Epizyme Provides Business Update and Reports First Quarter 2021 Financial Results

May 6, 2021

Total Revenue of $7.6 Million for 1Q 2021; TAZVERIK® Net Product Revenues of $6.2 Million

Ongoing TAZVERIK Clinical Trials in both Follicular Lymphoma and Prostate Cancer Demonstrate Encouraging Preliminary Safety and Activity Data

Investigational New Drug (IND) Submission for Novel SETD2 Inhibitor Program Planned for Mid-2021

Conference Call Today, Thursday, May 6 at 7:30 a.m. ET

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 6, 2021-- Epizyme (Nasdaq: EPZM), a fully integrated, commercial-stage biopharmaceutical company developing and delivering novel epigenetic therapies, today provided business and portfolio updates and reported first quarter 2021 financial results.

“Adoption of TAZVERIK has steadily increased as we continue to navigate the unique launch environment presented by COVID-19. We saw month-over-month commercial demand growth, with March 2021 representing our most successful month since launch and we look to build on this momentum as the pandemic-associated challenges begin to ease,” said Robert Bazemore, President and Chief Executive Officer of Epizyme. “TAZVERIK net revenues in the first quarter of 2021 increased by 37% from the fourth quarter of 2020, driven primarily by increased adoption in follicular lymphoma. The environment we operated in during the first quarter was not substantially different from the end of last year, however we are beginning to see some encouraging signs that things are slowly beginning to return to normal as vaccine adoption progresses.

“In early March, we hosted a strategic vision call to outline the pipeline-in-a-drug potential we see in TAZVERIK and plans to expand our portfolio starting with the anticipated IND submission for our novel SETD2 inhibitor in mid-2021. We plan to share additional pre-clinical data supporting the advancement of our SETD2 program at the European Hematology Association Congress 2021. During the Vision Call we also shared encouraging preliminary safety and activity data from ongoing combination trials in follicular lymphoma and prostate cancer and look forward to providing a steady stream of data updates from these and our many other planned and ongoing trials over the next few years.”

Recent Progress

- **Commercial Execution:** TAZVERIK generated net product revenue in **Epithelioid Sarcoma (ES)** and **Follicular Lymphoma (FL)** of $6.2 million in the first quarter of 2021, with March 2021 representing our highest level of commercial demand since launch. Commercial bottle demand growth was 31% in the first quarter compared to the fourth quarter of 2020, while total revenue grew by 37%. New prescribing accounts increased 38% in the first quarter of 2021 compared to the fourth quarter of 2020, including broader adoption among community practice. This is despite the continued negative impact COVID-19 had on patient visits to physicians and new patient starts across all lines of treatment as well as the ability of our field-based teams to fully access physicians treating ES and FL patients.
- **EZH-302 Phase 1b/3 Confirmatory Study of TAZVERIK in Follicular Lymphoma:** The combination of TAZVERIK with R^2 (Lenalidomide and Rituximab) is being evaluated in a Phase 1b/3 confirmatory study in relapsed / refractory FL patients. Preliminary safety and activity data of 13 patients from the 400 mg, 600 mg and 800 mg cohorts of the Phase 1b safety run-in were presented during Epizyme’s Vision Call in March showing encouraging initial treatment responses in each dose group, and adverse events that were in line with expectations based on the respective safety profiles of the individual agents. Epizyme plans to submit an update to this safety run-in for presentation at the 2021 ASH Annual Meeting later this year.

  Based on recent discussions with the U.S. Food and Drug Administration (FDA), Epizyme has aligned on an important change to the Phase 3 protocol whereby the second interim analysis will include an efficacy evaluation once 65% of progression free survival (PFS) events have occurred. This allows access to efficacy data earlier than previously expected and may provide an opportunity to stop the study early should the predefined treatment effect be realized. Based on these discussions with FDA, Epizyme has also expanded the Phase 1b portion of the study to include a minimum of 15 patients in the cohorts of 600 mg BID and 800 mg BID to help inform selection of the Phase 3 dose. Enrollment is nearly complete in these two cohorts and patients are being evaluated for follow-up of three months before initiating the Phase 3 randomization portion of the trial.

- **Additional Ongoing Clinical Trials of Tazemetostat in Follicular Lymphoma:** EZH-1401, the Company’s Phase 2 trial evaluating TAZVERIK plus Rituxan in relapsed / refractory FL continues to move forward as planned and is actively enrolling. Patient enrollment also continues in the Lymphoma Study Association (LYSA) trial in front-line FL and Diffuse Large B-cell Lymphoma (DLBCL), as well as other investigator sponsored trials.
- **EZH-1101 Phase 1b/2 Study of Tazemetostat in Prostate Cancer:** The combination of tazemetostat with standard-

of-care treatments, enzalutamide or abiraterone, was evaluated in the Phase 1b safety run-in portion of the EZH-1101 trial which enrolled a total of 21 men with metastatic prostate cancer. The Phase 1b protocol allowed patients to enroll who had previously failed enzalutamide, abiraterone, first generation anti-androgen receptor therapies or short course chemotherapy. In the study, patients received either abiraterone plus tazemetostat plus prednisone or enzalutamide plus tazemetostat. Based on encouraging preliminary safety and activity data, particularly in the enzalutamide plus tazemetostat group, Epizyme has initiated enrollment in the Phase 2 efficacy portion of this study which will evaluate enzalutamide plus tazemetostat compared to enzalutamide alone. Epizyme plans to submit an update to the Phase 1b safety run-in for presentation at a medical congress later this year.

- **EZH-301 Confirmatory Phase 1b/3 Study of TAZVERIK in Epithelioid Sarcoma:** The combination of TAZVERIK with doxorubicin compared with doxorubicin plus placebo is being evaluated in a Phase 1b/3 confirmatory study as a front-line treatment for ES patients. We have completed the planned enrollment in the Phase 1b safety run-in portion of the trial and the Phase 3 efficacy expansion portion of the trial remains on track for initiation. Preliminary data from the Phase 1b portion of this study has been accepted as a poster presentation at the 2021 ASCO Annual Meeting in June.
- **Tazemetostat Basket Trials in Additional Hematologic Malignancies and Solid Tumors:** Epizyme plans to initiate two signal finding basket studies to evaluate tazemetostat safety and efficacy across multiple new types of hematologic malignancies and solid tumors. With this approach, the Company plans to study multiple combinations with standard-of-care therapies and novel mechanisms of action to expand the potential of tazemetostat. Epizyme plans to initiate both basket studies in the second half of 2021.
- **Planned IND Submission for Epizyme's Novel SETD2 Inhibitor:** Based on the potential of SETD2 inhibition in multiple settings, including high risk t(4;14) multiple myeloma and in other B-cell malignancies such as large-cell lymphoma, as monotherapy and in combination with existing and emerging therapies including tazemetostat, Epizyme is planning to submit an Investigational New Drug (IND) application with the FDA in mid-2021 and expects to initiate a first-in-human clinical trial this year.

First Quarter 2021 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $298.9 million as of March 31, 2021, as compared to $373.6 million as of December 31, 2020.
- **Revenue:** Total revenue for the first quarter of 2021 was $7.6 million, compared to $1.4 million for the first quarter of 2020. Total revenue for the first quarter of 2021 comprised of $6.2 million in net sales of TAZVERIK in the U.S. and $1.4 million in collaboration and other revenue.
- **Operating Expenses:** Total GAAP operating expenses were $72.0 million for the first quarter of 2021 compared to $52.7 million for the first quarter of 2020. Total non-GAAP adjusted operating expenses were $63.7 million for the first quarter of 2021 compared to $45.7 million for the first quarter of 2020.
    - **Cost of revenue**: GAAP cost of revenue, which reflects the costs of TAZVERIK units sold, amortization of intangible assets, third-party royalties on net product revenue and costs of tazemetostat API and drug product sold to the Company's licensees or collaborators, was $2.9 million for the first quarter of 2021 compared to $0.6 million in the first quarter of 2020. Non-GAAP adjusted cost of revenue was $1.8 million for the first quarter of 2021 compared to $0.3 million for the first quarter of 2020.
    - **R&D expenses:** GAAP R&D expenses were $32.7 million for the first quarter of 2021 compared to $25.2 million for the first quarter of 2020. Non-GAAP adjusted R&D expenses were $30.3 million for the first quarter of 2021 compared to $22.9 million for the first quarter of 2020.
    - **SG&A expenses:** GAAP SG&A expenses were $36.4 million for the first quarter of 2021 compared to $27.0 million for the first quarter of 2020. Non-GAAP adjusted SG&A expenses were $31.5 million for the first quarter of 2021 compared to $22.5 million for the first quarter of 2020.
- **Net Loss (GAAP):** Net loss attributable to common stockholders was $70.3 million, or $0.69 per share, for the first quarter of 2021, compared to $50.9 million, or $0.51 per share, for the first quarter of 2020.

2021 Financial Guidance

- Based on its current operating plans, Epizyme expects its current cash runway to extend into 2023. Additionally, the Company expects its non-GAAP adjusted operating expenses for 2021 to be between $235 and $255 million.
- 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 6, at 7:30 a.m. ET. To participate in the conference call, please dial (877) 844-6886 (domestic) or (970) 315-0315 (international) and refer to conference ID 4139845. 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 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 non-GAAP adjusted operating expenses to total 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 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 and other serious diseases through novel epigenetic medicines. In addition to an active research and discovery pipeline, Epizyme has one U.S. FDA approved product, TAZVERIK® (tazemetostat), for the treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma (ES) who are not eligible for complete resection; adult patients with relapsed or refractory follicular lymphoma (FL) 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; and 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(s). The Company is also exploring the treatment potential of tazemetostat in investigational clinical trials in other solid tumors and hematological malignancies, as a monotherapy and combination therapy in both relapsed and front-line disease settings. By focusing on the genetic drivers of disease, Epizyme seeks to match medicines with the patients who need them. For more information, visit www.epizyme.com.

TAZVERIK® is a registered trademark of Epizyme, Inc.

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; 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; 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 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.

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EPIZYME, INC
CONSOLIDATED BALANCE SHEET DATA (UNAUDITED)

(Amounts in thousands)

	March 31, 2021	December 31, 2020
Consolidated Balance Sheet Data:		
Cash and cash equivalents	$ 73,711	$ 168,215
Marketable securities	225,232	205,391
Intangible assets, net	45,964	47,002
Total assets	406,711	473,573
Total current liabilities	39,006	43,400
Related party long-term debt, net of debt discount	215,858	215,670
Related party liability related to sale of future royalties	14,646	14,176
Total stockholders' equity	123,031	184,897

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

	Three Months Ended March 31	
	2021	2020
Revenues		
Product revenue, net	$ 6,191	$ 1,284
Collaboration and other revenue	1,440	70
Total revenue	7,631	1,354
Operating expenses		
Cost of revenue	2,853	614
Research and development	32,704	25,163
Selling, general and administrative	36,411	26,927
Total operating expenses	71,968	52,704
Operating loss	(64,337)	(51,350)
Other income, net:		
Interest (expense) income, net	(5,476)	756
Other expense, net	9	(48)
Related party non-cash interest expense related to sale of future royalties	(470)	(295)
Other (expense) income, net:	(5,937)	413
Loss before income taxes	(70,274)	(50,937)
Income provision	-	-
Net loss	$ (70,274)	$ (50,937)
Net loss per share attributable to common stockholders - basic and diluted	$ (0.69)	$ (0.51)
Weighted-average common shares outstanding used in net loss per share attributable to common stockholders - basic and diluted	101,790	99,616

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	2021	2020
GAAP Cost of Revenue	$ 2,853	$ 614
Less: Depreciation and Amortization	(1,038)	(298)
Non-GAAP Adjusted Cost of Revenue	$ 1,815	$ 316

Reconciliation of GAAP to Non-GAAP Research and Development		
GAAP Research and Development	$ 32,704	$ 25,163
Less: Stock-Based Compensation Expenses	(2,230)	(2,162)
Less: Depreciation and Amortization	(143)	(138)
Non-GAAP Adjusted Research and Development	$ 30,331	$ 22,863
Reconciliation of GAAP to Non-GAAP Selling, General and Administrative:		
GAAP Selling, General and Administrative	$ 36,411	$ 26,927
Less: Stock-Based Compensation Expenses	(4,785)	(4,348)
Less: Depreciation and Amortization	(101)	(76)
Non-GAAP Adjusted Selling, General and Administrative	$ 31,525	$ 22,503
Reconciliation of GAAP to Non-GAAP Operating Expenses		
GAAP Operating Expenses	$ 71,968	$ 52,704
Less: Stock-Based Compensation Expenses	(7,015)	(6,510)
Less: Depreciation and Amortization	(1,282)	(512)
Non-GAAP Adjusted Operating Expenses	$ 63,671	$ 45,682

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