



Epizyme and Celgene Advance EPZ-5676 DOT1L Inhibitor Clinical Program to Benefit Cancer Patients with Acute Leukemias, Achieving \$25 Million Clinical Proof of Concept Milestone

– Epizyme Also Achieves \$4 Million Development Candidate Milestone with GSK –

– 2013 End-of-Year Cash Guidance Increased –

– Five Clinical Proof of Concept Programs Planned in 2014 –

Cambridge, Mass. – January 6, 2014 – Epizyme, Inc. (NASDAQ: EPZM), a clinical stage biopharmaceutical company creating innovative personalized therapeutics for patients with genetically defined cancers, today announced the achievement of the proof of concept (POC) milestone in the EPZ-5676 DOT1L inhibitor clinical program, earning a \$25 million payment under the company’s collaboration with Celgene Corporation. The milestone was triggered by objective responses in patients with translocations of the MLL gene (MLL-r). These patients are currently enrolled in the fourth dose cohort in the dose escalation stage of the ongoing Phase 1 clinical study and are receiving uninterrupted treatment with EPZ-5676.

Epizyme also announced today that a development candidate milestone has been achieved for one of the three histone methyltransferase (HMT) targets included in the company’s collaboration with GlaxoSmithKline (GSK), earning a \$4 million payment.

“2013 was a year of important accomplishments for Epizyme,” said Robert Gould, Ph.D., chief executive officer, Epizyme. “We have achieved the proof of concept milestone for EPZ-5676, our first-in-class DOT1L inhibitor, in our Celgene collaboration, initiated an ongoing Phase 1 study of EPZ-6438, our first-in-class EZH2 inhibitor, in our Eisai collaboration, achieved a Development Candidate milestone in our GSK collaboration, and continue to advance our pipeline of personalized therapeutics for patients with genetically defined cancers.”

“We are very pleased with EPZ-5676’s emerging clinical profile and progress as a potential personalized therapeutic for patients with genetically defined acute leukemias,” said Dr. Gould. “We look forward to presenting the data from our ongoing Phase 1 study of EPZ-5676, including the dose escalation stage that has completed enrollment and the adult MLL-r expansion stage that is now enrolling patients, at a medical conference in 2014.”

Additionally, the European Medicines Agency's Committee for Orphan Medicinal Products recommended orphan drug designation for EPZ-5676 to the European Commission in December 2013. EPZ-5676 was granted orphan drug designation by the U.S. Food and Drug Administration in May 2013.

Including the Celgene POC milestone and the GSK development candidate milestone, Epizyme estimates a 2013 end-of-year cash and account receivables position of approximately \$145 million versus previous guidance of an end-of-year cash position of more than \$115 million.

Epizyme plans to have as many as five clinical proof of concept programs ongoing in 2014. For EPZ-5676, Epizyme's first-in-class DOT1L inhibitor, these include the ongoing adult MLL-r expansion stage, MLL-r in pediatric patients, and adult MLL-PTD patients. For EPZ-6438, Epizyme's first-in-class EZH2 inhibitor, these include adult non-Hodgkin lymphoma patients and also pediatric and young adult patients with synovial sarcomas, pending completion of the ongoing Phase 1 study.

About EPZ-5676 and Epizyme's Collaboration with Celgene

Epizyme is developing EPZ-5676, a small molecule inhibitor of DOT1L created with Epizyme's proprietary product platform, for the treatment of patients with acute leukemia in which the MLL gene is rearranged due to a chromosomal translocation (MLL-r) or a partial tandem duplication (MLL-PTD). Due to these rearrangements, DOT1L is misregulated, resulting in the increased expression of genes causing leukemia.

Epizyme believes that EPZ-5676 was the first HMTi to enter human clinical development. Epizyme is currently conducting a two-stage Phase 1 study. The dose escalation stage has completed enrollment, and the adult MLL-r expansion stage is now enrolling patients. Additional information about this ongoing Phase 1 study can be found here: <http://clinicaltrials.gov/show/NCT01684150>

Epizyme retains all U.S. rights to EPZ-5676 and has granted Celgene an exclusive license to EPZ-5676 outside of the United States. Epizyme is working with Abbott to develop a companion diagnostic to identify MLL-r patients. Additional information about Epizyme's partnerships is available here: www.epizyme.com/about-us/partnerships/

About Epizyme's Collaboration with GSK

In January 2011, Epizyme entered into a collaboration and license agreement with GSK to discover, develop and commercialize novel small molecule HMT inhibitors directed to three targets from Epizyme's product platform. Additional information about the GSK collaboration is available here: www.epizyme.com/about-us/partnerships/.

About EPZ-6438 and Epizyme's Collaboration with Eisai

Epizyme is developing EPZ-6438, a small molecule inhibitor of EZH2 created with our proprietary product platform, for the treatment of non-Hodgkin lymphoma patients

who have an oncogenic (cancer-causing) point mutation in EZH2. In many human cancers, misregulated EZH2 enzyme activity results in misregulation of genes that control cell proliferation – without these control mechanisms, cancer cells are free to grow rapidly.

In June 2013, Epizyme initiated a Phase 1/2 clinical trial of EPZ-6438 in patients with advanced solid tumors or with relapsed or refractory B-cell lymphoma. This program is currently in the dose escalation phase. The company believes EPZ-6438 is the second HMTi to enter human clinical development, following Epizyme's DOT1L inhibitor, EPZ-5676.

Additional information about this program, including clinical trial information, may be found here: <http://clinicaltrials.gov/ct2/show/NCT01897571>.

Epizyme granted Eisai a worldwide license to EPZ-6438 (Eisai refers to this therapeutic candidate as E7438), subject to Epizyme's right to opt in for co-development, co-commercialization and profit share arrangement with Eisai in the United States. Epizyme is working with Roche and Eisai to develop a companion diagnostic to identify patients with EZH2 point mutations. Additional information about these partnerships may be found here: <http://www.epizyme.com/about-us/partnerships/>.

About Epizyme, Inc.

Epizyme, Inc. is a clinical stage biopharmaceutical company creating personalized therapeutics for patients with genetically defined cancers. Epizyme has built a proprietary product platform that the company uses to create small molecule inhibitors of a 96-member class of enzymes known as histone methyltransferases, or HMTs. HMTs 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 HMTs, 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 a personalized approach to cancer treatment.

For more information, visit www.epizyme.com and connect with us on Twitter at [@EpizymeRx](https://twitter.com/EpizymeRx).

Cautionary Note on Forward-Looking Statements

Any statements in this press release about future expectations, plans and prospects for the Company, including statements about the Company's strategy, future operations, clinical development of the Company's therapeutic candidates, expectations regarding the Company's cash balance and future expectations and plans and prospects for the Company 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: the uncertainties inherent in the initiation of future clinical trials, expectations of expanding ongoing clinical trials, availability and timing of data from ongoing clinical trials, whether interim results from a clinical trial will be predictive of the final results of the trial or results of early clinical trials will be indicative of the results of future trials, expectations for regulatory approvals, development progress of the Company's companion diagnostics, availability of funding sufficient for 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 or companion diagnostics and other factors discussed in the "Risk Factors" section of the Company's 10-Q filed with the Securities and Exchange Commission on October 23, 2013. In addition, the forward-looking statements included in this press release represent the Company's views as of 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. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date hereof.

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