Epizyme Reports Updated Data from Phase 2 Trial of Tazemetostat in Patients with Relapsed or Refractory Follicular Lymphoma

June 21, 2019

Durable and Clinically Meaningful Responses Observed in Follicular Lymphoma Patients Regardless of EZH2 Mutational Status

Tazemetostat NDA Submission for Follicular Lymphoma On Track for Fourth Quarter 2019

Company to Host Conference Call Today at 8:30 a.m. EDT

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 21, 2019-- Epizyme, Inc. (Nasdaq: EPZM), a late-stage biopharmaceutical company developing novel epigenetic therapies, today reported positive interim data from an ongoing Phase 2 trial of its lead candidate, tazemetostat, as a monotherapy for patients with relapsed or refractory follicular lymphoma (FL) who have received at least two prior lines of systemic therapy. The data show that tazemetostat demonstrated meaningful clinical activity and was generally well tolerated in both patients with EZH2 activating mutations and those with wild-type EZH2.

The data will be presented today in an oral presentation entitled “Interim update from a Phase 2 multicenter study of tazemetostat, an EZH2 inhibitor, in patients with relapsed or refractory follicular lymphoma” at the International Conference on Malignant Lymphoma (ICML) by Franck Morschhauser, M.D., Ph.D., Centre Hospitalier Régional Universitaire de Lille, France, an investigator in the Phase 2 trial.

“FL is an indolent, incurable disease, for which patients are in need of new effective and tolerable treatment options,” said Dr. Shefali Agarwal, chief medical officer of Epizyme. “We continue to be encouraged by the demonstration of clinical activity and tolerability seen with tazemetostat treatment in these relapsed or refractory patients. We are pleased with the activity and durability we are seeing in both cohorts, and expect to see the data in patients with EZH2 mutations to continue to mature, given some patients are newer on study. Preparations for our NDA submission for tazemetostat for FL are underway, and we remain on track for submission in the fourth quarter of this year. We look forward to advancing those efforts, and further engaging with the FDA on our confirmatory study plans, as we work toward our goal of bringing tazemetostat to these patients.”

Follicular Lymphoma Phase 2 Cohort Design
Follicular lymphoma patients who had been previously treated with two or more systemic therapies were enrolled into two cohorts in the Phase 2 study. One cohort enrolled patients with EZH2 activating mutations and completed target enrollment of 45 patients in December 2018. A second cohort enrolled patients with wild-type EZH2, which completed enrollment of 54 patients in 2017. The study enrolled a difficult to treat population. In the cohort of patients with EZH2 activating mutations, 40% of patients were refractory to their last treatment; 40% were refractory to a rituximab regimen; and 22% were double refractory. In the wild-type EZH2 cohort, 37% were refractory to their last treatment; 61% were refractory to a rituximab regimen; and 39% were double refractory. All patients were treated with 800 mg of tazemetostat, administered orally twice a day. The primary endpoint of the study is objective response rate (ORR) as assessed by the investigator defined as a complete response (CR) or partial response (PR). Secondary endpoints include duration of response, overall survival and progression free survival and safety.

Interim Efficacy Data
All data are reported as of a June 7, 2019 data cutoff date. In the cohort of patients with EZH2 activating mutations, 43 patients were evaluable for efficacy. The ORR in this cohort was 77%, and 100% of patients experienced a reduction in tumor burden, with no patients having experienced progressive disease as best response. Seven percent of patients achieved a CR, 70% achieved a PR and 23% achieved stable disease (SD) as best response. Of those patients with SD, 9% remain on study with the potential to respond. At the time of this analysis, the median duration of response (DOR) was 8.3 months, with several new responders included since the prior data cutoff. The median progression-free survival (PFS) was 11.1 months and median follow-up time was 15.9 months.

In the cohort of FL patients with wild-type EZH2, 53 patients were evaluable for efficacy, as one patient withdrew consent for personal reasons within the first two weeks of treatment and is censored from the database. The ORR in this cohort was 34%, and 71% of patients experienced a reduction in tumor volume. Six percent of patients achieved a CR, 28% achieved a PR and 30% of patients achieved SD as best response. The median DOR is now mature at 13 months. The median PFS was 5.7 months and median follow-up time was 24.9 months.

Updated efficacy findings are summarized below:

<table>
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<tr>
<th>Best Response</th>
<th>FL with EZH2 MT</th>
<th>FL with EZH2 WT</th>
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<tbody>
<tr>
<td>Evaluable for efficacy on June 7, 2019</td>
<td>n =43</td>
<td>n =53</td>
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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.

About Epizyme, Inc.
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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; whether the NDA submission referred to in this release will be accepted for review under the

<table>
<thead>
<tr>
<th>Objective Response Rate (CR + PR)</th>
<th>77% (n=33)</th>
<th>34% (n=18)</th>
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<tbody>
<tr>
<td>Complete Response (CR)</td>
<td>7% (n=3)</td>
<td>6% (n=3)</td>
</tr>
<tr>
<td>Partial Response (PR)</td>
<td>70% (n=30)</td>
<td>28% (n=15)</td>
</tr>
<tr>
<td>Stable Disease (SD)</td>
<td>23% (n=10)</td>
<td>30% (n=16)</td>
</tr>
<tr>
<td>SD study drug ongoing</td>
<td>9% (n=4)</td>
<td>n=0</td>
</tr>
<tr>
<td>Progressive Disease</td>
<td>n=0</td>
<td>36% (n=19)</td>
</tr>
<tr>
<td>Overall Survival (OS)</td>
<td>Not reached$^1$</td>
<td>38.4 months</td>
</tr>
<tr>
<td>Median Duration of Response (DOR)</td>
<td>8.3 months$^1$ (36 weeks)</td>
<td>13 months (56.1 weeks)</td>
</tr>
<tr>
<td>Median Progression-Free Survival (PFS)</td>
<td>11.1 months$^1$ (48.1 weeks)</td>
<td>5.7 months (24.6 weeks)</td>
</tr>
</tbody>
</table>

1. Data continue to mature

Interim Safety Data
Favorable safety and tolerability have been observed with tazemetostat in these Phase 2 study cohorts. Interim safety results at the time of this analysis show only 5% of FL patients discontinued treatment due to treatment-related adverse events (AEs) and 9% had dose reductions due to treatment-related AEs. Treatment-related AEs of Grade 3 or higher were reported in 17% of patients, the most frequent of which included thrombocytopenia (3%), anemia (2%), asthenia (2%), vomiting (1%) and fatigue (1%).

“...continue to provide confidence in our planned NDA submission for tazemetostat in FL in the fourth quarter,” said Robert Bazemore, president and chief executive officer of Epizyme. “We believe strongly in tazemetostat’s potential to make a difference for these patients, and our ultimate goal is to reach FL patients across all lines of therapy. With several combination studies planned for this year with tazemetostat, we are making progress toward that goal. I am incredibly thankful to our team for their hard work in advancing tazemetostat, and to the patients, caregivers and physicians who have participated in our clinical program, making this all possible.”

Investor Conference Call
Epizyme will host an investor conference call and webcast today at 8:30 a.m. To participate in the call, please dial (877) 844-6886 (domestic) or (970) 315-0315 (international) and refer to conference ID 7765222. A live webcast will be available in the investor section of the company’s website at www.epizyme.com. The webcast will be archived on the website for 60 days.

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.

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“The data reported today are meaningful for our FL program and importantly, continue to provide confidence in our planned NDA submission for tazemetostat in FL in the fourth quarter,” said Robert Bazemore, president and chief executive officer of Epizyme. “We believe strongly in tazemetostat’s potential to make a difference for these patients, and our ultimate goal is to reach FL patients across all lines of therapy. With several combination studies planned for this year with tazemetostat, we are making progress toward that goal. I am incredibly thankful to our team for their hard work in advancing tazemetostat, and to the patients, caregivers and physicians who have participated in our clinical program, making this all possible.”

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accelerated approval process or at all, or approved on a timely basis or at all; 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.

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