made two, recent key hires to prepare for the intended regulatory engagement and determination of potential registration pathways in 2017. Pamela Strode was appointed to the position of Vice President of Regulatory Affairs and Quality Assurance, and Ray Mankoski, M.D., Ph.D. was appointed as Vice President of Medical Affairs.

Third Quarter 2016 Financial Results and Guidance

- **Cash Position**: Cash, cash equivalents and marketable securities were $263.3 million as of September 30, 2016, as compared to $208.3 million as of December 31, 2015.
- **Revenue:** Collaboration revenue was $6.6 million and $7.5 million for the three and nine months ended September 30, 2016, respectively, compared to $0.4 million and $2.0 million for the three and nine months ended September 30, 2015, respectively. The increase was driven predominantly by the recognition of the $6.0 million milestone earned upon GlaxoSmithKline's (GSK) initiation of patient dosing in a Phase 1 clinical trial of GSK3326595, a PRMT5 inhibitor invented by Epizyme and licensed to GSK. GSK holds worldwide rights to the compound, and Epizyme may receive significant additional payments from GSK if future milestones are met for the program, plus up to double digit royalties on worldwide net sales should this product candidate progress through the clinic to commercialization.
- **R&D Expenses:** Research and development (R&D) expenses were $23.9 million and $63.1 million for the three and nine months ended September 30, 2016, respectively, compared to $16.8 million and $94.4 million for the three and nine months ended September 30, 2015, respectively. The increase in R&D expenses for the three months ended September 30, 2016, is primarily due to the expansion of the tazemetostat clinical development program, increased spending on tazemetostat preclinical activities, and increased discovery and spending on high-priority, earlier-stage programs. The period-over-period decrease from the nine months ended September 30, 2015 was driven by the inclusion of the $40.0 million payment to Eisai for the reacquisition of the tazemetostat worldwide rights, excluding Japan, in R&D expenses in the first quarter of 2015. The Company expects that research and development expenses will continue to increase in the fourth quarter of 2016.
- **G&A Expenses:** General and administrative (G&A) expenses were $7.5 million and $20.8 million for the three and nine months ended September 30, 2016, respectively, as compared to $6.7 million and $17.9 million for the three and nine months ended September 30, 2015, respectively. The increase is primarily due to the staffing of key leadership roles in the first half of 2016. G&A expenses were flat compared to the second quarter of 2016, and we expect G&A expenses to remain relatively constant through the fourth quarter of 2016.
- **Net Loss:** Net loss was $24.3 million and $75.2 million for the three and nine months ended September 30, 2016, respectively, compared to a net loss of $23.1 million and $110.2 million for the three and nine months ended September 30, 2015, respectively.
- **Financial Guidance:** Epizyme reiterates its belief that its cash, cash equivalents and marketable securities of $263.3 million as of September 30, 2016 will be sufficient to fund the Company's planned operations into at least the second quarter of 2018.

Conference Call Information
Epizyme will host a conference call and audio webcast today at 8:30 a.m. Eastern Time to discuss its third quarter 2016 financial results and business updates. To participate in the conference call, please dial (877) 844-6886 (domestic) or (970) 315-0315 (international) and refer to conference ID 96812020. The webcast can be accessed under "Events and Presentations" in the Investor Relations section of the company's website at www.epizyme.com.

About Epizyme, Inc.
Epizyme, Inc. is a clinical-stage biopharmaceutical company creating novel epigenetic therapeutics for cancer patients. Epizyme has built a proprietary product platform that the Company uses to create small molecule inhibitors of chromatin modifying proteins (CMPs), such as histone methyltransferases or HMTs. CMPs are part of the system of gene regulation, referred to as epigenetics, that controls gene expression. Genetic alterations can result in changes to the activity of CMPs, making them oncogenic (cancer-causing). By focusing on the genetic drivers of cancers, Epizyme's targeted science seeks to match the right medicines with the right patients.

For more information, visit www.epizyme.com and connect with us on Twitter at @EpizymeRx.

Cautionary Note on Forward-Looking Statements
Any statements in this press release about future expectations, plans and prospects for Epizyme, Inc. and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: uncertainties inherent in the initiation of future clinical studies and in the availability and timing of data from ongoing clinical studies; whether interim results from a clinical trial will be predictive of the final results of the trial; whether results from preclinical studies or earlier clinical studies will be predictive of the results of future trials; whether results from clinical studies will warrant meetings with regulatory authorities or submissions for regulatory approval; expectations for regulatory approvals to conduct trials or to market products; whether the Company's cash resources will be sufficient to fund the Company's foreseeable and unforeseeable

operating expenses and capital expenditure requirements; other matters that could affect the availability or commercial potential of the Company's therapeutic candidates; and other factors discussed in the "Risk Factors" section of the Company's most recent Form 10-Q filed with the SEC and in the Company's other filings from time to time with the SEC. In addition, the forward-looking statements included in this press release represent the Company's views as of the date hereof and should not be relied upon as representing the Company's views as of any date subsequent to the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so.

Tecentriq™ is a trademark of Genentech, Inc., (South San Francisco, CA, USA), a member of the Roche Group.

EPIZYME, INC.
CONSOLIDATED BALANCE SHEET DATA (UNAUDITED)
(Amounts in thousands)

	September 30, 2016	December 31, 2015
Cash and cash equivalents	$ 66,028	$ 208,323
Marketable securities	197,315	—
Total assets	278,986	217,903
Deferred revenue	29,287	30,709
Total stockholders' equity	233,796	169,532

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2016	2015	2016	2015
Collaboration revenue	$ 6,584	$ 358	$ 7,529	$ 2,005
Operating expenses:				
Research and development	23,888	16,788	63,078	94,390
General and administrative	7,522	6,676	20,792	17,883
Total operating expenses	31,410	23,464	83,870	112,273
Loss from operations	(24,826)	(23,106)	(76,341)	(110,268)
Other income, net	490	41	1,145	118
Net loss	$ (24,336)	$ (23,065)	$ (75,196)	$ (110,150)
Loss per share allocable to common stockholders:				
Basic	$ (0.42)	$ (0.56)	$ (1.32)	$ (2.81)
Diluted	$ (0.42)	$ (0.56)	$ (1.32)	$ (2.81)
Weighted average shares outstanding:				
Basic	57,970	41,461	56,828	39,204
Diluted	57,970	41,461	56,828	39,204

Contacts

Media

Julie DiCarlo, Epizyme, Inc.

jdicarlo@epizyme.com

(617) 401-0721

Investors

Monique Allaire, THRUST IR

monique@thrustir.com

(617) 895-9511

Primary Logo

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