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Epizyme Announces Acceptance of Investigational New Drug Application for Tazemetostat in Patients with INI1-Negative Tumors or Synovial Sarcoma

- *Phase 2 study in adults and phase 1 study in pediatric patients with INI1-negative tumors or synovial sarcoma to begin in the second half of 2015*

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Epizyme, Inc. (NASDAQ:EPZM), a clinical stage biopharmaceutical company creating novel epigenetic therapies for patients with cancer, today announced the U.S. Food and Drug Administration (FDA) has accepted the company's investigational new drug (IND) application for tazemetostat for the treatment of adults and pediatric patients with INI1-negative tumors or synovial sarcoma. In the second half of 2015, Epizyme plans to initiate a multi-center phase 2 study in adults and a multi-center phase 1 study in children to evaluate tazemetostat in patients with relapsed or refractory INI1-negative tumors or synovial sarcoma.

"Patients with INI1-negative tumors have a life-threatening disease and few treatment options. Our development approach reflects Epizyme's strategy for aggressively advancing tazemetostat for indications with high unmet need," said Peter Ho, M.D., Ph.D., Chief Development Officer. "These clinical studies and our IND enable the expansion of our clinical development program, as we aim to establish tazemetostat's benefit globally in multiple therapeutic areas where it has shown promise in early research."

"We believe the treatment of INI1-negative tumors offers an opportunity for us to establish a strong clinical profile for tazemetostat in multiple patient populations and reinforces Epizyme's leadership position in the field of targeted epigenetic therapeutics," added Robert Gould, Ph.D., President and Chief Executive Officer. "These new registration-supporting studies in INI1-negative tumors and synovial sarcoma will complement our ongoing 5-arm phase 2 study of tazemetostat in non-Hodgkin lymphoma, which is actively enrolling patients."

INI1 is a critical component of the SWI/SNF regulatory complex, a chromatin remodeler that acts in opposition to EZH2. INI1-negative tumors have altered SWI/SNF function, resulting in aberrant and oncogenic EZH2 activity. This activity can be targeted by small molecule inhibitors of EZH2 such as tazemetostat. INI1-negative tumors are generally aggressive and are poorly served by current treatments. For example, current treatment of MRT, a well-studied INI1-negative tumor, consists of surgery, chemotherapy and radiation therapy, which are associated with limited efficacy and significant treatment-related morbidity. The annual incidence of patients with INI1-negative tumors and synovial sarcoma in major markets, including the U.S., E.U. and Japan, is approximately 2,400.[1]

The adult phase 2 multicenter study will enroll up to 90 patients in three cohorts. The first cohort will be comprised of patients with malignant rhabdoid tumor (MRT), rhabdoid tumor of the kidney (RTK) and atypical teratoid / rhabdoid tumor (ATRT). The second cohort will be comprised of patients with other INI1-negative tumors including epithelial sarcoma, epithelioid malignant peripheral nerve sheath tumor, extraskeletal myxoid chondrosarcoma, myoepithelial carcinoma, and renal medullary carcinoma. The third cohort will be comprised of patients with synovial sarcoma. Dosing in all three cohorts will be at the recommended phase 2 dose of 800 mg twice per day (BID) with a tablet formulation, which Epizyme is also using in its ongoing phase 2 trial in non-Hodgkin lymphoma. The primary endpoint is overall response rate (ORR) for patients with INI1-negative tumors and progression-free survival (PFS) for patients with synovial sarcoma. Secondary endpoints include duration of response, overall survival (OS), PFS for patients with INI1-negative tumors, safety and pharmacokinetics (PK).

The pediatric phase 1 multicenter study will enroll approximately 40 patients in a dose escalation design, followed by dose expansion, with an oral suspension of tazemetostat. The study will enroll subjects with INI1-negative tumors or synovial sarcoma. INI1-negative tumors include MRT, ATRT, RTK, and other INI1-negative tumors as previously described. The primary endpoint of study is safety with the objective of establishing the recommended phase 2 dose in pediatric patients. Secondary endpoints include PK, ORR, duration of response, PFS and OS.

Epizyme will present a clinical update for the phase 1 portion of the ongoing phase 1/2 trial of tazemetostat at ESMO's European Cancer Conference on September 26, 2015. This update will include safety data from the entire cohort and efficacy data from patients with solid tumors including INI1-negative tumors.

About EZH2 in Cancer

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, INI1-negative cancers such as malignant rhabdoid tumors, epithelioid sarcomas, and a range of other solid tumors including synovial sarcoma.

About the Tazemetostat Clinical Program

In addition to the aforementioned studies in patients with INI1-negative tumors and synovial sarcoma, Epizyme is evaluating tazemetostat in patients with relapsed or refractory non-Hodgkin lymphoma (NHL) and solid tumors in a phase 1/2 study. The dose escalation and dose expansion cohorts from the ongoing phase 1 part of the study are fully enrolled.

The phase 2 NHL study is the phase 2 portion of the phase 1/2 study. This trial is a five-arm, multi-center, international study that will assess the safety and activity of tazemetostat in patients with relapsed or refractory non-Hodgkin lymphoma. The study will enroll up to 30 patients in each arm, prospectively stratified for EZH2 mutation status and cell-of-origin, assuming each arm of the study achieves its primary response rate goal in its first stage. The five study arms are enrolling relapsed/refractory patients with:

- Germinal center DLBCL with mutant EZH2
- Germinal center DLBCL with wild-type EZH2
- Follicular lymphoma with mutant EZH2
- Follicular lymphoma with wild-type EZH2
- Non-germinal center DLBCL

The Company also plans to initiate additional clinical evaluations of tazemetostat, including a combination with R-CHOP in patients with DLBCL, and a combination with a B-cell signaling agent or other emerging targeted therapies for B-cell lymphomas.

About Tazemetostat

Epizyme is developing tazemetostat for the treatment of non-Hodgkin lymphoma patients and patients with INI1-negative tumors or synovial sarcoma. Tazemetostat is a first-in-class small molecule inhibitor of EZH2 created by Epizyme using its proprietary product platform. In many human cancers, aberrant EZH2 enzyme activity results in misregulation of genes that control cell proliferation resulting in the rapid and unconstrained growth of tumor cells. Tazemetostat is the WHO International Non-Proprietary Name (INN) for compound EPZ-6438.

Additional information about the ongoing phase 1/2 program, including clinical trial information, may be found here: https://clinicaltrials.gov/ct2/show/NCT01897571.

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 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 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 will be predictive of the final results of the trial or 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 our Form 10-Q most recently filed with the SEC, and in our 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. 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.

[1] *According to a report by Clarion Healthcare commissioned by Epizyme.*

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