Epizyme Announces Positive Pre-NDA Meeting for Tazemetostat for Follicular Lymphoma, Pipeline Updates and Third Quarter 2019 Results

October 30, 2019

Pre-NDA Meeting Supports Registration Strategy for Tazemetostat for Follicular Lymphoma Patients with and without EZH2 Activating Mutations and Planned NDA Submission in December 2019

Updated Phase 2 Follicular Lymphoma Data Selected for Oral Presentation at ASH

Finalized U.S. Launch Readiness for Epithelioid Sarcoma with January 23, 2020 PDUFA Date

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 30, 2019-- Epizyme, Inc. (Nasdaq: EPZM), a late-stage biopharmaceutical company developing novel epigenetic therapies, today announced recent tazemetostat program updates, including successfully completing a pre-NDA meeting with the U.S. Food and Drug Administration (FDA) for its tazemetostat program for follicular lymphoma (FL), G9a program updates and third quarter 2019 financial results.

"We are very pleased with the outcome of our recent pre-NDA meeting and the continued alignment with FDA on our registration strategy for FL patients, regardless of their EZH2 status, who have received at least two prior systemic therapies," said Dr. Shefali Agarwal, chief medical officer of Epizyme. "FL remains an incurable disease, and we believe strongly in the potential of tazemetostat to make a difference for these patients. We are on track to submit our FL NDA for accelerated approval in December and look forward to continuing to engage with FDA as we work to bring tazemetostat to both FL and epithelioid sarcoma patients in the U.S. next year."

Tazemetostat Program Updates

- **Pre-NDA Meeting Supports Planned NDA Submission for FL:** During a recent pre-NDA meeting, Epizyme gained alignment with the FDA that the proposed data package is sufficient to support a submission for accelerated approval of tazemetostat as a monotherapy for relapsed or refractory FL patients, both with EZH2 activating mutations and wild-type EZH2, who have received at least two prior systemic therapies. Epizyme is on track to submit the NDA for this indication in December 2019.

- **Mature Phase 2 Data to be Reported in Oral Presentation at ASH:** Epizyme's abstract on data from its ongoing Phase 2 trial in FL as of a June 7, 2019 data cutoff has been selected for an oral presentation on Saturday, Dec. 7 at the 2019 American Society of Hematology (ASH) Annual Meeting. Updated data, as assessed by both investigators and independent reviewers from a later data cutoff than the abstract submission, will be presented and will serve as the basis for the planned FL NDA submission.

- **Gained Alignment with FDA on Single Confirmatory Trial for FL:** Epizyme gained alignment with FDA on a single confirmatory trial to support a submission for full approval. This global, randomized, adaptive trial will evaluate the combination of tazemetostat with "R^2" (Revlimid® plus Rituxan®), an approved chemo-free treatment regimen, for FL patients in the second-line or later treatment setting. The trial is expected to enroll approximately 500 FL patients, stratified based on their EZH2 mutation status. Site initiation is underway and the safety run-in portion of the trial is on track to begin in the fourth quarter of 2019.

- **Preparing for Epithelioid Sarcoma (ES) U.S. Commercial Launch with Jan. 23, 2020 PDUFA Date:** Priority Review was granted by FDA for Epizyme's NDA for accelerated approval of tazemetostat for patients with metastatic or locally advanced ES who are not eligible for curative surgery. To support a potential early 2020 approval and launch, the company's go-to-market strategy has been finalized. An experienced commercial and medical affairs team is now in place to expand the knowledge and awareness of ES among the treating and patient communities and ensure seamless patient access to tazemetostat, if approved.

- **ES Confirmatory Trial Ready to Begin in Fourth Quarter:** Epizyme has begun initiating sites for its confirmatory trial to support a submission for full approval of tazemetostat for ES. This global, randomized, controlled trial will assess the

combination of tazemetostat plus doxorubicin, a commonly used systemic treatment, compared with doxorubicin alone as a front-line treatment. The trial is expected to enroll approximately 150 patients, with the safety run-in portion to begin in the fourth quarter of 2019.

- **Combination Trial Open for Castration-Resistant Prostate Cancer (CRPC):** Epizyme is conducting a Phase 1b/2 clinical trial in chemo-naïve patients with metastatic CRPC, assessing tazemetostat with enzalutamide or with abiraterone, the standard-of-care treatments for this patient population. Epizyme recently presented preclinical data at the AACR-NCI-EORTC International Conference on Molecular Targets, which demonstrated that tazemetostat in combination with an androgen signaling inhibitor (ASI) increased tumor growth inhibition more than either agent alone. Site initiation is underway and the dose-escalation Phase 1b portion of the trial is on track to begin in the fourth quarter of 2019.

G9a Program Update

- Epizyme has decided to refocus its preclinical program targeting G9a on other potential development candidates and discontinue development of EZM-8266. This decision was made after a review of development path implications of a preclinical toxicology finding of EZM-8266. The company is evaluating next steps for its G9a program to develop an oral, disease-modifying approach to treating a variety of hemoglobinopathies, including sickle cell disease.

Leadership Team Expansion

- Epizyme further strengthened its management team with the appointment of Mark De Rosch, Ph.D., to chief regulatory officer. Dr. De Rosch joined Epizyme from Nightstar Therapeutics, where he served as senior vice president, regulatory affairs and quality assurance, and brings more than 25 years of global regulatory strategy and operations experience, including having successfully led the regulatory strategy and marketing approval of Kalydeco™, the first disease-modifying treatment for people with cystic fibrosis when at Vertex Pharmaceuticals. Dr. De Rosch earned a B.S. in chemistry/biochemistry from the University of Wisconsin, and an M.S. and Ph.D. in inorganic chemistry from the University of California, San Diego.

“Over the course of 2019, we’ve made significant progress building out critical functions, advancing and expanding tazemetostat development, and continuing our evolution toward becoming a commercial company,” said Robert Bazemore, president and chief executive officer of Epizyme. “I am proud of what we have achieved thus far, with much more to come in the next several months. We have multiple trials to initiate, a second NDA to submit and a first U.S. commercial launch to execute, if approved. We are thrilled to be on the cusp of delivering tazemetostat to patients and look forward to continued progress.”

Third Quarter 2019 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities were $292.9 million as of Sept. 30, 2019.
- **Revenue:** Collaboration revenue for the third quarter of 2019 was $5.7 million, compared to no revenue for the third quarter of 2018. This collaboration revenue was earned as part of the Company’s Boehringer Ingelheim collaboration, which includes a $1.25 million quarterly installment in connection with the Company’s research activities.
- **R&D Expenses:** Research and development (R&D) expenses were $26.6 million for the third quarter of 2019, compared to $27.0 million for the third quarter of 2018. The decrease primarily relates to decreases in clinical trial expenses and tazemetostat manufacturing costs, offset by an increase in discovery research activities related to tazemetostat in other indications.
- **G&A Expenses:** General and administrative (G&A) expenses were $17.1 million for the third quarter of 2019, compared to $11.5 million for the third quarter of 2018. The increase is due primarily to pre-commercialization activities and staffing, as well as increased personnel related expenses.
- **Net Loss Attributed to Common Stockholders**: Net loss attributable to common stockholders was $36.1 million, or $0.40 per share, for the third quarter of 2019, compared to $37.5 million, or $0.54 per share, for the third quarter of 2018.

Financial Guidance
Based on its current operating plan, Epizyme continues to expect its cash runway to extend into the first quarter of 2021.

About Epizyme, Inc.
Epizyme, Inc. is a late-stage biopharmaceutical company committed to rewriting treatment for cancer and other serious diseases through novel epigenetic medicines. Epizyme is broadly developing its lead product candidate, tazemetostat, an oral, first-in-class EZH2 inhibitor, with studies underway in both solid tumors and hematological malignancies, as a monotherapy and combination therapy in relapsed and front-line disease. The company is also exploring additional molecules in its novel G9a inhibitor program. By focusing on the genetic drivers of disease, Epizyme's science seeks to match targeted medicines with the patients who need them. 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: uncertainties inherent in the initiation of future clinical studies and in the availability and timing of data from ongoing clinical studies; whether interim results from a

clinical trial will be predictive of the final results of the trial; whether results from preclinical studies or earlier clinical studies will be predictive of the results of future 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; expectations for regulatory approvals, including accelerated approval, to conduct trials or to market products; 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 potential of the company's therapeutic candidates; and other factors discussed in the "Risk Factors" section of the company's most recent 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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CONDENSED CONSOLIDATED BALANCE SHEET DATA (UNAUDITED)

(Amounts in thousands)

	September 30, 2019	December 31, 2018
Consolidated Balance Sheet Data:		
Cash, cash equivalents, and marketable securities	$ 292,861	$ 240,304
Total assets	334,197	275,501
Current portion of deferred revenue	1,794	13,300
Deferred revenue, net of current portion	3,806	3,806
Total stockholders’ equity	293,738	233,009

CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS (UNAUDITED)
(Amounts in thousands except per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	**2018**	**2019**	**2018**
Collaboration revenue	$ 5,715	$ —	$ 19,506	$ 12,000
Operating expenses:				
Research and development	26,579	27,027	94,382	83,994
General and administrative	17,089	11,528	44,773	31,801
Total operating expenses	43,668	38,555	139,155	115,795
Operating loss	(37,953)	(38,555)	(119,649)	(103,795)
Other income, net:				
Interest income, net	1,879	1,069	5,790	3,121

Other (expense), net	(15)	(6)	(34)	(11)
Other income, net	1,864	1,063	5,756	3,110
Net loss	$ (36,089)	$ (37,492)	$ (113,893)	$ (100,685)
Other comprehensive income (loss):				
Unrealized (loss) gain on available-for-sale securities	(99)	3	203	26
Comprehensive loss	$ (36,188)	$ (37,489)	$ (113,690)	$ (100,659)

Reconciliation of net loss to net loss attributable to common stockholders:

Net loss	$ (36,089)	$ (37,492)	$ (113,893)	$ (100,685)
Accretion of convertible preferred stock	—	—	(2,940)	—
Net loss attributable to common stockholders	$ (36,089)	$ (37,492)	$ (116,833)	$ (100,685)
Net loss per share attributable to common stockholders - basic and diluted	$ (0.40)	$ (0.54)	$ (1.33)	$ (1.45)
Weighted-average common shares outstanding used in net loss per share attributable to common stockholders - basic and diluted	91,044	69,539	88,145	69,472

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