Epizyme Presents Updates from SYMPHONY-1 Tazemetostat + R² Combination Study in Relapsed/Refractory Follicular Lymphoma at the 2022 ASCO Annual Meeting

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Updated Activity Data from Phase 1b Portion of the Study Shows Continued Improvement in Both Objective and Complete Response Rates

Update Includes Response Data for Sub-Group of Patients Who Are Rituximab-Refractory and with POD24

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 2, 2022-- Epizyme, Inc. (Nasdaq: EPZM), a fully integrated, commercial-stage biopharmaceutical company developing and delivering transformative therapies for cancer patients against novel epigenetic targets, announced updated safety and activity data from the Phase 1b safety run-in portion of its Phase 1b/3 confirmatory study evaluating the investigational use of tazemetostat, a first-in-class, oral, selective inhibitor of EZH2, in combination with rituximab + lenalidomide (R^2) in patients with relapsed/refractory follicular lymphoma (R/R FL). These patients have been treated with at least one prior systemic therapy, including patients who are rituximab-refractory and/or relapsed within 24 months (POD24). These data will be presented at the 2022 American Society of Clinical Oncology (ASCO) Annual Meeting on Saturday, June 4, 2022 during the Hematologic Malignancies Poster Session.

The updated interim analysis of the Phase 1b study includes 44 FL patients who received treatment with tazemetostat and R^2 (400 mg [n=4], 600 mg [n=19], or 800 mg [n=21]) as of the January 22, 2022 data cutoff. The safety profile of the tazemetostat and R^2 combination was consistent with the prescribing information for both tazemetostat and R^2, respectively. Additionally, there was no clear dose response for treatment-emergent adverse events (TEAEs) or dose modifications.

Thirty-eight of the 44 patients were evaluable for tumor assessments as of the data cutoff, with 36 patients responding to treatment. The activity findings showed an objective response rate (ORR) of 95 percent (50% complete response [CR] rate and 45% partial response [PR] rate). Two patients achieved stable disease, and two patients had progressive disease (one from the 400-mg cohort and one from the 600-mg cohort). Median progression-free survival (PFS) and duration of response were not yet reached as the study is ongoing.

This analysis also provides more in-depth characterization of enrolled patients and their response to therapy. For patients who are rituximab-refractory the ORR was 100 percent (n=13), with six patients (46%) achieving a CR. For patients with POD24, 100 percent (n=10) achieved an ORR, with four patients (40%) achieving a CR. For patients with wild type EZH2, the ORR was 94 percent (n=30), with 15 patients (47%) achieving a CR. For EZH2 mutation positive patients, the ORR was 100 percent (n=5), with three patients (60%) achieving a CR.

“Following the previous data presentation at ASH in 2021, it is encouraging to see an increase in objective and complete response rates for patients treated with tazemetostat in combination with R^2, especially in a difficult to treat population who are rituximab-refractory and with POD24. We believe the improvement in ORR and CR builds upon the findings from our preclinical data, which showed a potential synergistic effect of tazemetostat with lenalidomide and an additive effect with rituximab,” said Dr. Shefali Agarwal, Senior Medical Advisor, and interim Chief Medical and Development Officer at Epizyme. “We will continue to follow these patients and look forward to sharing follow-up data, as available, in addition to enrolling patients globally for the Phase 3 portion of the study.”

SYMPHONY-1 (EZH-302) is an international, multicenter, randomized, double-blind, active-controlled, 3-stage, biomarker-enriched, confirmatory Phase 1b/3 study, which is designed to evaluate the safety and efficacy of tazemetostat in combination with R^2 in patients with R/R FL after at least one prior line of therapy. The Phase 1b portion of the study is designed to determine the recommended Phase 3 dose (RP3D), activity, and safety of tazemetostat and R^2. In addition to the safety run-in analysis, the study also assessed the pharmacokinetics and continues to assess clinical activity of tazemetostat when administered in combination with R^2.

The Phase 1b safety run-in component evaluated tazemetostat at three dose levels (400 mg, 600 mg, and 800 mg orally twice daily [BID]) in 28-day cycles with standard-dose R^2 using a 3 + 3 design. Rituximab was administered at 375 mg/m^2 intravenously on days 1, 8, 15 and 22 of cycle 1, then on day 1 of cycles 2 to 5. Lenalidomide was administered at 20 mg (creatinine clearance ≥60 mL/min) or 10 mg (if creatinine clearance <60 mL/min) orally once daily on days 1 to 21 every 28 days for 12 cycles. In the Phase 3 component, approximately 500 patients will be randomly assigned to receive the RP3D of tazemetostat at 800mg BID + R^2 or placebo + R^2. The study will also include a maintenance arm with tazemetostat or placebo following the first year of treatment with tazemetostat + R^2 or placebo + R^2.

Treatment with tazemetostat and R^2 was generally well tolerated and the adverse events were consistent with those contained in the prescribing information for both tazemetostat and R^2, respectively. Grade 3/4 TEAEs were observed in 25 patients (57%); the most common grade 3/4 TEAE was neutrophil count decrease/neutropenia (30%). Fourteen patients (32%) reported SAEs (serious adverse events).

A table of the activity findings as of the data cutoff are below:

Best Overall Response (BOR) Rate[a], n (%)	**Tazemetostat + R^2 (n = 38)[b]**
Objective Response Rate (ORR)	36 (95)
Complete Response[c] (CR)	19 (50)
Partial Response (PR)	17 (45)

Stable Disease (SD) 2 (5)

[a] Overall, there were 31 PET-CT-based responses and 7 CT-based responses.

[b] Six patients were not included in the initial efficacy assessments.

[c] For CR, 18 were PET-CT-based responses and 1 was a CT-based response.

CT, computed tomography; PET, positron emission tomography; R^2, lenalidomide + rituximab.

“The preliminary efficacy data and consistent safety profile we see in this SYMPHONY-1 patient population is an exciting update for our tazemetostat clinical program and reinforces our belief that tazemetostat has the potential to become a backbone of therapy in FL,” said Grant Bogle, President and Chief Executive Officer at Epizyme. “The data shared at ASCO this weekend are the first of several tazemetostat combination studies across both solid tumor and hematologic malignancies that we look forward to sharing as the data mature later this year and into next.”

In addition to the SYMPHONY-1 presentation (Abstract #7572), the Company has one additional tazemetostat study being presented during the ASCO Annual Meeting. The EZH-102 study (Abstract #10040) is a Phase 1, multicenter, open-label, dose escalation (Phase 1a) and dose expansion (Phase 1b) study evaluating tazemetostat monotherapy in pediatric patients with R/R SMARCB1 (INI1 negative) tumors.

About TAZVERIK® (tazemetostat)

TAZVERIK is a methyltransferase inhibitor indicated for the treatment of:

- Adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection.
- Adult patients with relapsed or refractory follicular lymphoma whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least two prior systemic therapies.
- Adult patients with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options.

These indications are approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

The most common (≥20%) adverse reactions in patients with epithelioid sarcoma are pain, fatigue, nausea, decreased appetite, vomiting and constipation. The most common (≥20%) adverse reactions in patients with follicular lymphoma are fatigue, upper respiratory tract infection, musculoskeletal pain, nausea and abdominal pain.

View the U.S. Full Prescribing Information here: Epizyme.com

About Epizyme, Inc.

Epizyme, Inc. is a fully integrated, commercial-stage biopharmaceutical company committed to its mission of rewriting treatment for cancer through novel epigenetic medicines. The Company is focused on creating medicines that are targeted at specific causes of diseases, that are orally administered, tolerable, easy to take and based on a deep understanding of the patients that may benefit from them. The Company aspires to change the standard-of-care for patients and physicians by developing medicines with fundamentally new mechanisms of action. For more information, visit www.epizyme.com.

TAZVERIK® is a registered trademark of Epizyme, Inc.

R^2, Revlimid + Rituximab. Revlimid (lenalidomide) is a registered trademark of Celgene Corporation, a Bristol Myers Squibb company.

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, including, without limitation, Epizyme’s views with respect to the safety and activity of tazemetostat based on the updated data from the Phase 1b safety-run in portion of Epizyme’s SYMPHONY-1 trial, the potential benefit associated with tazemetostat, clinical development plans for tazemetostat, and expectations around timing of additional data 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: whether commercial sales of TAZVERIK for epithelioid sarcoma and follicular lymphoma in the approved indications will be successful; whether tazemetostat will receive marketing approval for epithelioid sarcoma or follicular lymphoma in other jurisdictions, full approval in the United States or approval in any other indication; whether results from preclinical studies or earlier clinical studies will be predictive of the results of future trials, such as the ongoing confirmatory trials of TAZVERIK; whether interim results of clinical studies will be predictive of the final results of the studies; 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 the company will receive regulatory approvals, including accelerated approval, to conduct trials or to market products; the impact of the COVID-19 pandemic on the company’s business, results of operations and financial condition; 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 success of tazemetostat; and other factors discussed in the “Risk Factors” section of the company’s most recent Form 10-K and 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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