Epizyme®

Rewriting Treatments for People with Cancer and Other Serious Diseases

August 9, 2021

Nasdaq: EPZM

FORWARD-LOOKING STATEMENTS

Any statements in this presentation 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 the refinement of the company's commercial strategy and cost reductions will achieve the company's objectives; 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 presentation 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.

EPIZYME

A FULLY INTEGRATED COMMERCIAL ENTERPRISE

TAZVERIK™ (tazemetostat) tablets

APPROVED FOR 2 INDICATIONS

JAN 2020
Accelerated approval granted in epithelioid sarcoma (ES)

JUNE 2020
Accelerated approval granted in follicular lymphoma (FL)

MULTI-BILLION DOLLAR

GLOBAL MARKET OPPORTUNITY

CONFIRMATORY TRIALS REMAIN ON TRACK

ENCOURAGING INITIAL SAFETY RUN-IN RESULTS

HIGH-VALUE RESEARCH PIPELINE

ADVANCING TOWARD CLINIC

IND CLEARANCE FOR NOVEL SETD2 INHIBITOR

FIRST-IN-HUMAN TRIAL EXPECTED TO INITIATE THIS YEAR

TAZVERIK™
(tazemetostat) tablets

- NOVEL MECHANISM OF ACTION
- ACTIVITY DEMONSTRATED IN MULTIPLE CANCERS
- GENERALY WELL-TOLERATED; LOW DISCONTINUATION RATES
- POTENTIAL FOR EXTENDED TREATMENT DURATION
- BROAD THERAPEUTIC POTENTIAL IN SOLID TUMORS AND HEME MALIGNANCIES
- COMBINATION OPPORTUNITIES WITH SOC TREATMENTS

CONTINUED PROGRESS ACROSS BUSINESS UNITS IN 2Q

TAZVERIK (tazemetostat) tablets
HUTCHMED

LAUNCHED EZH2 NOW TESTING PROGRAM WITH QUEST DIAGNOSTICS

COMMERCIAL AND DEVELOPMENT COLLABORATION WITH HUTCHMED IN CHINA

IND CLEARANCE FOR EPIZYME'S NOVEL SETD2 INHIBITOR, EZM-0414

CLINICAL AND PRECLINICAL DATA PRESENTED AT EHA AND ASCO

EZH-1101 PHASE 1B/2 STUDY IN PROSTATE CANCER NOW OVER 1/3 ENROLLED

REVISED COMMERCIAL STRATEGY AND OPERATING PLAN

STRATEGIC COLLABORATION WITH HUTCHMED FOR TAZVERIK®

Overview of Collaboration

Product: TAZVERIK® (tazemetostat)

Exclusive/co-exclusive License:

- Research & Development
- Manufacturing & Commercialization
- Territory: Greater China

R&D Synergies: investigate combos with HUTCHMED's novel oncology medicines portfolio

China Commercial: initially develop & seek approval in various hematological and solid tumors:

- Epithelioid sarcoma (ES)
- Follicular lymphoma (FL)
- Diffuse large b-cell lymphoma (DLBCL)

Ex-China impact: accelerate global development (HUTCHMED will contribute to global study/studies)

Key Financial Terms

Upfront: US$25 million

Development & Regulatory Milestones: up to $110 million, across up to 8 potential indications

Sales Milestones: up to $175 million

Royalties: Tiered royalties of mid-teen to low-twenties % based on annual sales in Greater China

Warrant Rights:

- HUTCHMED has option to acquire Epizyme shares
- Term: 4 years
- Amount: up to $65 million
- Exercise Price: $11.50/share

COMBINATION POTENTIAL FOR TAZVERIK® WITH HUTCHMED'S ASSETS

TAZVERIK (tazemetostat) tablets
HUTCHMED

	NEAR TERM		LONGER TERM	
SOLID TUMORS	**+ FRUQUINTINIB (VEGFRi)** *(China approved for CRC; Global Ph III ongoing)*	Lung	**+ HMPL-295 (ERKi)** *(China Ph I ongoing)*	K-Ras mutant tumors
		Ovarian		
	+ SURUFATINIB (VEGFRi/FGFRi/CSF1Ri) *(China approved for NET; U.S. NDA & EMA MAA submitted)*	Tumors w/ neuroendocrine differentiation (NED), *e.g. NEPC*	**+ IMMUNOTHERAPIES, e.g. HMPL-A83 (CD47)** *(IND-enabling stage)*	Macrophage-targeting such as breast cancer
		Sarcoma *(suru. in U.S. Ph Ib)*		
HEMATOLOGICAL MALIGNANCIES	**+ HMPL-689 (PI3Kδi)** *(China reg. Ph II initiated; U.S./E.U. Ph II ongoing)*	DLBCL	**+ HMPL-760 (BTKi)**	NHL
		TCL	**+ HMPL-A83 (CD47)**	
			+ Bi-specific Abs	1L NHL

2021 HIGHLIGHTS & EXPECTED MILESTONES

TAZVERIK™ (tazemetostat) tablets
HUTCHMED

- Implement revised commercial strategy and continue to expand adoption of TAZVERIK® (tazemetostat) in FL and ES
- EZM-0414 IND clearance received; clinical trial initiation expected 2H 2021
- Follow-up data from Phase 1b safety run-ins for EZH-302 in FL and EZH-1101 in mCRPC 2H 2021
- Anticipate advancing to the efficacy stages of our ES, FL and prostate cancer clinical programs
- Planned initiation of novel basket trials in both heme and solid tumors in 2H 2021
- Anticipated alignment with EMA on registration path for TAZVERIK in Europe

2Q 2021 FINANCIAL RESULTS

STATEMENT OF OPERATIONS	THREE MONTHS ENDED JUNE 30	
	2021	**2020**
Total Revenue	**$13.0M**	**$2.5M**
TAZVERIK Net Sales	$8.0M	$2.2M
Collaboration Revenue	$5.0M	$0.2M
Total Operating Expenses	**$71.2M**	**$60.0M**
Research and Development	$34.9M	$26.3M
Selling, General and Administrative	$33.9M	$32.7M
Net Loss Attributable to Common Stockholders	**$64.4M** ($0.63 per share)	**$58.4M** ($0.58 per share)

BALANCE SHEET AND 2021 FINANCIAL GUIDANCE

BALANCE SHEET	JUNE 30, 2021	DECEMBER 31, 2020
Cash, Cash Equivalents, and Marketable Securities	$244.0M	$373.6M

Full year 2021 non-GAAP adjusted cash expenses anticipated to be between $220 – $230M

Cash runway expected to be sufficient to fund operations into 4Q 2022

EPIZYME OVER THE NEXT 5 YEARS

THE NEXT EPIsode
REWRITING ONCOLOGY TREATMENT WITH EPIGENETICS

MAXIMIZE COMMERCIAL EFFECTIVENESS	TAZVERIK adopted as backbone therapy for FL TAZVERIK utilized in multiple combination regimens
BUILD ON TAVZERIK'S PIPELINE-IN-A-DRUG POTENTIAL	TAZVERIK approved in additional heme and solid tumor indications Robust flow of data read-outs
EXPAND PIPELINE & PORTFOLIO TO OVERCOME UNDRUGGABLE TARGETS	Progress three new programs into the clinic starting with novel SETD2 inhibitor, EZM-0414 Robust flow of data read-outs
COLLABORATE TO EXPAND PATIENT REACH & BUILD VALUE	TAZVERIK partnered to reach ex-US markets Multiple clinical and scientific collaborations

TAZVERIK™ (tazemetostat) tablets

SAFETY INFORMATION

MOST COMMON ADVERSE REACTION (≥20%, ANY GRADE)

- ES: Pain, fatigue, nausea, decreased appetite, vomiting and constipation
- FL: Fatigue, upper respiratory infection, musculoskeletal pain, nausea and abdominal pain

WARNINGS & PRECAUTIONS

- Secondary malignancies: Across clinical trials of 729 adults who received TAZVERIK 800 mg twice daily, myelodysplastic syndrome or acute myeloid leukemia occurred in 0.7% of patients. One pediatric patient developed T-cell lymphoblastic lymphoma.
- Embryo-fetal toxicity

DRUG INTERACTION

- Strong and Moderate Cytochrome P450 (CYP)3A Inhibitors: Avoid coadministration of strong and moderate CYP3A inhibitors with TAZVERIK. Reduce the dose of TAZVERIK if coadministration of moderate CYP3A inhibitors cannot be avoided
- Strong and Moderate CYP3A Inducers: Avoid coadministration with TAZVERIK