Epizyme Announces Publication of Tazemetostat Phase 1 Clinical Data in The Lancet Oncology

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Study Evaluated the Safety of Tazemetostat and Established the Recommended Phase 2 Dose; Anti-Tumor Activity Observed in Multiple Tumor Types

CAMBRIDGE, Mass., April 09, 2018 (GLOBE NEWSWIRE) -- Epizyme, Inc. (NASDAQ:EPZM), a clinical-stage company developing novel epigenetic therapies, announced today its first-in-human data on the effects of EZH2 inhibition in patients with advanced solid tumors and B-cell non-Hodgkin lymphoma (NHL) was published in the peer-reviewed *The LancetOncology.* The objectives of the Phase 1 dose-escalation portion of the study were to evaluate the safety and tolerability of orally dosed tazemetostat, a first-in-class selective inhibitor of EZH2. The study established the recommended dose for the Phase 2 expansion study and demonstrated favorable safety findings and anti-tumor activity.

“Today's publication in *The Lancet Oncology* reports the safety and tolerability endpoints for tazemetostat in this study, which enabled further evaluation of EZH2 inhibition in INI1- and SMARCA4-negative solid tumors and NHL,” said Professor Antoine Italiano, MD, Ph.D. of Institut Bergonie and lead author of the paper. “I’m also encouraged by the preliminary anti-tumor activity observed in this study.”

The open-label Phase 1 study was designed to evaluate the maximally tolerated dose and supported defining the recommended Phase 2 dose (RP2D) of tazemetostat. Tazemetostat was dosed twice daily as a single agent in patients with relapsed or refractory B-cell NHL (n=21) or with advanced solid tumors (n=43) including molecularly defined INI1- or SMARCA4-negative tumors. Additional study objectives were to evaluate the adverse events (AE), pharmacokinetics (PK), pharmacodynamics (PD) and preliminary anti-tumor activity of the agent.

The results of the safety, PK and PD analyses helped determine the RP2D of 800 mg twice daily. The most common treatment-related adverse events, regardless of attribution, were grade 1 or 2 asthenia, anorexia, anemia, muscle spasms, nausea and vomiting. One single dose-limiting toxicity of grade 4 thrombocytopenia was identified at the highest dose of 1600 mg, but no other grade 3 or 4 toxicities were observed at a frequency greater than five percent.

Anti-tumor activity was seen across several tumor types. In B-cell NHL, durable objective responses were observed in eight patients. Three patients had a complete response (CR), one with diffuse large B-cell lymphoma (DLBCL) and two with follicular lymphoma (FL). Five additional patients experienced a partial response (PR): three with DLBCL, one with FL and one with marginal zone lymphoma.

Of the patients with solid tumors enrolled in this study, 13 had INI1- or SMARCA4-negative tumors. Activity was observed in five of these patients, including a CR in one patient with a malignant rhabdoid tumor, and a PR in one patient with SMARCA4-negative malignant rhabdoid tumor of the ovary (MRTO). Prolonged stable disease was observed in a patient with MRTO and two patients with epithelioid sarcoma (ES) experienced prolonged stable disease greater than 20 months.

“We are excited to see these data published in *The Lancet Oncology*, knowing that few Phase 1 studies are selected. We believe this is an important confirmation of our science as we continue to advance tazemetostat—a potent, selective, orally available EZH2 inhibitor," said Robert Bazemore, president and chief executive officer of Epizyme. "Additionally, we would like to thank the investigators, patients and caregivers for their participation in this study, and for contributing to our understanding of tazemetostat as we work to address a significant medical need.”

The results from this early phase study laid the groundwork for further exploration of tazemetostat in larger trials as a targeted approach to treat molecularly defined tumors predicted to be dependent on EZH2 activity, such as ES and NHL. Phase 2 studies in adults and a Phase 1 study for children, adolescents and young adults are currently enrolling patients living with these types of cancer.

The paper titled “Tazemetostat, an EZH2 inhibitor, in relapsed or refractory B-cell non-Hodgkin lymphoma and advanced solid tumours: a first-in-human, open-label, phase 1 study” was authored by researchers from Institut Bergonié, Institut Gustave Roussy and Université de Bordeaux, as well as members from Epizyme’s Research and Clinical Development teams. The paper is available online today by clicking here and will be published in the May issue, available April 25, 2018.

About the Tazemetostat Clinical Trial Program
Tazemetostat, a first-in-class EZH2 inhibitor, is currently being studied as a monotherapy in ongoing Phase 2 programs in certain molecularly defined solid tumors, including epithelioid sarcoma and other INI1-negative tumors; both follicular lymphoma (FL) and diffuse large B-cell lymphoma (DLBCL) forms of non-Hodgkin lymphoma (NHL); mesothelioma; and combination studies in DLBCL and NSCLC.

About Epizyme, Inc.
Epizyme, Inc. is a clinical-stage biopharmaceutical company committed to rewriting treatment for cancer and other serious diseases through novel epigenetic medicines. Epizyme is broadly developing its lead product candidate, tazemetostat, a first-in-class EZH2 inhibitor, with studies underway in both solid tumors and hematological malignancies, as a monotherapy and combination therapy in relapsed and front-line disease. The company is also developing a novel G9a program with its next development candidate, EZM8266, which is targeting sickle cell disease. By focusing on the genetic drivers of disease, Epizyme's science seeks to match targeted medicines with the patients who need them. For more information, visit www.epizyme.com.

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 and in the 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; whether results from preclinical studies or earlier clinical studies will be predictive of the results of future trials; whether results from clinical studies will warrant meetings with regulatory authorities, submissions for regulatory approval or review by governmental authorities under the accelerated approval process; whether Fast Track Designation and Orphan Drug Designations will provide the benefits for which tazemetostat is eligible; expectations for regulatory approvals to conduct trials or to market products; whether the company's cash resources will be sufficient to fund 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 and other factors discussed in the "Risk Factors" section of the company's most recent Form 10-Q filed with the SEC and in the company's 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 and should not be relied upon as representing the company's views as of any date subsequent to 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.

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