Epizyme Announces Registration Path for Tazemetostat for Follicular Lymphoma and Provides Pipeline Updates and 2019 Guidance

January 4, 2019

Path Defined to Submit for Accelerated Approval in All FL Patients after at least Two Prior Lines of Therapy Based on Fully Enrolled Phase 2 Study

Operating Runway Extended into the Second Quarter of 2020

Conference Call to be Held Today, Jan. 4, at 8:30 a.m. ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 4, 2019--Epizyme, Inc. (Nasdaq: EPZM), a clinical-stage company developing novel epigenetic therapies, today announced a comprehensive set of pipeline updates, including that the company has identified a path to submission for accelerated approval of tazemetostat for patients with relapsed and/or refractory follicular lymphoma (FL), both with and without EZH2 activating mutations. The company recently conducted a productive meeting with the U.S. Food and Drug Administration (FDA) to discuss the FL registration strategy based on the current patient population in its ongoing Phase 2 clinical trial. Following the discussion, Epizyme has defined a registration strategy for tazemetostat in both EZH2 mutant and wild type FL patient populations, where patients’ disease has progressed following two or more lines of therapy. Based on this, the company anticipates submitting a New Drug Application (NDA) for this indication in the fourth quarter of 2019. In addition, the company provided an update on its clinical and preclinical pipeline and anticipated milestones for 2019.

"Follicular lymphoma is an incurable cancer today, and in the third line and later settings, there are limited effective treatment options. Defining a clear path to a regulatory submission for tazemetostat for this patient population marks a huge step forward for patients and an opportunity to change the course of FL treatment," said Shefali Agarwal, M.D., chief medical officer of Epizyme. "This FL NDA submission would mark the second for tazemetostat in one year, following our first submission for epithelioid sarcoma, which is on track for the second quarter of 2019. If successful, tazemetostat is poised to be the first commercially available EZH2 inhibitor. We look forward to advancing our submission preparations and further engaging with FDA, as we work expeditiously to bring tazemetostat to the patients who need it."

Tazemetostat Registration Update for Follicular Lymphoma

- **Phase 2 Study Fully Enrolled**: The ongoing Phase 2 study has been fully enrolled and based on discussions with FDA, is expected to provide the necessary relapsed and/or refractory FL patients needed for an NDA submission, with 45 patients with EZH2 activating mutations and 54 patients with wild-type EZH2.
- **Registration Path Identified for NDA Submission in Follicular Lymphoma**: Epizyme recently met with FDA to review its planned registration strategy for tazemetostat for patients with FL who have been previously treated with two or more systemic therapies, which represents a population of unmet medical need. The company has identified a path to a submission for accelerated approval for patients with both mutant and wildtype EZH2, based on the ongoing Phase 2 study. Epizyme will further advance the Phase 2 study, with updated data to be reported at a medical meeting in mid-2019 and an NDA submission targeted for the fourth quarter of 2019.
- **Confirmatory Program Could Support Expansion into Earlier Treatment Lines of Follicular Lymphoma**: As part of an accelerated approval strategy, Epizyme plans to conduct a confirmatory program to support full approval of tazemetostat in FL, while also supporting its potential expansion into the second-line treatment of FL. Under its Fast Track designation, the company intends to engage with FDA in the first half of 2019 to discuss the confirmatory program and will share details upon initiation.

Tazemetostat Registration Update for Epithelioid Sarcoma

- **NDA Submission for Epithelioid Sarcoma on Track for Second Quarter of 2019**: Epizyme is advancing preparations for its first NDA submission for tazemetostat in the second quarter of 2019 using the accelerated approval pathway for the treatment of patients with epithelioid sarcoma (ES). ES is an ultra-rare and difficult-to-treat sarcoma with no specifically indicated FDA-approved therapies today. If approved, tazemetostat could be the first treatment specifically indicated for patients with ES. The company has begun pre-commercial activities, with plans to commercialize tazemetostat on its own in the U.S.

Tazemetostat Program Expansion Updates
• **Combination Study to Begin in Follicular Lymphoma in 2019:** Based on the monotherapy efficacy and safety data generated to-date, Epizyme plans to explore the potential of tazemetostat in earlier lines of FL as combination therapy. The company is assessing the opportunity to conduct a combination study that would compare the chemo-free combination of rituximab and Revlimid® (R²) with tazemetostat versus R² with placebo in patients with relapsed or refractory FL. Epizyme plans to provide an update on its combination study plans once they have been finalized.

• **R-CHOP Combination Data Further Support Tazemetostat Combination Potential:** Under its collaboration agreement with Epizyme, the Lymphoma Study Association (LYSA) reported data at the 2018 American Society of Hematology Annual Meeting on the combination of tazemetostat with R-CHOP as a front-line treatment for patients with diffuse large B-cell lymphoma. The data showed that the combination of the two agents was generally well-tolerated, confirmed the recommended tazemetostat dose for the combination to be 800mg twice-daily and demonstrated clinical activity, with 87 percent of patients experiencing a metabolic complete response. Based on these data, Epizyme is considering opportunities to expand the evaluation of this combination into patients with FL.

• **Plans in Place to Expand Tazemetostat into New Indications and Combinations:** Based on its mechanism of action, favorable safety reported and demonstrated activity in multiple tumor types and treatment settings, Epizyme plans to expand tazemetostat’s potential utility into additional combinations and indications. The company has identified the next set of clinical assessments for tazemetostat, including a combination study in castration-resistant prostate cancer that is slated to begin in mid-2019, and assessment in platinum-resistant tumors, such as small-cell lung cancer, triple-negative breast cancer and ovarian cancer, slated to begin in the second half of 2019.

• **Genentech and Epizyme to Close Tecentriq® Combination Assessment in NSCLC:** As part of a collaboration agreement, Genentech/Roche initiated assessment of tazemetostat in combination with Tecentriq for the treatment of non-small cell lung cancer (NSCLC) in an arm of its MORPHEUS NSCLC Trial. Before patients had been enrolled in the study, recruitment was halted due to the partial hold placed on tazemetostat studies. Epizyme has since reopened enrollment in the U.S. and Germany for studies for which it is the sponsor. Due to the hold and strategic reprioritizations, the companies have jointly opted not to move forward with the NSCLC combination study.

**Preclinical and Discovery Pipeline Update**

• **EZM8266 on Track to Begin Clinical Development:** Throughout 2018, Epizyme conducted IND-enabling studies on its next development candidate, EZM8266, a novel G9a inhibitor for the treatment of sickle cell disease. The company is on track to begin clinical development of EZM8266 in the second half of 2019 with a dose-finding and safety study.

• **Two Research Programs to Be Advanced under Boehringer Ingelheim Collaboration:** In November 2018, Epizyme entered a strategic collaboration with Boehringer Ingelheim focused on the research, development and commercialization of novel small molecule inhibitors directed toward two previously unaddressed epigenetic targets as potential therapies for people with cancer. Specifically, these targets are enzymes within the helicase and histone acetyltransferase (HAT) families that when dysregulated have been linked to the development of cancers that currently lack therapeutic options.

**Updated Financial Guidance**

• Based on enhanced operating efficiencies, partner revenues and proceeds from the company’s underwritten public offering completed in October 2018, Epizyme has extended its expected capital runway into the second quarter of 2020 based on current operating plans.

“We are at a point in our company’s evolution where we are beginning to realize the true value of all of the hard work to which we have dedicated ourselves over the past several years. 2019 is set to be a year of pivotal milestones for Epizyme, providing validation of our expertise in drug development and bringing us closer to achieving our mission of helping patients,” said Robert Bazemore, president and chief executive officer of Epizyme. “With defined registration paths for tazemetostat in two indications and plans to expand into other combinations and indications, tazemetostat has the potential to generate significant value for the patients and physicians who need new treatment options, and for Epizyme. Outside of tazemetostat, our research capabilities provide additional advantages to our company, and we are excited to be moving EZM8266 into the clinic and working with our partners to advance earlier programs. I am proud of what we have accomplished, and look forward to what is ahead as we transition to a commercial-stage company that can truly have an impact on patients.”

**Conference Call Information**

Epizyme will host a conference call today, Jan. 4, at 8:30 a.m. ET to review this corporate update. To participate in the conference call, please dial (877) 844-6886 (domestic) or (970) 315-0315 (international) and refer to conference ID 7289720. A live webcast and slides will be available in the investor section of the company’s website at [www.epizyme.com](http://www.epizyme.com). The webcast and slides will be archived for 60 days following the call and presentation.

**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 also is 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](http://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 relating to the Company’s ability to resume enrollment in its tazemetostat trials and the timing of such resumption, and the impact of the safety finding in the company’s pediatric trial on enrollment of patients in ongoing and future trials of tazemetostat following the lifting of the partial clinical hold and the resumption of enrollment; 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. 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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Source: Epizyme, Inc.

Media:
Erin Graves, (617) 500-0615
Epizyme, Inc.
media@epizyme.com

Investors:
Monique Allaire, (617) 896-9511
THRUST Strategic Communications
monique@thrustsc.com