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Epizyme Announces First Patient Dosed in Global Clinical Program Evaluating Tazemetostat in Genetically Defined Solid Tumors

- U.S. study sites now enrolling adults in registration-supporting phase 2 study
- U.S. study sites now enrolling pediatric patients in phase 1 dose escalation study

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Epizyme, Inc. (NASDAQ: EPZM), a clinical stage biopharmaceutical company creating novel epigenetic therapies for cancer patients, announced today that the first patient has been dosed in the phase 2 study of tazemetostat in adult patients with genetically defined tumors. The phase 1 dose escalation study in pediatric patients with the same tumor types is also now open for enrollment. The cancers being studied in these trials, INI1-negative tumors, certain SMARCA4-negative tumors and synovial sarcomas, are aggressive cancers that are poorly served by current treatments. The first sites activated for adult enrollment are Northwestern University, MD Anderson Cancer Center and Cincinnati Children's Hospital and the first sites activated for pediatric enrollment are the Dana Farber Cancer Institute and Cincinnati Children's Hospital. Additional study sites in the U.S., Canada, Europe and Australia are planned to be added over the upcoming months.

"Life-threatening rare tumors such as rhabdoid tumors, epithelioid sarcomas and synovial sarcomas affect children and young adults who are in need of novel effective therapies since the standard approaches are only marginally useful," said George Demetri, M.D., Director, Center for Sarcoma and Bone Oncology, Dana-Farber Cancer Institute and Professor of Medicine, Harvard Medical School. "We are enthusiastic about evaluating tazemetostat in our patients with these forms of sarcomas since the molecular mechanism is so compelling, especially with the recent identification of mutations in INI1 or SMARCA4 as genetic drivers for these cancers."

"This important study will enroll children with cancers such as malignant rhabdoid tumor, based on unique genetic defects that appear to result in biological sensitivity to EZH2 inhibition," said Susan Chi, M.D., Director of the Pediatric Brain Tumor Clinical Trials Program, Dana-Farber Cancer Institute and Assistant Professor of Pediatrics, Harvard Medical School. "For children with these deadly diseases, tazemetostat potentially represents a meaningful option when other treatments have been exhausted."

"Initiation of the clinical program in genetically defined solid tumors is an important milestone for Epizyme and expands tazemetostat development beyond non-Hodgkin lymphoma," said Peter Ho, M.D., Ph.D., Chief Medical Officer, Epizyme. "We are excited to advance the study of tazemetostat in these patients."

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, rhabdoid tumor of the kidney and atypical teratoid rhabdoid tumor, all of which are characterized by INI1- or SMARCA4-negativity. The second cohort will be comprised of patients with non-rhabdoid 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 in which INI1 is dysregulated by a reciprocal translocation between chromosome 18 and the X chromosome. Patients will be dosed at 800 mg twice daily with tablets taken orally. 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), and PFS for patients with INI1-negative tumors, as well as 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 patients with the same INI1-negative tumors, SMARCA4-negative tumors or synovial sarcoma as in the adult study. The primary endpoint of the study is safety, with the objective of establishing the recommended phase 2 dose in pediatric patients. Secondary endpoints include pharmacokinetics, objective response rate, duration of response, progression free survival, and overall survival.

INI1-negative or certain SMARCA4-negative tumors are characterized as aggressive cancers with few to no approved treatments today. For example, current treatment of malignant rhabdoid tumors, an INI1-negative tumor, consists of surgery, chemotherapy and radiation therapy, which are associated with limited efficacy and significant treatment-related morbidity.

In August, the FDA's Division of Oncology Products 2 accepted Epizyme's IND application to study adult and pediatric patients with INI1-negative solid tumors or synovial sarcoma in the U.S.

Interim data from Epizyme's phase 2 study of tazemetostat in adult patients with genetically defined solid tumors are anticipated to be presented at a medical conference in late 2016.

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 lymphoma, INI1-negative or certain SMARCA4-negative cancers such as malignant rhabdoid tumors and epithelioid sarcomas, synovial sarcoma, and a range of other solid tumors.

About Tazemetostat

Epizyme is developing tazemetostat for the treatment of patients with non-Hodgkin lymphoma and for patients with INI1-deficient solid tumors. Tazemetostat is a first-in-class small molecule inhibitor of EZH2 created by Epizyme using its proprietary product platform. In some 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 this program, including clinical trial information for the adult five -arm NHL study, can be found here: https://clinicaltrials.gov/ct2/show/NCT01897571

Clinical trial information for the adult INI1-negative tumors, certain SMARCA4-negative tumors or synovial sarcoma trial can be found here: https://clinicaltrials.gov/ct2/show/NCT02601950

Clinical trial information for the pediatric INI1-negative tumors, certain SMARCA4-negative tumors or synovial sarcoma trial can be found here: https://clinicaltrials.gov/ct2/show/NCT02601937

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 chromatin modifying proteins (CMPs), such as histone methyltransferases or HMTs. CMPs 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 CMPs, 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 such as the results referred to in this release will be predictive of the final results of the trial or the results of future trials; expectations for regulatory approvals to conduct trials or to market products; 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 Form 10-Q filed with the SEC on November 9, 2015, 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.

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