Epizyme Reports Updated Data from Phase 2 Trial of Tazemetostat for Epithelioid Sarcoma at 2019 ASCO Annual Meeting

June 3, 2019

New Clinical Data Presented Today Included in Recently Submitted NDA to FDA

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 3, 2019--Epizyme, Inc. (Nasdaq: EPZM), a late-stage biopharmaceutical company developing novel epigenetic therapies, today reported updated data on tazemetostat from the epithelioid sarcoma cohort of its ongoing Phase 2 study in patients with molecularly defined solid tumors. The data will be presented today in an oral presentation entitled “Safety and efficacy of tazemetostat, a first-in-class EZH2 inhibitor, in patients with epithelioid sarcoma” at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting by Silvia Stacchiotti, M.D., Fondazione IRCCS Istituto Nazionale Tumori, Milan, and an investigator in the Phase 2 clinical trial.

In July 2017, Epizyme completed enrollment of 62 patients in the epithelioid sarcoma cohort of its Phase 2 trial. Updated data reported today from that cohort are as of a September 17, 2018 cutoff date. Findings include that treatment with tazemetostat resulted in a 15% objective response rate (ORR) and a 26% disease control rate (DCR). The median duration of response (DOR) has not yet been reached. Among the 62 patients, tazemetostat continues to be generally well-tolerated with favorable safety.

"Today, there are limited effective and tolerable treatment options available for patients with epithelioid sarcoma, a rare and aggressive cancer that affects people in the prime of their lives,” said Dr. Shefali Agarwal, chief medical officer of Epizyme. “We are pleased that the data presented today are consistent with what we have seen throughout our development of tazemetostat for epithelioid sarcoma, demonstrating meaningful clinical activity and good tolerability. Importantly, the totality of these data formed the foundation for our first NDA submission, which we just announced last week. If we are successful, tazemetostat would be the first FDA-approved EZH2 inhibitor. We are thankful to the patients, physicians and caregivers who have participated in our study and hope that tazemetostat may positively impact patients with this devastating cancer in the future.”

Efficacy Data
The epithelioid sarcoma cohort in Epizyme’s Phase 2 study represents the largest prospective study of epithelioid sarcoma with any approved or investigational anticancer treatment to date. Epithelioid sarcoma is an ultra-rare and aggressive soft tissue sarcoma, characterized by a loss of the INI1 protein. It is most commonly diagnosed in young adults (20-40 years old) and is often fatal, with a median overall survival (OS) of less than one year in patients with metastatic disease.

The fully enrolled cohort includes 24 treatment-naive patients and 38 relapsed and/or refractory patients for a total of 62 adult and pediatric epithelioid sarcoma patients (at least 16 years of age). Patients enrolled were administered 800 mg of tazemetostat orally twice daily. The primary endpoint of the study is ORR, comprised of complete and partial responses as measured by RECIST 1.1. Secondary endpoints include DOR, DCR, OS and safety.

Updated findings are summarized below, based on a September 17, 2018 data cut-off date.

<table>
<thead>
<tr>
<th>Key Efficacy Endpoint</th>
<th>Treatment-naive (n=24)</th>
<th>Relapsed and/or Refractory (n=38)</th>
<th>Total (n=62)</th>
</tr>
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<tbody>
<tr>
<td>Objective Response Rate, n (%)</td>
<td>6 (25%)</td>
<td>3 (8%)</td>
<td>9 (15%)</td>
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<tr>
<td>Median Duration of Response, weeks</td>
<td>41.1 (34.1, not reached)</td>
<td>Not reached (40.1, not reached)</td>
<td>Not reached (34.1, not reached)</td>
</tr>
<tr>
<td>Disease Control Rate*, n (%) (95% confidence interval)</td>
<td>10 (42%) (22.1, 63.4)</td>
<td>6 (16%) (6.0, 31.3)</td>
<td>16 (26%) (15.5, 38.5)</td>
</tr>
<tr>
<td>Median Overall Survival, weeks (95% confidence interval)</td>
<td>Not reached</td>
<td>47.4</td>
<td>82.4 (47.4, not reached)</td>
</tr>
</tbody>
</table>

*Comprised of confirmed objective responses for any duration or disease stabilization of 32 weeks or more
Tazemetostat Safety Data
Favorable safety and tolerability have been observed with tazemetostat in this Phase 2 study cohort. The majority of treatment-emergent adverse events (TEAEs) were grade 1 or 2, with only 13 percent of patients experiencing grade 3 or higher treatment-related TEAEs. Reported TEAEs regardless of attribution with an incidence of 10% or greater were fatigue (39%), nausea (35%), cancer pain (32%), decreased appetite (26%), constipation (21%), vomiting (24%), cough and headache (18% each), diarrhea, weight decrease and anemia (16% each), dyspnea (13%) and plural effusion (11.5%). Two percent of patients were dose-reduced due to an adverse event and one patient discontinued treatment due to an adverse event in the Phase 2 cohort.

The safety data from the 62 epithelioid sarcoma patients in the study cohort are consistent with the overall safety observed to date in over 800 people in the tazemetostat clinical program.

Tazemetostat NDA Submission for Epithelioid Sarcoma
In May, Epizyme announced that it submitted the New Drug Application (NDA) for tazemetostat for the treatment of patients with metastatic or locally advanced epithelioid sarcoma not eligible for curative surgery to the US. Food and Drug Administration (FDA). The FDA has a 60-day filing review period to determine whether the NDA is complete and acceptable for filing.

About Epithelioid Sarcoma
Epithelioid sarcoma is an ultra-rare soft tissue sarcoma characterized by a loss of the protein INI1. Patients are most commonly diagnosed as young adults, between 20 and 40 years of age. Median overall survival from initial diagnosis is 30 months. Epithelioid sarcoma becomes more aggressive after recurrence or metastases, with a typical survival of less than one year for patients with metastatic disease.

About the Tazemetostat Clinical Trial Program
Tazemetostat, an oral, potent, first-in-class EZH2 inhibitor, is currently being studied as a monotherapy in ongoing clinical programs in patients with certain molecularly defined solid tumors, including epithelioid sarcoma and other INI1-negative tumors, and in patients with follicular lymphoma, both with and without EZH2 activating mutations. Multiple clinical studies are underway through collaborations assessing tazemetostat as a combination treatment for patients with diffuse large B-cell lymphoma. Epizyme also plans to conduct multiple additional clinical trials designed to evaluate the potential benefit of tazemetostat in earlier lines of therapy for follicular lymphoma, as well as new combinations and cancer indications.

About Epizyme, Inc.
Epizyme, Inc. is a late-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.

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, including accelerated approval, 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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