Epizyme Reports First Quarter 2022 Financial Results and Provides Business Update

May 10, 2022

TAZVERIK® (tazemetostat) Net Product Revenue of $8.7 Million for 1Q 2022, Supported by Streamlined Operating Expenses which Decreased by 17% in 1Q 2022 vs. 1Q 2021

First Patient Dosed in the Randomized Phase 3 Portion of SYMPHONY-1 (EZH-302), Epizyme's Phase 1b/3 Confirmatory Study Assessing Tazemetostat in Combination with R^2 in Follicular Lymphoma (FL)

Updated Data from the Phase 1b Portion of SYMPHONY-1 to be Presented at ASCO; Additional Updates Anticipated in 2H 2022 from Tazemetostat and EZM0414 (SETD2 inhibitor) Studies

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 10, 2022-- Epizyme (Nasdaq: EPZM), a fully integrated, commercial-stage biopharmaceutical company developing and delivering transformative therapies for cancer patients against novel epigenetic targets, today reported first quarter 2022 financial results and provided a business update.

"The relapsed or refractory follicular lymphoma treatment landscape is rapidly changing, and we believe TAZVERIK® is poised to grow at an accelerated rate as the year progresses. We saw encouraging progress in important commercial metrics during the first quarter despite some seasonal impact related in part to the Medicare Part D drug benefit design and year-end prescription variability, which we continue to evaluate. TAZVERIK demand experienced a strong rebound in March, and we entered the second quarter with positive momentum. We believe that TAZVERIK has the potential to reach many more patients based on changes in the current treatment options for patients in the R/R FL market and the updated NCCN Guidelines® for FL," said Grant Bogle, President and Chief Executive Officer. "We are also continuing to advance our key clinical programs and look forward to sharing updated SYMPHONY-1 data from the Phase 1b cohort at ASCO."

Recent Progress

- **TAZVERIK® (tazemetostat) commercial progress:**
  - TAZVERIK generated net product revenue of $8.7 million for the first quarter of 2022, including $0.5 million related to the sale of TAZVERIK commercial product for third-party pharmaceutical company use in clinical trials. TAZVERIK commercial net sales in the first quarter of 2022 were $8.1 million, representing an increase of approximately 10% when compared to $7.4 million in the fourth quarter of 2021.
  - Commercial demand increased 16% in the first quarter of 2022 versus the fourth quarter of 2021 levels while total demand (commercial demand and free goods supplied through the patient assistance program) in the first quarter of 2022 was similar to fourth quarter 2021 levels. The Company believes the difference in total demand as compared with commercial demand was related, in part, to limitations of the Medicare Part D drug benefit design and year-end prescription variability, which followed a similar pattern in 2021. While total demand was soft in the beginning of the quarter, it rebounded in March to its highest monthly level since launch. Additional time is needed to fully evaluate and understand seasonality and fluctuations.
  - Recent market research suggests that TAZVERIK market share continues to grow in the third-line setting for both EZH2 mutation-positive and wild-type populations, consistent with the Company's commercial focus and messaging. The amount of free goods supplied to patients through Epizyme's patient assistance program represented approximately 15% of total demand for the first quarter of 2022. This rate was consistent with the first quarter of 2021.
- **National Comprehensive Cancer Network® (NCCN) released updated NCCN Guidelines® for B-Cell Lymphomas:** The recently updated NCCN Guidelines for grade 1-2 follicular lymphoma (FL) now include tazemetostat as a suggested treatment regimen in the second line for elderly or infirm patients with EZH2 wild type or unknown relapsed/refractory (R/R) disease in patients who have no satisfactory alternative treatment options. For third-line and subsequent therapy, tazemetostat is a suggested treatment regimen for patients with EZH2 mutation-positive disease or patients with EZH2 wild-type or unknown R/R disease who have no satisfactory alternative treatment options.
- **Global enrollment open and actively screening in the randomized Phase 3 portion of SYMPHONY-1 (EZH-302):** Dosing of the first patient was recently completed in the Phase 3 portion of the SYMPHONY-1 study, and the study is open globally and is actively screening and enrolling patients. SYMPHONY-1 is the confirmatory study assessing tazemetostat in combination with rituximab + lenalidomide (R^2) compared with R^2 plus placebo in patients with R/R FL previously treated with at least one systemic therapy, including those who are rituximab-refractory and/or have experienced progression of disease within two years (POD24). Updated data from the Phase 1b portion of SYMPHONY-1 was accepted for a poster presentation, which will be shared at the upcoming American Society of Clinical Oncology Annual Meeting in Chicago from

June 3-7. Data to be presented include updated overall response rate and complete response rate data as well as a subgroup analysis of rituximab-refractory and POD24 patients. The Company continues to follow this Phase 1b cohort of patients and plans to present additional updated data later this year.

- **LYSA Phase 2 study enrollment nearly complete; top-line results expected in second half of 2022:** Enrollment in the FL arm is complete for the Phase 2 portion of the Lymphoma Study Association (LYSA) study, a Phase 1b/2 combination study of tazemetostat with R-CHOP in high-risk, front-line FL and diffuse large B-cell lymphoma (DLBCL) patients. Epizyme, in collaboration with LYSA, anticipates presenting top-line results from the Phase 2 portion of the study in the second half of 2022.
- **CELLO-1 Phase 2 study 85% enrolled; updated safety run-in data and interim data from the Phase 2 portion of the study expected in second half of 2022:** The Phase 2 portion of the CELLO-1 study (EZH-1101), which is evaluating tazemetostat plus enzalutamide compared to enzalutamide monotherapy in metastatic castration-resistant prostate cancer patients, is approximately 85% enrolled toward a target of 80 patients. In 2022, Epizyme expects to complete enrollment in the randomized Phase 2 portion of the study and present updated data from the safety run-in portion as well as interim safety and efficacy data from the Phase 2 portion of the study in the second half of the year.
- **We continue to screen patients in ARIA (EZH-1501), the Phase 1b/2 tazemetostat hematological basket study, and SET-101, the Phase 1/1b study of EZM0414**. Epizyme plans to provide updates on these programs in the second half of 2022.

First Quarter 2022 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $199.7 million as of March 31, 2022, compared to $176.8 million as of December 31, 2021.
- **Revenue:** Total revenue was $8.7 million for the first quarter of 2022, an increase of 14% vs. $7.6 million for the first quarter of 2021. Net product revenue of TAZVERIK in the U.S was $8.7 million for the first quarter of 2022, an increase of 40% vs. $6.2 million for the first quarter of 2021.
- **Operating Expenses:** Total GAAP operating expenses were $59.6 million for the first quarter of 2022, a decrease of 17% vs. $72.0 million for the first quarter of 2021, reflecting focused efforts on streamlining operations. Total non-GAAP adjusted operating expenses were $53.0 million for the first quarter of 2022, compared to $63.7 million for the first quarter of 2021.
    - **R&D expenses:** GAAP R&D expenses were $29.8 million for the first quarter of 2022, compared to $32.7 million for the first quarter of 2021. Non-GAAP adjusted R&D expenses were $27.8 million for the first quarter of 2022, compared to $30.3 million for the first quarter of 2021.
    - **SG&A expenses:** GAAP SG&A expenses were $27.2 million for the first quarter of 2022, compared to $36.4 million for the first quarter of 2021, representing a 25% decrease following the previously announced operating expense and workforce reductions. Non-GAAP adjusted SG&A expenses were $23.6 million for the first quarter of 2022, compared to $31.5 million for the first quarter of 2021.
- **Net Loss (GAAP):** Net loss attributable to common stockholders was $55.5 million, or $0.38 per share, for the first quarter of 2022, compared to $70.3 million, or $0.69 per share, for the first quarter of 2021.

A reconciliation of non-GAAP adjusted financial measures directly comparable to GAAP financial measures is presented in the table attached to this press release.

Conference Call Information
Epizyme will host a conference call today, May 10, at 8:30 a.m. ET. To participate, please dial (877) 844-6886 (domestic) or (970) 315-0315 (international) and refer to conference ID 5369344. A webcast, as well as supplemental slides to support the webcast, will be available in the investor section of the Company's website at www.epizyme.com, and will be archived for 60 days following the call.

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 measures: total non-GAAP adjusted operating expenses on a historical basis, non-GAAP adjusted R&D expenses on a historical basis and non-GAAP adjusted SG&A expenses on a historical basis. Epizyme derives these non-GAAP financial measures by excluding certain expenses and other items from the respective GAAP financial measure, that is most directly comparable to each non-GAAP financial measure. Specifically, the non-GAAP financial measures exclude stock-based compensation expense and depreciation and amortization of intangibles. The Company's management believes that these non-GAAP financial measures are useful to both management and investors in analyzing its ongoing business and operating performance. Management does not intend the presentation of these non-GAAP financial measures 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, these non-GAAP financial measures may differ from similarly named measures used by other companies.

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 studies.

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 prioritization of the company's development activities and cost reductions will achieve the company's objectives or forecasted cost savings; 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 preclinical data referenced 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 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.

TAZVERIK® is a registered trademark of Epizyme, Inc.

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

NCCN Guidelines® is a registered trademark of National Cancer Comprehensive Network.

EPIZYME, INC
CONSOLIDATED BALANCE SHEET DATA (UNAUDITED)
(Amounts in thousands)

	March 31, 2022	December 31, 2021
Consolidated Balance Sheet Data:		
Cash and cash equivalents	$ 77,421	$ 98,336
Marketable securities	122,309	78,454
Intangible assets, net	41,811	42,849
Total assets	312,186	289,000
Total current liabilities	38,967	45,196
Deferred revenue	11,950	11,950
Related party long-term debt, net of debt discount	216,670	216,461
Related party liability related to sale of future royalties, net of current portion	15,824	15,654
Total stockholders' equity (deficit)	11,121	(20,688)

EPIZYME, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS (UNAUDITED)
(Amounts in thousands except per share data)

	Three Months Ended March 31	
	2022	**2021**
Revenues		
Product revenue, net	$ 8,656	$ 6,191
Collaboration and other revenue	40	1,440
Total revenue	8,696	7,631
Operating expenses		
Cost of revenue	2,637	2,853
Research and development	29,781	32,704
Selling, general and administrative	27,204	36,411
Total operating expenses	59,622	71,968
Operating loss	(50,926)	(64,337)
Other (expense) income, net:		
Interest expense, net	(5,480)	(5,476)
Other (expense) income, net	(48)	9
Change in fair value of of warrants to purchase common stock	1,350	-
Related party non-cash interest expense related to sale of future royalties	(370)	(470)
Other expense, net:	(4,548)	(5,937)
Loss before income taxes	(55,474)	(70,274)
Income tax provision	(31)	-
Net loss	$ (55,505)	$ (70,274)
Net loss per share attributable to common stockholders - basic and diluted	$ (0.38)	$ (0.69)
Weighted-average common shares outstanding used in net loss per share attributable to common stockholders - basic and diluted	144,201	101,790

EPIZYME, INC.
Reconciliation of Selected GAAP Measures to Non-GAAP Measures (UNAUDITED)
(Amounts in thousands)

	Three Months Ended March 31	
Reconciliation of GAAP to Non-GAAP Cost of Revenue	**2022**	**2021**
GAAP Cost of Revenue	$ 2,637	$ 2,853
Less: Depreciation and Amortization	(1,038)	(1,038)
Non-GAAP Adjusted Cost of Revenue	$ 1,599	$ 1,815
Reconciliation of GAAP to Non-GAAP Research and Development		
GAAP Research and Development	$ 29,781	$ 32,704
Less: Stock-Based Compensation Expenses	(1,792)	(2,230)
Less: Depreciation and Amortization	(148)	(143)
Non-GAAP Adjusted Research and Development	$ 27,841	$ 30,331
Reconciliation of GAAP to Non-GAAP Selling, General and Administrative:		
GAAP Selling, General and Administrative	$ 27,204	$ 36,411
Less: Stock-Based Compensation Expenses	(3,497)	(4,785)
Less: Depreciation and Amortization	(112)	(101)
Non-GAAP Adjusted Selling, General and Administrative	$ 23,595	$ 31,525
Reconciliation of GAAP to Non-GAAP Operating Expenses		
GAAP Operating Expenses	$ 59,622	$ 71,968
Less: Stock-Based Compensation Expenses	(5,289)	(7,015)
Less: Depreciation and Amortization	(1,298)	(1,282)

Non-GAAP Adjusted Operating Expenses	$ 53,035	$ 63,671

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