Epizyme Presents Pre-Clinical Data and Early Clinical Observations from Ongoing Phase 1 Trial of EZH2 Inhibitor EPZ-6438 (E7438) at ASH Meeting on Lymphoma Biology

--In three dose cohorts completed to date: maximum tolerated dose (MTD) not reached; pharmacokinetics (PK) were dose-proportional; pharmacodynamic (PD) evidence of target inhibition was observed; objective responses were seen in two NHL patients --

-- Ongoing enrollment in dose cohorts 4 and 5 --

-- More complete Phase 1 data to be presented in late 2014 --

-- Initiation of Phase 2 studies in non-Hodgkin lymphoma (NHL) and INI1-deficient tumors planned in late 2014, pending review of Phase 1 results --

Colorado Springs, Colo., August 12, 2014 - Epizyme, Inc. (NASDAQ: EPZM), a clinical stage biopharmaceutical company creating innovative personalized therapeutics for patients with genetically defined cancers, reported pre-clinical data and early clinical observations from an ongoing Phase 1 trial, being conducted in collaboration with Eisai, the Institut Gustave Roussy, and the Institut Bergonie, of EZH2 inhibitor EPZ-6438 (E7438) in patients with advanced solid tumors and B-cell lymphomas. These data were presented today by Robert Copeland, Ph.D., Chief Scientific Officer, Epizyme, during an oral session on novel therapeutics in lymphoma at the American Society of Hematology (ASH) meeting on Lymphoma Biology, held August 10-13 in Colorado Springs, Colorado. The presentation is available on the Epizyme website at http://www.epizyme.com/?p=1053.

“EPZ-6438 is the first EZH2 inhibitor to enter the clinic. We are very pleased to see that the maximum tolerated dose has not been reached and that there was a clear PK and PD dose relationship through the first three cohorts that have been evaluated,” said Robert Gould, Ph.D., Chief Executive Officer, Epizyme. “Additionally, we saw two objective responses among NHL patients enrolled in the first three cohorts of the Phase 1 dose escalation study. We plan to present the full results of the ongoing Phase 1 dose escalation study at a scientific conference later in 2014. Pending review of those results, we expect to initiate two Phase 2 studies in 2014: one in NHL and one in INI1-deficient tumors, such as malignant rhabdoid tumors.”

Pre-Clinical Findings
Pre-clinical data have shown the utility of single-agent EZH2 inhibitors in both EZH2 mutant and EZH2 wild type germinal center (GC) NHL models. Data presented today showed that in pre-clinical studies in GC NHL cell lines, combining EPZ-6438 with CHOP, a chemotherapy cocktail regimen that is a standard of care in NHL, resulted in strong synergy of lymphoma cell killing. When EPZ-6438 was combined with each individual component of the CHOP regimen, the synergy was greatest with prednisone, the corticosteroid component of CHOP. Prednisone greatly enhanced the potency of EPZ-6438 for killing EZH2 mutant-bearing lymphoma cell lines, and broadened the activity of EPZ-6438 to all GC NHL cell lines, regardless of EZH2 mutational status. Combining EPZ-6438 with dexamethasone, another corticosteroid, yielded similar synergistic results. Synergy was also observed in both EZH2 mutant and wild type cell lines when EPZ-6438 was combined with B-cell signaling pathway agents and BCL2 antagonists.

Early Clinical Observations
The primary objective of the ongoing Phase 1 dose escalation study is to evaluate the safety
and tolerability of EPZ-6438 and determine the maximum tolerated dose (MTD) or recommended Phase 2 dose (RP2D); the secondary objectives are to determine pharmacokinetics (PK) and pharmacodynamics (PD) of EPZ-6438. The study to date consists of five dosing cohorts, with evaluation of doses of 100 mg to 1600 mg BID, orally administered in 28-day cycles without a drug holiday in patients with advanced solid tumors or with relapsed or refractory B-cell lymphoma. Three of five dosing cohorts (100, 200 and 400 mg) have been completed with 12 evaluable patients dosed, four of whom were NHL patients. Dose cohorts evaluating 800 mg and 1600 mg are ongoing.

Early clinical observations from the three completed cohorts include:

- MTD has not been reached; there were no DLTs or AE-related treatment discontinuations
- PK was dose-proportional across these three cohorts
- PD evidence of target inhibition was observed in skin
- Two NHL patients achieved objective responses: a partial response in a patient with relapsed transformed diffuse large B-cell lymphoma (DLBCL), and an ongoing partial response in a patient with primary refractory mediastinal B-cell lymphoma (PMBCL)
- Additionally, a patient with follicular lymphoma with EZH2 mutation had stable disease

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 germinal center (GC) non-Hodgkin lymphomas, INI1-deficient cancers such as synovial sarcoma and malignant rhabdoid tumors, and a range of other solid tumors.

About EPZ-6438
Epizyme and its partner Eisai are developing EPZ-6438, a small molecule inhibitor of EZH2 created with Epizyme’s proprietary product platform, for the treatment of non-Hodgkin lymphoma patients. 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 (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 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/

In June 2013, Epizyme and Eisai initiated a Phase 1/2 clinical trial of EPZ-6438 (E7438) in patients with advanced solid tumors or B-cell lymphomas. This program is currently in the dose escalation phase. 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

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, availability and timing of data from ongoing clinical studies, whether interim results from a clinical trial such as the results reported in this release will be predictive of the final results of the trial or results of early clinical studies 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 May 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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