Epizyme DOT1L Inhibitor EPZ-5676 Shows Clinical and Biological Activity in Adult Patients with Acute Leukemias in Phase 1 Trial

- Three objective responses: Two complete responses (CRs) in 54 mg/m^2/day dose cohort and one partial response (PR) in 90 mg/m^2/day dose cohort, as of October 6, 2014 data cut-off
- Additional biological activity observed: Resolution of cutaneous leukemia in two patients, leukemia cell differentiation effects in eight patients
- Overall, eight of 34 MLL-r or MLL-PTD patients and nine of 42 patients overall across all dose levels showed biological or clinical activity
- Majority of adverse events were Grade 1 or Grade 2
- Expansion cohort at 54 mg/m^2/day now open to enrollment

San Francisco, Calif., December 8, 2014 – Epizyme, Inc. (NASDAQ: EPZM), a clinical stage biopharmaceutical company creating innovative personalized therapeutics for patients with genetically defined cancers, announced today the presentation of results from the company's Phase 1 trial of EPZ-5676, a potent and selective inhibitor of the DOT1L histone methyltransferase (HMT). Epizyme, along with its partner Celgene, is developing EPZ-5676 for the treatment of acute leukemia with alterations in the *MLL* gene (MLL-r) or partial tandem duplications within *MLL* (MLL-PTD). The trial found that EPZ-5676 was generally safe and well tolerated across all dose cohorts and showed clinical and biological activity. These data will be presented today by Eytan M. Stein, M.D., Memorial Sloan Kettering Cancer Center, at the 56th annual meeting of the American Society of Hematology (ASH) in San Francisco, Calif.

Forty-two heavily pre-treated acute leukemia patients were enrolled and evaluable for anti-leukemic activity as of the data cut-off of October 6, 2014. Thirty-four of these patients had MLL-r or MLL-PTD.

- Eight of the 34 MLL-r or MLL-PTD patients across all dose levels, and nine patients overall, showed biological or clinical activity
- Two of five MLL-r patients enrolled in the 54 mg/m^2/day dose cohort achieved CRs (one morphologic CR and one cytogenetic CR); one patient of 23 enrolled in the 90 mg/m^2/day dose cohort achieved a PR
- The two patients with CRs had MLL-r with an (11;19) translocation, and the patient with the PR had a trisomy 11, which is associated with MLL-PTD
- Two patients, including one with CR, experienced resolution of leukemia cutis, and eight patients experienced leukemia cell differentiation characterized by

morphological maturation or non-malignant leukocytosis

“In this heavily pre-treated patient population, there is a significant unmet need,” said Dr. Stein. “MLL-r acute leukemias are particularly difficult to treat, and the safety profile and clinical and biological activity we have seen with EPZ-5676, including two complete responses, are encouraging.”

“We are pleased to have seen objective responses as well as resolution of leukemia cutis and differentiation effects among patients in this study,” said Peter Ho, M.D., Ph.D., Chief Development Officer, Epizyme. “Based on the clinical activity we observed at intermediate dose cohorts, we plan to enroll up to 20 additional MLL-r or MLL-PTD patients at 54 mg/m^2/day to explore further the single agent activity of EPZ-5676 at this dose and to better characterize the molecular profile of responding patients.”

The objectives of this Phase 1, open-label, dose escalation study are to determine the maximum tolerated dose or recommended Phase 2 dose, and to characterize the safety, tolerability, pharmacokinetics, pharmacodynamics and anti-leukemic activity of EPZ-5676 in adult patients with relapsed/refractory leukemia, including those with MLL-r or MLL-PTD.

Thirty-one percent of patients had one prior therapy, 31 percent had two prior therapies, 24 percent had three prior therapies, and 14 percent had four or more prior therapies. Thirty-eight percent of patients had received prior allogeneic hematopoietic cell transplant.

Adverse events assessed by investigators to be drug-related were seen in 38 percent of patients. The majority were Grade 1 or Grade 2 gastrointestinal events. Three patients experienced Grade 3 leukocytosis, and one patient experienced Grade 3 anemia. Two dose-limiting toxicities occurred at 90 mg/m^2/day: one Grade 4 reversible cardiac failure with concurrent sepsis and one Grade 4 reversible hypophosphatemia.

Pharmacokinetic and pharmacodynamic data were consistent with results reported by the Company in its November 6, 2014 press release.

Investor Event and Webcast

Epizyme will host a live event with audio webcast of its discussion of the Company’s clinical programs and pipeline at the ASH annual meeting on Monday, December 8, 2014, at 12:30 p.m. PT (3:30 p.m. ET).

The webcast will be available in the Events and Presentations section under the Investor Relations section of the Company's website at www.epizyme.com, and an archived replay of the webcast will be available for 30 days after the presentation.

About EPZ-5676
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 HMT inhibitor to enter human clinical development. Epizyme is currently conducting a two-stage Phase 1 study in adult MLL-r and MLL-PTD patients and in May 2014, initiated a Phase 1 study of EPZ-5676 in pediatric patients with rearrangements of the *MLL* gene. The adult dose escalation stage has completed enrollment, and a dose expansion cohort of adult MLL-r and MLL-PTD patients is open for enrollment. Additional information about these ongoing Phase 1 studies may be found here: http://clinicaltrials.gov/show/NCT01684150

EPZ-5676 has been granted orphan drug designation for the treatment of acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) by the Food and Drug Administration in the U.S. and by the European Commission in Europe.

Epizyme retains all U.S. rights to EPZ-5676 and has granted Celgene an exclusive license to EPZ- 5676 outside of the U.S. Additional information about Epizyme's collaborations is available here: 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.

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 or expansion of ongoing clinical studies, whether results of preclinical studies or early clinical studies such as the clinical data reported in this release will be indicative of the results of future trials; expectations for regulatory approvals, , availability of funding sufficient for the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements, and other factors discussed in the "Risk Factors" section of the Company's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission in November 2014. 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.

Media/Investors:
Manisha Pai
Epizyme, Inc.
617.229.7560
mpai@epizyme.com