Phase 1 Dose Escalation Data for Epizyme EZH2 Inhibitor EPZ-6438 (E7438) Shows Single Agent Activity in B-Cell Non-Hodgkin Lymphomas and Malignant Rhabdoid Tumor

- *Partial response or better seen in four of 10 evaluable patients with relapsed or refractory non-Hodgkin lymphoma (NHL), including three of five evaluable patients with diffuse large B-cell lymphoma (DLBCL)*
    - *Ongoing complete response observed in one DLBCL patient*
- *Ongoing partial response seen in one malignant rhabdoid tumor patient, one of two evaluable solid tumor patients with INI1-deficient tumors*
- *Majority of adverse events were Grade 1 or Grade 2, with only one Grade 3 or Grade 4 treatment-related adverse event*
    - *No AEs required treatment discontinuation or dose reduction*
- *800 mg oral BID under consideration by Data Monitoring Committee as the recommended Phase 2 dose*
- *Company to hold conference call and webcast with slides on Thursday, November 20, 2014, at 8:00 a.m. ET*

Barcelona, Spain, November 20, 2014 – Epizyme, Inc. (NASDAQ: EPZM), a clinical stage biopharmaceutical company creating innovative personalized therapeutics for patients with genetically defined cancers, today announced results from the Phase 1 dose escalation study of the investigational EZH2 inhibitor EPZ-6438 (referred to as E7438 by Eisai) administered orally as a single agent in patients with advanced solid tumors and B-cell non-Hodgkin lymphomas. These data will be presented today at 12:10 p.m. CET/6:10 a.m. ET by EORTC Scientific Chair Jean-Charles Soria, M.D., Ph.D., on behalf of study investigator Vincent Ribrag, M.D., both of the Institut Gustave Roussy, at the 26th Annual EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. The slides will be posted to the Epizyme website, www.epizyme.com, before the Company's conference call.

"The single agent activity seen with EPZ-6438 in both non-Hodgkin lymphoma patients and the malignant rhabdoid tumor patient in this Phase 1 study is very encouraging," said Professor Ribrag. "This is true particularly given the advanced nature of disease and the extent of prior treatment failures in many of these patients."

This open-label, multicenter, Phase 1 study investigated EPZ-6438 as a single agent in patients with advanced B-cell non-Hodgkin lymphomas (diffuse large B-cell lymphoma = 6, follicular lymphoma = 5, marginal zone lymphoma = 1) or advanced solid tumors (colorectal = 4, INI1-deficient malignant rhabdoid tumor = 1, INI1-deficient synovial sarcoma = 1, other solid tumors = 6). The study objectives included establishment of the maximum tolerated or recommended Phase 2 dose, safety, tolerability, pharmacokinetics and preliminary evaluation of anti-tumor activity. Patients on study

were heavily pre-treated, with fourteen patients having received between two and four prior therapies and nine having received more than four prior therapies. Five dosing cohorts were studied: 100 mg (n=6), 200 mg (n=3), 400 mg (n=3), 800 mg (n=6) and 1600 mg (n=6).

As of October 20, 2014, the following activity was observed in the 20 patients with advanced B-cell NHL or advanced solid tumors who were evaluable for efficacy:

- Four of 10 evaluable NHL patients achieved a partial response (PR) or better, including one complete response (CR)
- Among five evaluable DLBCL patients, three achieved a PR or better: One patient with a PR reported in August 2014 subsequently evolved to a CR upon continued treatment and remains on study at 41 weeks of treatment; one of the two patients who achieved a PR remains on study
- Among four evaluable patients with follicular lymphoma (FL), one achieved a partial response and remains on study; three achieved stable disease (SD) and of these, two remain on study
- Confirmatory sequencing in a central laboratory showed all 10 NHL patients evaluable for efficacy had wild-type EZH2, and responses were observed in both germinal center origin and non-germinal center origin disease
- One patient with an INI1-deficient malignant rhabdoid tumor achieved a PR and remains on study; 10 patients with solid tumors were evaluable for efficacy, including two patients with INI1-deficient solid tumors
- EPZ-6438 was well tolerated, and the majority of adverse events were Grade 1 or Grade 2
- Responses were seen across a range of doses to 800 mg BID

“These results provide encouraging evidence of anti-tumor activity with EPZ-6438, in both NHL and malignant rhabdoid tumors, including the potential for responses to improve with continued treatment,” said Peter Ho, M.D., Ph.D., Chief Development Officer, Epizyme. “Given the clinical activity we saw in both wild type EZH2 and non-germinal center lymphoma patients, our plan for the first Phase 2 NHL study is to evaluate EPZ-6438 in DLBCL and FL patients with and without EZH2 mutations.”

All 24 patients were evaluated for safety and tolerability as of the safety data cut-off of September 24, 2014. Twenty of 24 patients were evaluable for efficacy as of October 20, 2014. EPZ-6438 was administered orally, twice daily in 28-day cycles to all patients.

The majority of adverse events were Grade 1 or Grade 2. Adverse events occurring in more than 10 percent of patients were asthenia, decreased appetite and nausea. The only Grade 3 or Grade 4 treatment-related adverse event observed was Grade 4 thrombocytopenia in one patient at 1600 mg, which met the criteria for a dose-limiting toxicity. No AEs required treatment withdrawal or dose reduction; however, three AEs resulted in dose interruption.

EPZ-6438 was rapidly absorbed and eliminated, with a terminal half-life of three to six hours. In addition, H3K27Me3 inhibition in the skin, a marker of biologic activity, was correlated to treatment exposure, with near maximal inhibition predicted by pharmacokinetic exposure at 800 mg.

Among patients with non-Hodgkin lymphoma, clinical activity of EPZ-6438 did not require mutation within EZH2, as confirmatory sequencing showed all subjects evaluable for efficacy and analyzed for EZH2 were wild type. In addition, four of the five evaluable DLBCL patients had lymphoma of non-germinal center origin, and responses were observed in both germinal and non-germinal center subtypes. Currently, a Phase 2 dose of 800 mg BID is under consideration. A final recommendation for the Phase 2 dose will be approved by the Data Monitoring Committee based on efficacy, safety, and PK/PD parameters.

Conference Call and Webcast
Epizyme will host a conference call and live audio webcast with slides on Thursday, November 20, 2014, at 8:00 a.m. ET to discuss results from the Phase 1 study.

To participate in the conference call, please dial 1-877-844-6886 (domestic) or 1-970-315-0315 (international) and refer to conference ID 35051953. The live webcast can be accessed under “Events and Presentations” in the Investor Relations section of the Company’s website at www.epizyme.com.

Slides will be available on the Company’s website prior to the conference call.

About EZH2 Cancers
EZH2 is a histone methyltransferase (HMT) that is increasingly understood to play a potentially oncogenic role in a number of cancers. These include non-Hodgkin lymphomas and INI1-deficient cancers such as synovial sarcoma and malignant rhabdoid tumors.

About EPZ-6438
Epizyme and its partner Eisai are developing EPZ-6438 (E7438) for the treatment of non-Hodgkin lymphoma patients and patients with INI1-deficient solid tumors. EPZ-6438 is a small molecule inhibitor of EZH2 discovered by Epizyme. 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.

Epizyme granted Eisai a worldwide license to EPZ-6438, 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 non-wild type EZH2, where EZH2 contains point mutations. Additional information about these partnerships may be found here: http://www.epizyme.com/about-us/partnerships/

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?term=7438&rank=1

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, 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 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.

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