# Epizyme Provides Business Highlights, Preliminary Fourth Quarter and Full Year 2021 Financials and Clinical Trial Updates

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*-- Preliminary TAZVERIK® (tazemetostat) Net Product Revenue Expected to be Between $11.2-11.7 Million and Between $30.6-31.1 Million for 4Q 2021 and Full-Year 2021, Respectively; Preliminary TAZVERIK Commercial Net Sales Expected to be Between $7.0-7.5 Million and Between $23.2-23.7 Million for 4Q 2021 and Full-Year 2021, Respectively --*

*-- SYMPHONY-1 Phase 3 Global Startup Activities Ongoing --*

*-- Three New Clinical Studies Open for Enrollment and Actively Screening for Patients --*

*-- Total Non-GAAP Operating Expenses Forecasted to be Between $170-190 Million for 2022 --*

*-- Company Provides Initial Guidance for Potential 2022 Clinical Milestones --*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 10, 2022-- Epizyme (Nasdaq: EPZM), a fully integrated, commercial-stage biopharmaceutical company developing and delivering novel epigenetic therapies, today provided an update on recent business highlights and its outlook for 2022.

“For Epizyme, 2021 was defined by key organizational changes that reduced our overall operating expenses while we accelerated TAZVERIK commercial adoption. As most recently reported at the American Society of Hematology annual meeting in December 2021, substantial progress on tazemetostat combination trials was made throughout 2021. Additionally, we initiated SET-101, the first-in-human study of EZM0414, our novel, first-in-class, oral SETD2 inhibitor and consummated a commercialization and development collaboration with HUTCHMED intended to bring TAZVERIK to patients in greater China and accelerate development of tazemetostat in combination with other active agents,” said Grant Bogle, President and Chief Executive Officer of Epizyme.

“Looking ahead to 2022, we plan to continue our focus on accelerating commercial adoption of TAZVERIK and advancing key clinical trial programs. We look forward to initiating the global Phase 3 portion of our SYMPHONY-1 study, which compares tazemetostat plus $R^2$ to $R^2$ plus placebo in R/R FL patients, gaining a greater understanding and insight into the ability of TAZVERIK to combine safely with other active agents both in hematological and solid tumor indications and sharing the initial safety results for EZM0414 from the SET-101 study. I look forward to providing updates on these important areas as we seek to progress our vision for growth.”

**Recent TAZVERIK® (tazemetostat) Commercial Progress**

- Epizyme expects TAZVERIK net product revenue of between $11.2-11.7 million for the fourth quarter of 2021, including between $4.1-4.3 million related to the sale of TAZVERIK commercial product for third-party pharmaceutical company use in clinical trials. TAZVERIK commercial net sales in the fourth quarter of 2021 are expected to be between $7.0-7.5 million, representing an increase of approximately 35% when compared to $5.2 million in the third quarter of 2021.
- For the full-year ended December 31, 2021, Epizyme expects TAZVERIK net product revenue of between $30.6-31.1 million, including between $7.3-7.5 million related to sales of TAZVERIK commercial product for third-party pharmaceutical company use in clinical trials. TAZVERIK commercial net sales for the full-year 2021 are expected to be between $23.2-23.7 million.
- The amount of free goods supplied to patients through Epizyme’s patient assistance program is expected to represent approximately 30% of total end user demand for the fourth quarter of 2021 and 25% for the full-year 2021.
- Total end user demand in the fourth quarter of 2021 is expected to represent at least a 14% increase over third quarter 2021 levels. This increase was driven primarily by sales for follicular lymphoma (FL).

**Recent Pipeline Highlights**

- **SYMPHONY-1:** During the December 2021 American Society of Hematology (ASH) annual meeting, Epizyme shared encouraging updated safety and activity data from the Phase 1b portion of its Phase 1b/3 confirmatory study, SYMPHONY-1. The ongoing study is evaluating tazemetostat in combination with rituximab + lenalidomide ($R^2$) in patients with relapsed or refractory (R/R) FL previously treated with at least one systemic therapy, including those who are rituximab-refractory and/or have progression of disease within two years (POD24). Based on the Phase 1b safety run-in results, in December 2021 Epizyme submitted a protocol amendment to the FDA with 800mg twice-daily (BID) as the tazemetostat dose for the global Phase 3 portion of the trial.
- **EZH-1301 (Solid Tumor) and EZH-1501 (Hematological) Basket Studies:** During the fourth quarter of 2021, Epizyme initiated two basket studies – EZH-1301 and EZH-1501, to evaluate tazemetostat combinations in patients with solid

tumors and hematological malignancies, respectively.
- **SET-101:** Epizyme announced the initiation of its first-in-human study of EZM0414, Epizyme's novel, first-in-class, oral SETD2 inhibitor, which is being developed for the treatment of adult patients with R/R multiple myeloma (MM) or R/R diffuse large B-cell lymphoma (DLBCL) in November 2021, and that the FDA granted Fast Track designation for EZM0414 in adult patients with DLBCL. Epizyme also shared preclinical data on EZM0414 along with the SET-101 Phase 1/1b clinical trial design at the 2021 ASH conference.

**2022 Projected Milestones**

- **SYMPHONY-1:** Epizyme continues to follow the 40 patients treated in the Phase 1b safety run-in portion of the study. Follow-up data from the safety run-in are anticipated to be presented at a medical conference later this year. Global startup activities for the Phase 3 randomized portion of the study are currently underway.
- **CELLO-1**: CELLO-1, an open-label, randomized Phase 1b/2 study, is evaluating tazemetostat plus enzalutamide compared to enzalutamide monotherapy in metastatic castration-resistant Prostate Cancer patients (mCRPC). The Phase 2 efficacy portion of the study is more than one-half enrolled towards a target of 80 patients. Epizyme expects to complete enrollment in 2022. Patients from the Phase 1b portion of the study continue to be followed and Epizyme expects to present updated data from these patients in 2022.
- **LYSA Study**: Patient enrollment is expected to complete in the ongoing Lymphoma Study Association (LYSA) Phase 2 clinical trial investigating tazemetostat plus R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone) in front-line high-risk FL and DLBCL in the first quarter of 2022. Epizyme expects that interim results from the trial in DLBCL and FL patients will be presented at a medical conference in 2022.
- **EZH-1301 (Solid Tumor) and EZH-1501 (Hematological) Basket Studies:** The Company recently opened sites for these two basket studies, which sites are actively screening patients for enrollment in each of the studies. Epizyme plans to provide updates as the studies reach key enrollment milestones, as well as preliminary data in 2022.
- **Additional Tazemetostat Studies:** Epizyme continues to advance additional clinical studies evaluating tazemetostat, including FDA post-marketing commitments.
- **SET-101:** Epizyme recently opened sites for the dose escalation portion of the SET-101 trial, which are actively screening patients for enrollment in this first-in-human study and which Epizyme expects will enroll between 30-36 patients. Epizyme plans to provide updates as the study reaches key enrollment milestones along with preliminary safety data in 2022.
- **Cash Runway:** Epizyme continues to expect its current cash runway to extend into the fourth quarter of 2022.
- **2022 Operating Expense Guidance:** The Company expects 2022 non-GAAP adjusted operating expenses of between $170-190 million.

The Company's estimates of net product revenue and commercial net sales of TAZVERIK and its ability to fund operations are preliminary and unaudited, represent management estimates as of the date of this release and are subject to completion of the Company's financial closing procedures. As a result, the Company's actual financial results may differ materially from the preliminary estimated financial information set forth above. The Company's independent registered public accounting firm has not conducted an audit or review of, and does not express an opinion or any other form of assurance with respect to, the estimates of net product revenue of TAZVERIK, commercial net sales, end user demand or estimates as to cash runway and operating expenses.

**About Non-GAAP Financial Measures**

In addition to financial information prepared in accordance with the U.S. generally accepted accounting principles (GAAP), this press release includes the following non-GAAP financial measure: total non-GAAP adjusted operating expenses on a projected basis. Epizyme derives this non-GAAP financial measure by excluding certain expenses and other items from the GAAP financial measure that is most directly comparable to each non-GAAP financial measure. Specifically, the non-GAAP financial measure excludes stock-based compensation expense and depreciation and amortization of intangibles. The Company's management believes that this non-GAAP financial measure is useful to both management and investors in analyzing its ongoing business and operating performance. Management does not intend the presentation of this non-GAAP financial measure to be considered in isolation or as a substitute for results prepared in accordance with GAAP, but as a complement to provide greater transparency. In addition, this non-GAAP financial measure may differ from similarly named measures used by other companies. A quantitative reconciliation of projected non-GAAP adjusted operating expenses to projected GAAP adjusted operating expenses is not available without unreasonable effort primarily due to the Company's inability to predict with reasonable certainty the amount of future stock-based compensation expense.

**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 is 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 EZM0414**

EZM0414 is a potent, selective, oral, small molecule, investigational drug agent that inhibits the histone methyltransferase, SETD2, which plays a role in oncogenesis. SETD2 methylates histone as well as non-histone proteins, and this activity is involved in several key biological processes including transcriptional regulation, RNA splicing, and DNA damage repair. Based on the preclinical data on SETD2 inhibition by EZM0414 in multiple settings, including high risk t(4;14) multiple myeloma (MM) and in other B-cell malignancies such as diffuse large B-cell lymphoma (DLBCL), the Company is conducting SET-101, a Phase 1/1b study of EZM0414, for the treatment of adult patients with relapsed or refractory MM and DLBCL.

**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.

**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: whether commercial sales of TAZVERIK for epithelioid sarcoma and follicular lymphoma in the approved indications will be successful or will increase to the levels anticipated or at all; whether the refinement of the company's commercial strategy and cost reductions will achieve the company's objectives or forecasted cost savings; whether the Company identifies items during its financial statement closing process that result in adjustments to the estimates, preliminary figures and guidance included in this press release; 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; uncertainties inherent in the initiation of future clinical studies and in the availability and timing of data from ongoing clinical studies; whether results from preclinical studies, such as the data reported in this release with respect to EZM0414, or earlier clinical studies of the company's product candidates will be predictive of the results of future trials, such as the ongoing confirmatory trials of TAZVERIK; 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; whether the company's collaborations and licensing agreements with third parties will be successful; uncertainties as to 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 or 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.

TAZVERIK® is a registered trademark of Epizyme, Inc.

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

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