Epizyme Reports Fourth Quarter and Full Year 2021 Financial Results and Provides Business Update

March 1, 2022

TAZVERIK® (tazemetostat) Net Product Revenue of $11.6 Million for 4Q 2021; $30.9 Million for FY 2021

$85 Million in Gross Proceeds Raised in January 2022 Public Offering, Combined with Recent Expense Reductions Announced Today, Extends Cash Runway into 3Q 2023

Company Engaged in Global Start-up Activities for SYMPHONY-1; Data Updates Expected Across Pipeline Programs in 2022

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 1, 2022-- Epizyme (Nasdaq: EPZM), a fully integrated, commercial-stage biopharmaceutical company developing and delivering transformative therapies for cancer against novel epigenetic targets, today reported fourth quarter and full year 2021 financial results and provided business and portfolio updates.

“Epizyme entered 2022 demonstrating continued progress on our commercial efforts to drive prescription growth for TAZVERIK as a monotherapy, as well as advancing our key combination clinical studies, which we believe have the potential to significantly expand the value and reach of TAZVERIK among physicians and patients as the data mature,” said Grant Bogle, President and Chief Executive Officer. “In support of our commercialization and development efforts, we continue to make operational changes to reduce our expenses and extend our cash runway, while strategically deploying our resources to the areas we believe may be of highest impact for the company and its stakeholders.”

Recent Highlights and 2022 Projected Milestones

- **TAZVERIK® (tazemetostat) commercial progress:**
  - TAZVERIK generated net product revenue of $11.6 million for the fourth quarter and $30.9 million for the full year 2021, including $4.2 million and $7.4 million, respectively, 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 were $7.4 million, representing an increase of approximately 42% when compared to $5.2 million in the third quarter of 2021.
  - The amount of free goods supplied to patients through Epizyme’s patient assistance program represented approximately 29% of total end user demand for the fourth quarter of 2021 and approximately 24% for the full-year 2021.
  - Total end user demand in the fourth quarter of 2021 represented a 14% increase over third quarter 2021 levels. This increase was driven primarily by sales for follicular lymphoma (FL).
- **Global start-up of Phase 3 portion of SYMPHONY-1 study underway; updated safety run-in data from Phase 1b portion expected in 2022:** After completing the 30-day waiting period for its protocol amendment submitted to the U.S. Food and Drug Administration (FDA) in December 2021 with 800 mg twice-daily as the recommended Phase 3 dose, Epizyme accelerated global start-up activities, including sites in greater China with our collaboration partner HUTCHMED, for the Phase 3 portion of the SYMPHONY-1 (EZH-302) study, a confirmatory study assessing tazemetostat in combination with rituximab + lenalidomide (R^2) compared with R^2 plus placebo 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. The Company is currently screening patients in the Phase 3 portion and expects to enroll the first patient in the first quarter of 2022. Follow-up data from the Phase 1b safety run-in portion of the study are expected to be presented at a medical conference later this year.
- **LYSA Phase 2 study enrollment nearly complete; interim results expected in second half of 2022:** Enrollment 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, is nearly complete with 111 patients out of a target of approximately 122 patients in DLBCL and 61 patients out of a target of approximately 62 patients in FL enrolled as of February 23, 2022. Epizyme, in collaboration with LYSA, anticipates presenting interim results from the Phase 2 portion of the study in the second half of 2022.
- **CELLO-1 Phase 2 study ~75% enrolled; updated safety run-in data and interim data expected in second half of 2022:** The Phase 2 efficacy 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 (mCRPC), is approximately 75% enrolled toward a target of 80 patients. Epizyme expects to complete enrollment in the randomized Phase 2 portion of the study in 2022 and anticipates presenting updated data from the safety run-in portion as well as interim data from the Phase 2 portion of the study in the second half of 2022.
- **Initiated Phase 1b/2 tazemetostat hematological basket study (EZH-1501):** During the fourth quarter of 2021, Epizyme

initiated EZH-1501, its Phase 1b/2 signal finding basket study evaluating tazemetostat combinations in patients with hematological malignancies. Epizyme has entered into a clinical supply agreement with Roche for the bispecific cohort of the Company's Phase 1b/2 basket study. This cohort will evaluate the investigational use of TAZVERIK® (tazemetostat), in combination with mosunetuzumab, Roche's investigational CD20xCD3 T-cell engaging bispecific antibody, for patients with R/R FL who have received two or more prior lines of therapy. Epizyme plans to provide updates as EZH-1501 reaches key enrollment milestones and plans to provide preliminary data from EZH-1501 in the second half of 2022.

- **Initiated first-in-human study of EZM0414 (SET-101)**: During the fourth quarter of 2021, Epizyme initiated the SET-101 study, a first-in-human Phase 1/1b study of EZM0414, Epizyme's novel, first-in-class, oral SETD2 inhibitor, in adult patients with R/R multiple myeloma (MM) and R/R DLBCL. The Company expects to enroll between 30-36 patients in the Phase 1 dose escalation portion of the study. In October 2021, the FDA granted Fast Track designation for EZM0414 in adult patients with R/R DLBCL, and in January 2022, the FDA granted Orphan Drug designation for EZM0414 for MM. Epizyme plans to provide updates as the study reaches key enrollment milestones, along with preliminary data from SET-101 in 2022.

2022 Operating Plan Updates and Revised Financial Guidance

As part of Epizyme's ongoing efforts to execute more effectively and advance its long-term growth strategy, the Company announced the following:

- **External Spending and Workforce Reductions:** On March 1, 2022, the Company announced a further reduction of operating expenses, including a reduction in force of approximately 12% of its current employees. Estimated severance and termination costs of approximately $2.8-3.2 million are expected to be recorded in the first quarter of 2022.
- **Pipeline Reprioritization:** Given the breadth of Epizyme's current tazemetostat clinical development program, the Company has discontinued enrollment in its Phase 2 study of tazemetostat in combination with rituximab (SYMPHONY-2, EZH-1401), as well as its Phase 1/1b basket study evaluating tazemetostat combinations in patients with solid tumors (EZH-1301). The decision to discontinue enrollment in these studies was based on evolving market dynamics and a continued focus on optimizing the Company's investments and eliminating potentially overlapping studies. The Company continues to study tazemetostat in combination with other therapies for both hematologic and solid tumor malignancies, both in ongoing Company-sponsored studies as well as investigator-initiated studies.
- **Revised 2022 Financial Guidance:** 2022 total non-GAAP adjusted operating expenses are now expected to be between $160-180 million, compared to the prior guidance of $170-190 million. Based on the current operating plan, the Company expects that its existing cash, cash equivalents and marketable securities as of December 31, 2021, together with the $79.5 million in net proceeds raised from the common stock offering in January 2022, and expected cash generated from product sales, will be sufficient to fund planned operating expenses and capital expenditure requirements and pay debt service obligations as they become due, into the third quarter of 2023, without incorporating potential milestone payments, expense reimbursements from existing collaboration agreements or any future business development activities.

Fourth Quarter and Full Year 2021 Financial Results:

- **Cash Position:** Cash, cash equivalents and marketable securities were $176.8 million as of December 31, 2021.
- **Revenue:** Total revenue for the fourth quarter of 2021 was $11.6 million, compared to $4.5 million for the fourth quarter of 2020. Total revenue for the full year ended December 31, 2021 was $37.4 million, comprised of $30.9 million in net product revenue of TAZVERIK in the U.S. and $6.5 million in collaboration and other revenue.
- **Operating Expenses:** Total GAAP operating expenses were $62.9 million for the fourth quarter of 2021 and $275.4 million for the full year ended December 31, 2021, compared to $70.5 million for the fourth quarter of 2020 and $241.2 million for the full year ended December 31, 2020. Total non-GAAP adjusted operating expenses were $54.7 million for the fourth quarter of 2021 and $243.4 million for the full year ended December 31, 2021, compared to $62.8 million for the fourth quarter of 2020 and $209.6 million for the full year ended December 31, 2020.
    - **R&D expenses:** GAAP R&D expenses were $28.9 million for the fourth quarter of 2021 and $131.0 million for the full year ended December 31, 2021, compared to $33.7 million for the fourth quarter of 2020 and $110.9 million for the full year ended December 31, 2020. Non-GAAP adjusted R&D expenses were $26.6 million for the fourth quarter of 2021 and $122.0 million for the full year ended December 31, 2021, compared to $31.5 million for the fourth quarter of 2020 and $101.3 million for the full year ended December 31, 2020.
    - **SG&A expenses:** GAAP SG&A expenses were $30.9 million for the fourth quarter of 2021 and $134.0 million for the full year ended December 31, 2021, compared to $35.0 million for the fourth quarter of 2020 and $125.2 million for the full year ended December 31, 2020. Non-GAAP adjusted SG&A expenses were $25.9 million for the fourth quarter of 2021 and $115.1 million for the full year ended December 31, 2021, compared to $30.5 million for the fourth quarter of 2020 and $106.2 million for the full year ended December 31, 2020.
- **Net Loss (GAAP):** Net loss attributable to common stockholders was $50.7 million, or $0.49 per share, for the fourth quarter of 2021 and $251.1 million, or $2.45 per share, for the full year ended December 31, 2021, compared to $66.2 million, or $0.65 per share, for the fourth quarter of 2020 and $231.7 million, or $2.29 per share, for the full year ended December 31, 2020.

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, March 1, at 8:30 a.m. ET. To participate, please dial (877) 844-6886 (domestic) or (970) 315-0315 (international) and refer to conference ID 4082815. 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 and projected basis, non-GAAP adjusted cost of product revenue, 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. A quantitative reconciliation of projected total non-GAAP adjusted operating expenses to total GAAP 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 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 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.

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

	December 31, 2021	December 31, 2020
Consolidated Balance Sheet Data:		
Cash and cash equivalents	$ 98,336	$ 168,215
Marketable securities	78,454	205,391
Intangible, net	42,849	47,002
Total assets	289,000	473,573
Total current liabilities	45,196	43,400
Deferred revenue	11,950	-
Related party long-term debt, net of debt discount	216,461	215,670
Related party liability related to sale of future royalties, net of current	15,654	14,176
Total stockholders' equity (deficit)	(20,688)	184,897

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

	Three Months Ended December 31		Twelve Months Ended December 31	
	2021	2020	2021	2020
Revenues				
Product revenue, net	$ 11,558	$ 4,506	$ 30,922	$ 11,469
Collaboration and other revenue	24	3,869	6,505	4,293
Total revenue	11,582	8,375	37,427	15,762
Operating expenses				
Cost of revenue	3,154	1,823	10,498	5,067
Research and development	28,855	33,680	130,966	110,933
Selling, general and administrative	30,860	35,015	133,955	125,178
Total operating expenses	62,869	70,518	275,419	241,178
Operating loss	(51,287)	(62,143)	(237,992)	(225,416)
Other income, net:				
Interest (expense) income, net	(5,677)	(3,505)	(22,380)	(4,682)
Other expense, net	4	6	(66)	(99)
Change in fair value of Warrant liability	6,700	-	11,120	-
Related party non-cash interest expense related to sale of future royalties	(369)	(475)	(1,782)	(1,383)
Other (expense) income, net:	658	(3,974)	(13,108)	(6,164)
Loss before income taxes	(50,629)	(66,117)	(251,100)	(231,580)
Income provision	(22)	(116)	(22)	(114)
Net loss	$ (50,651)	$ (66,233)	$(251,122)	$(231,694)
Net loss per share attributable to common stockholders - basic and diluted	$ (0.49)	$ (0.65)	$ (2.45)	$ (2.29)
Weighted-average common shares outstanding used in net loss per share attributable to common stockholders - basic and diluted	104,196	101,596	102,646	100,960

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

	Three Months Ended December 31		Twelve Months Ended December 31	
Reconciliation of GAAP to Non-GAAP Cost of Revenue	**2021**	**2020**	**2021**	**2020**
GAAP Cost of Revenue	$ 3,154	$ 1,823	$ 10,498	$ 5,067
Less: Depreciation and Amortization	(1,038)	(1,038)	(4,154)	(2,998)
Non-GAAP Adjusted Cost of Revenue	$ 2,116	$ 785	$ 6,344	$ 2,069
Reconciliation of GAAP to Non-GAAP Research and Development				
GAAP Research and Development	$ 28,855	$ 33,680	$ 130,966	$ 110,933
Less: Stock-Based Compensation Expenses	(2,066)	(2,049)	(8,360)	(9,093)
Less: Depreciation and Amortization	(170)	(148)	(633)	(558)
Non-GAAP Adjusted Research and Development	$ 26,619	$ 31,483	$ 121,973	$ 101,282
Reconciliation of GAAP to Non-GAAP Selling, General and Administrative:				
GAAP Selling, General and Administrative	$ 30,860	$ 35,015	$ 133,955	$ 125,178
Less: Stock-Based Compensation Expenses	(4,818)	(4,372)	(18,427)	(18,515)
Less: Depreciation and Amortization	(122)	(124)	(459)	(428)
Non-GAAP Adjusted Selling, General and Administrative	$ 25,920	$ 30,519	$ 115,069	$ 106,235
Reconciliation of GAAP to Non-GAAP Operating Expenses				
GAAP Operating Expenses	$ 62,869	$ 70,518	$ 275,419	$ 241,178
Less: Stock-Based Compensation Expenses	(6,884)	(6,421)	(26,787)	(27,608)
Less: Depreciation and Amortization	(1,330)	(1,310)	(5,246)	(3,984)
Non-GAAP Adjusted Operating Expenses	$ 54,655	$ 62,787	$ 243,386	$ 209,586

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