Epizyme®

Developing and delivering transformative therapies for people living with cancer

May 2022

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 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 presentation 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 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-stage biopharmaceutical company dedicated to developing and delivering transformative therapies for cancer patients against novel epigenetic targets.

TAZVERIK Presents a Billion Dollar Plus Global Oncology Market Opportunity

TAZVERIK Label Expansion Trials are On Track. Encouraging SYMPHONY-1 Initial Safety Run-In Results

SET-101: Phase 1A Trial of EZM0414, A Novel SETD2 Inhibitor, Open and Actively Screening for Enrollment

High Value Research Pipeline Advancing Towards Clinic

Our Vision to Fuel Long-term Growth

1. MAXIMIZE COMMERCIAL EFFECTIVENESS
2. BUILD ON TAZVERIK'S PIPELINE-IN-A-DRUG POTENTIAL
3. EXPAND PIPELINE & PORTFOLIO TO OVERCOME UNDRUGGABLE TARGETS
4. COLLABORATE TO EXPAND PATIENT REACH & BUILD VALUE

TAZVERIK®
Commercial Progress

TAZVERIK®
(tazemetostat) tablets
200 mg

FIRST-IN-CLASS EZH2 INHIBITOR APPROVED FOR 2 INDICATIONS

JANUARY 2020

Accelerated approval granted in **epithelioid sarcoma (ES)**

JUNE 2020

Accelerated approval granted in **R/R follicular lymphoma (FL)**

- **BROAD THERAPEUTIC POTENTIAL IN SOLID TUMORS AND HEME MALIGNANCIES**
- **NOVEL MECHANISM OF ACTION, ORAL ADMINISTRATION**
- **ACTIVITY DEMONSTRATED IN MULTIPLE CANCERS**
- **GENERALLY SAFE AND WELL-TOLERATED; LOW DISCONTINUATION RATES**
- **POTENTIAL FOR EXTENDED TREATMENT DURATION**
- **COMBINATION OPPORTUNITIES WITH SOC AND NOVEL TREATMENTS BEING EVALUATED**

Epizyme®

Full prescribing information is available at www.TAZVERIK.com.
Not for promotional use.
R/R, relapsed/refractory; SOC, standards of care.

Commercial Strategies to Accelerate TAZVERIK Growth

TAZVERIK® (tazemetostat) tablets 200 mg

Simplified message

Define appropriate TAZVERIK patient

Increase understanding of wild-type dataset

Capitalize on changing market dynamics

Revised Commercial Strategy and Execution Are Leading to Improvements in TAZVERIK Awareness and Adoption Among Surveyed Physicians* Who Treat R/R FL Patients

TAZVERIK (tazemetostat) tablets 200 mg

Highest Unaided Awareness

Unaided awareness for TAZVERIK among treating physicians remains the **highest of any approved treatment for 3L+ FL**

Increased Prescribing

In 3L, current prescribing has **increased from 14% (Q4) to 18% (Q1)**

Increased Intent To Prescribe

Treating physicians indicate they **plan to prescribe TAZVERIK to ~23% of their 3L** patients

Increase in WT Use

Physicians report **increases in both current (12%) and projected future (18%) use in 3L FL**

Patient Satisfaction

~90% of physicians surveyed believe their patients are somewhat to extremely satisfied with TAZVERIK

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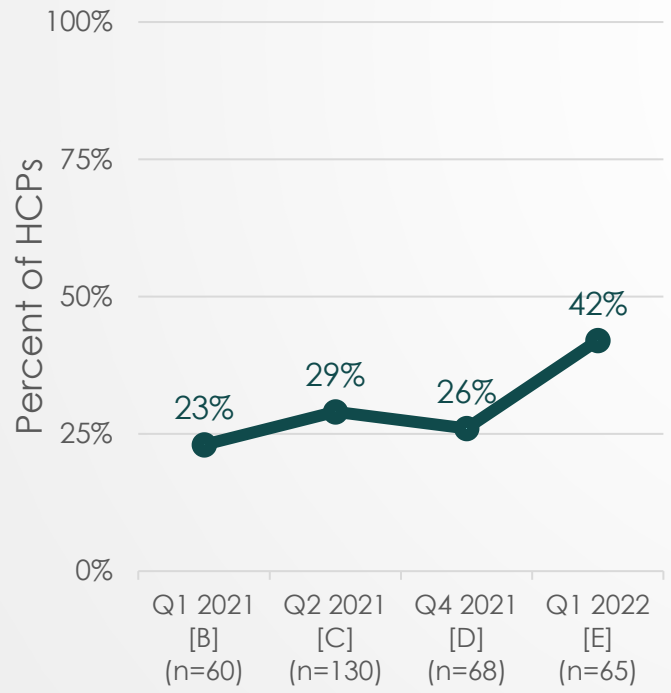
R/R, relapsed/refractory; FL, follicular lymphoma; WT, wild type; 3L, third line.
*Source: Based on Company-sponsored research of treating physicians: Wave 6 ATU, fielded Q1 2022. Share data is HCP reported.

Increase in Surveyed Physicians Who Perceive Third-Line, Wild-Type And Untested Patients As Appropriate For TAZVERIK

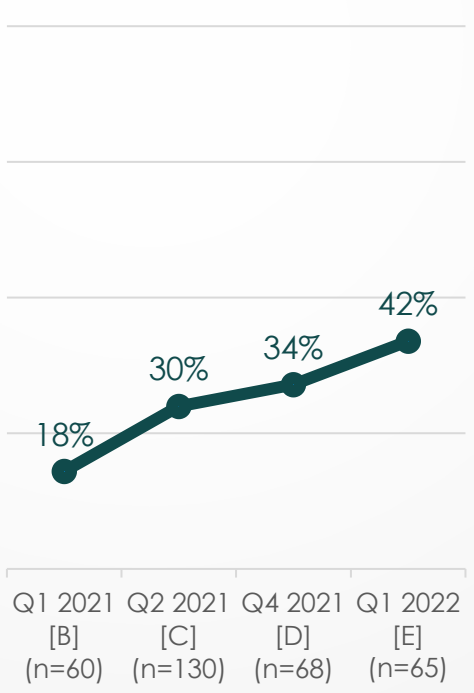
TAZVERIK (tazemetostat) tablets 200 mg

Percent of HCP Respondents Who Consider Respective Types of Patients Appropriate for TAZVERIK

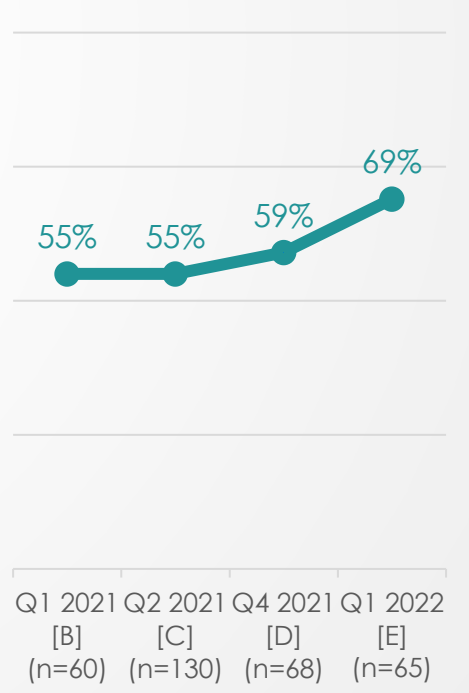
Third-line patients who are **EZH2 wild type**



Third-line patients with **untested EZH2** mutation status



Patients with **no satisfactory alternative treatment** (regardless of line of therapy)



Source: Based on Company-sponsored research: Wave 6 ATU, fielded Q1 2022.

Updated NCCN Guidelines® For B Cell Lymphomas

Supports Use Of TAZVERIK® (tazemetostat) as a Suggested Treatment Regimen

	2021 FL Guidelines (2A)	2022 FL Guidelines (2A)
2nd Line R/R FL	Not Included	Therapy for elderly or infirm EZH2 wild type or unknown R/R disease in patients who have no satisfactory alternative treatment options
3rd Line R/R FL	EZH2 mutation positive R/R disease after 2 prior therapies EZH2 wild type or unknown R/R disease in patients who have no satisfactory alternative treatment options	EZH2 mutation positive EZH2 wild type or unknown R/R disease in patients who have no satisfactory alternative treatment options

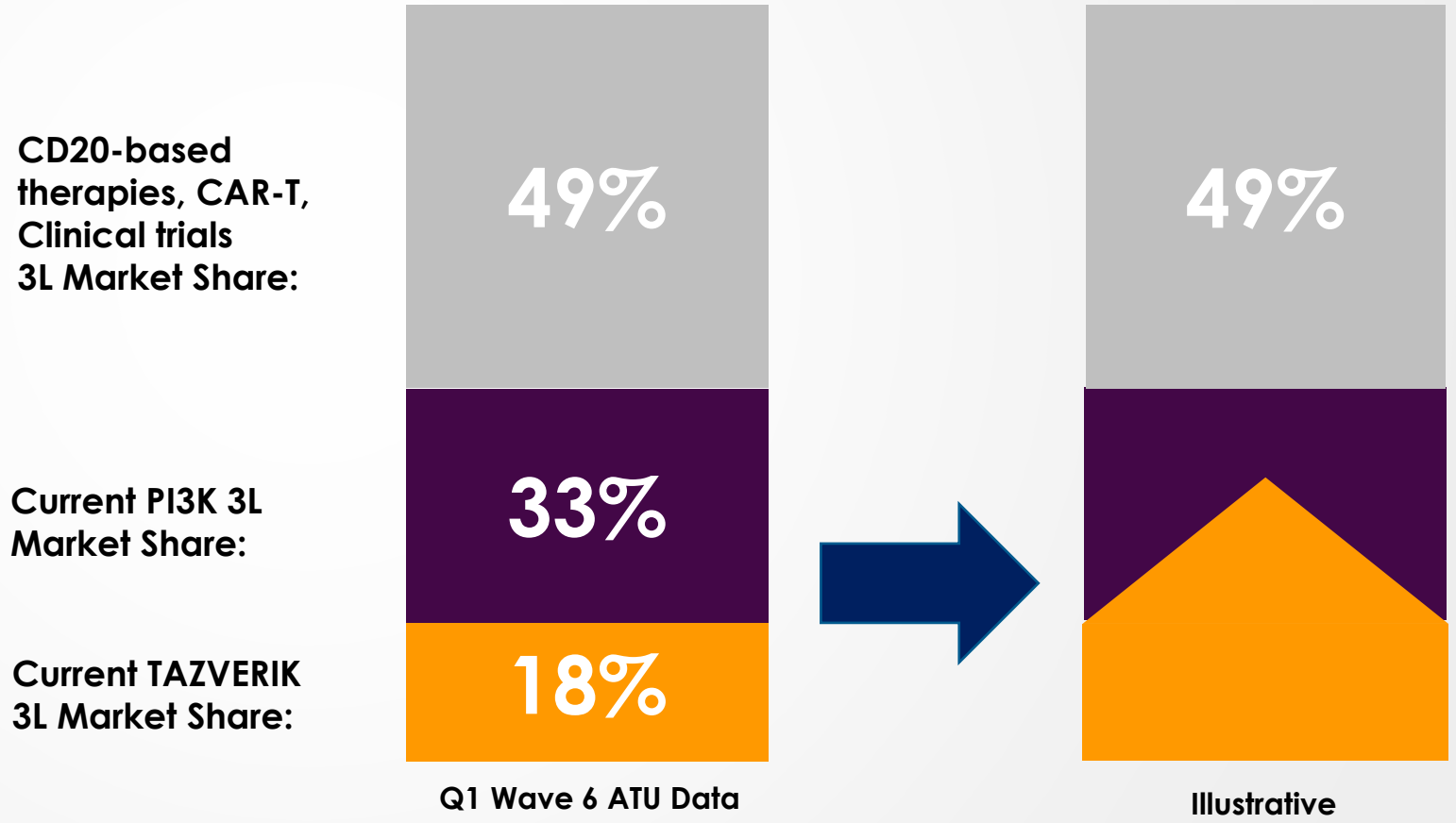
R/R, relapsed/refractory; FL, follicular lymphoma.
Source: NCCN v2.2022.

Recent Changes in Third-Line, Relapsed/Refractory FL Marketplace

3L R/R FL Marketplace

- PI3K class accounts for ~1/3 of the 3rd line market share*
- R/R FL treatment landscape shifting following withdrawal of 3 PI3Ks from FL indications^
- At April 21st ODAC meeting, panelists and FDA assessed risk-benefit profile of PI3K inhibitors in FL**
- TAZVERIK is now the only oral monotherapy approved in the 3L+ FL setting
- Presents a potential opportunity for TAZVERIK to Gain 3L Market Share

Market Share of Current 3L Therapies & Opportunities for TAZVERIK*



FL, follicular lymphoma; 3L, third line; PI3K, Phosphoinositide 3-kinases.
*Source: Based on Company-sponsored research: Wave 6 ATU, fielded Q1 2022.
^In December 2021, SecuraBio, Inc. announced it was withdrawing Copiktra's FL indication. This was followed by Gilead Sciences, Inc.'s announcement in January 2022 to withdraw Zydelig's FL indication and TG Therapeutics Inc.'s announcement in April to stop selling Ukoniq.
**April 21,2022 Meeting of the Oncologic Drugs Advisory Committee Meeting on PI3K Inhibitors in Hematologic Malignancies.

Tazemetostat Development Plans

Epizyme Development Plan for Tazemetostat in Heme Malignancies

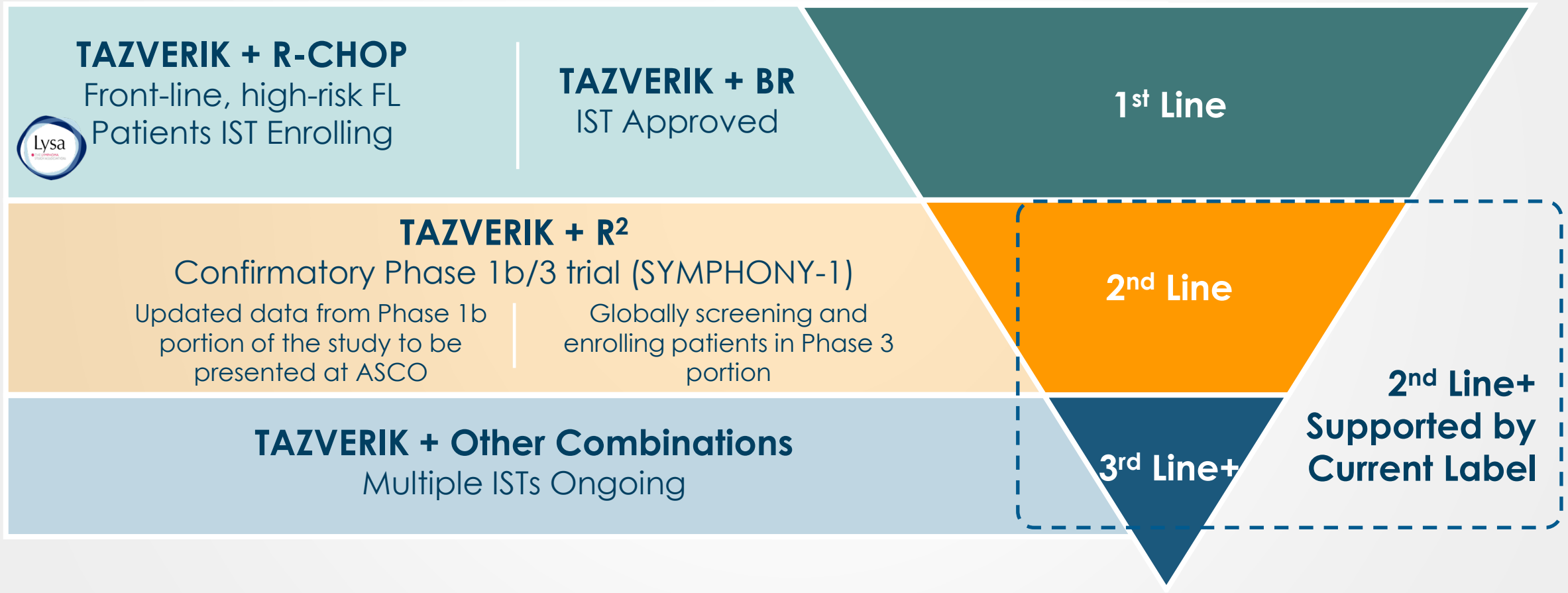
Indication	Study / Combo Drug (s)	Study Details	Planned Study Enrollment	Study Status
Follicular Lymphoma	**SYMPHONY-1** (EZH-302): R[2]	Second-Line+ FL; Phase 1b/3 Confirmatory Combination Trial	• Ph 1b, N = 40 • Ph 3, N = 500	• Updated Ph1b at ASCO • First patient dosed in global Ph3 portion • Enrollment open and actively screening globally
	LYSA[‡]: R-CHOP	High-Risk Front-Line FL	• N = 62	• Enrollment nearly complete • Top-line data anticipated 2H 2022
	Bendamustine + Rituximab	Front-Line FL	--	• Investigator Initiated Studies Ongoing
	Other ISTs Ongoing	Third-Line+		
DLBCL	**LYSA[‡]:** R-CHOP	High-Risk Front-Line DLBCL	• N = 122	• Enrollment nearly complete • Top-line data anticipated 2H 2022
Heme Basket: DLBCL, FL, MCL, MM	**ARIA** (EZH-1501) **Heme Basket Study**	**Len + CD19; R/R DLBCL***	• Ph 1b (per cohort), N = 2-9 • Ph 2 (per cohort), N = ~20	**Open for enrollment** *Stage-gated*
		Lenalidomide; R/R DLBCL*		
		Mosunetuzumab; R/R FL*		
		BTK Inhibitor; R/R MCL		
		Dara+Pom+Dex; R/R MM		

Note: highlighted studies are Epizyme's prioritized studies

[‡]LYSA Cooperative Group Phase 2 FL/DBCL study is an investigator sponsored trial (IST).
R2, Revlimid + rituximab is a registered trademark of Celgene Corporation, a Bristol Myers Squibb company. FL, follicular lymphoma; DLBCL, diffuse large B-cell lymphoma, MCL, mantle cell lymphoma, Dara+Pom+Dex, daratumumab plus pomalidomide and dexamethasone. MM, multiple myeloma.
^ : Roche clinical supply agreement for Mosunetuzumab (CD20xCD3).

Developing TAZVERIK® to Become the Backbone of Therapy for Patients with Follicular Lymphoma

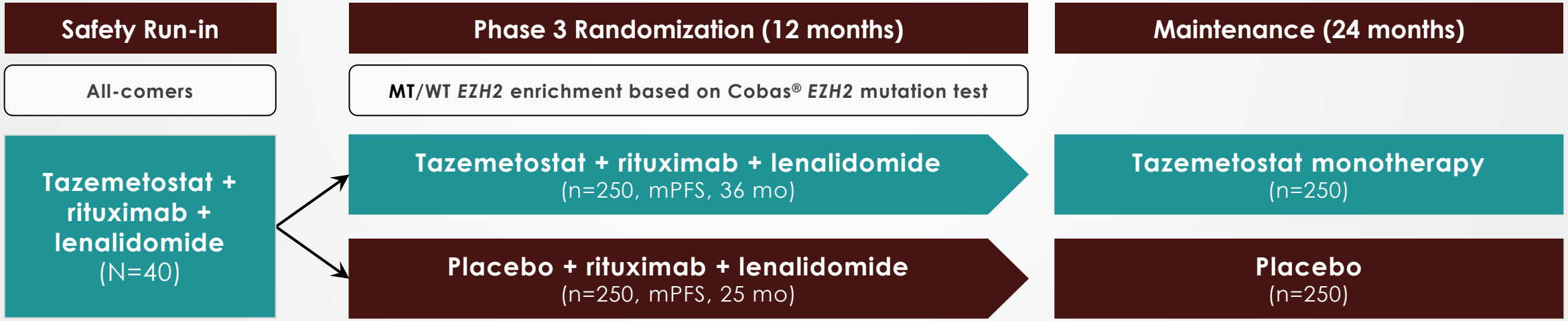
2022 Follicular Lymphoma Epidemiology
~13,700 Patients Diagnosed Annually in the U.S.*



*Decision Resources Group, NHL and CLL Disease Landscape and Forecast Report, April 2022.
R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone; BR, bendamustine and rituximab; R², Revlimid and rituximab, R2, Revlimid + rituximab is a registered trademark of Celgene Corporation, a Bristol Myers Squibb company. IST, investigator sponsored trial.

SYMPHONY-1: Phase 1b/3 Tazemetostat in Combination With R^2 in Patients With R/R FL

Population	Patients with relapsed / refractory FL who have been treated with at least 1 prior systemic therapy, including patients who are rituximab-refractory and/or POD24
Key Objectives	**Phase 1b (safety run-in)** Safety, pharmacokinetics, antitumor activity, RP3D **Phase 3 (efficacy)** Primary: PFS as determined by investigator; interim analyses for futility Secondary: PFS by IRC, response rate, duration of response, OS, QOL, safety



Stratification for randomized portion by EZH2 mutation status: treatment-sensitive vs refractory to prior rituximab-containing regimen, patients treated with 1 prior vs ≥2 prior systemic therapies

FL, follicular lymphoma; IRC, independent radiology committee; RP3D, recommended Phase 3 dose; mPFS, median progression-free survival; MT, mutation; OS, overall survival; PFS, progression-free survival; QOL, quality of life; R^2, rituximab + lenalidomide; R2, Revlimid + rituximab is a registered trademark of Celgene Corporation, a Bristol Myers Squibb company. R/R, relapsed or refractory; WT, wild-type.

Data on file. Cambridge, MA: Epizyme, Inc., 2021. https://clinicaltrials.gov/ct2/show/NCT04224493.

SYMPHONY-1 Interim Analysis: Safety Run-in Patient Background

Characteristic	Tazemetostat + R^2 (n=40)
Median age in years (range)	67 (39–83)
Male, n (%)	24 (60.0)
Age ≥ 65 years, n (%)	24 (60.0)
ECOG PS, n (%)	
0	28 (70.0)
1	12 (30.0)
Prior lines of systemic anticancer therapy, n (%)	
1	19 (47.5)
2	13 (32.5)
≥3	8 (20.0)
Median prior lines of systemic anticancer therapy (range)	2 (1–4)
Prior classes of treatment, n (%)	
Prior anti-CD20 antibody + chemotherapy (R/G-bendamustine, R/G-CHOP-based therapy) n, (%)	30 (75.0)
Prior anti-CD20 antibody-only therapy, n (%)	10 (25.0)

Updated data to be presented at ASCO

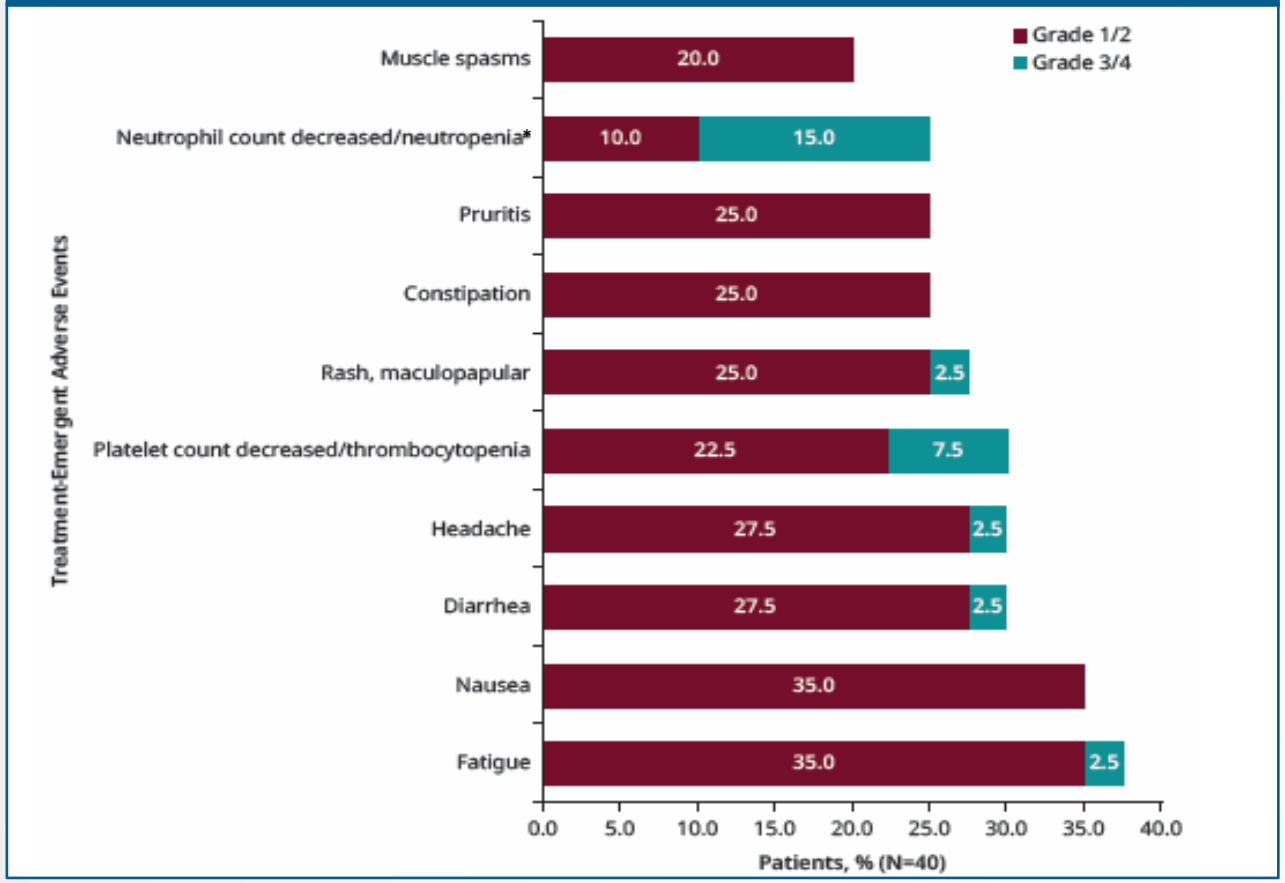
- Robust number of patients (40) enrolled across the three tazemetostat BID dose groups: 400 mg (n=4), 600 mg (n=18) or 800 mg (n=18)
- Median age was 67 years (range, 39–83) and median number of prior therapies was 2 (range, 1–4)
- 75% of patients had prior anti-CD20 antibody + chemotherapy treatment

Note: Data cut off as of September 29, 2021.

ECOG PS, Eastern Cooperative Oncology Group performance status; R/G, rituximab/obinutuzumab; R/G-CHOP, rituximab/obinutuzumab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R^2, rituximab + lenalidomide. BID, twice daily.

SYMPHONY-1 Interim Analysis: Safety Run-in Adverse Events

TEAEs Occurring in ≥20% of Patients in the Safety Population



Updated data to be presented at ASCO

- Cumulatively, Grade 3/4 TEAEs were observed in 17 (42.5%) patients
- The most common grade 3/4 TEAE (≥10%) was neutrophil count decrease/neutropenia (15.0%)

Note: Data cut off as of September 29, 2021.

Safety profile of tazemetostat + R^2 consistent with safety information for the individual tazemetostat and R^2 package inserts

*Growth factor support was administered only upon incidence of neutropenia and not given until after patients developed neutropenia.
TEAE, treatment-emergent adverse event.

SYMPHONY-1 Interim Analysis: Safety Run-in Response Rates

Updated data to be presented at ASCO

Response, n (%)	Tazemetostat + R^2 (n=35)
Overall Response Rate*	32 (91.4%)
Complete Response^	13 (37.1%)
Partial Response	19 (54.3%)
Stable Disease	3 (8.6%)
Progressive Disease	0

- 35 of 40 patients treated with tazemetostat + R^2 were evaluable for tumor assessments; 32 patients responded to treatment
- Duration-of-response data were not mature because of short follow-up
- As of data cutoff, no evaluable patient has exhibited Progressive Disease as best response

Note: Data cut off as of September 29, 2021.

Impressive overall response rate (ORR) findings – patients being followed for durability (DOR). Data support expansion to randomized Phase 3 portion of the trial in 500 patients with R/R FL, including rituximab-refractory patients

*For best overall response, there were 27 PET-CT–based responses and 8 CT-based responses.
^For CR, 12 were PET-CT–based responses and 1 was a CT-based response.
CR, complete response; CT, computed tomography; PET, positron emission tomography; PD, progressive disease; PR, partial response; R^2, rituximab + lenalidomide. R2, Revlimid + rituximab is a registered trademark of Celgene Corporation, a Bristol Myers Squibb company.

Epizyme Seeking to Establish a Benchmark for R^2 Use in Rituximab-Refractory/POD24 Patients, Which Represent 30-40% of Patients in 2L+ FL*

Background

- AUGMENT study evaluated R^2 vs. R in 2L+ R/R FL patients, but excluded rituximab-refractory patients
- There is a lack of data evaluating how R^2 performs in 2L+ R/R FL patient population, including rituximab-refractory and POD24 patients

Our Approach

- Design a prospective natural history study to understand R^2 outcomes in a more representative patient population consistent with patients enrolled in SYMPHONY-1

Our Goal

- Create a synthetic control arm for patients enrolled in Phase 1b portion of SYMPHONY-1 (n=40)

* Mozessohn et al, Rituximab Resistant Follicular Lymphoma: Predictors of Rituximab Resistance, Incidence of Transformation and Prognosis, Blood (2011) 118 (21): 4981; Casulo et al. Early Relapse of Follicular Lymphoma After Rituximab Plus Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone Defines Patients at High Risk for Death: An Analysis From the National LymphoCare Study; Journal of Clinical Oncology Vol 33, No 23, August 2015.

**Source: AUGMENT study conducted by BMS/Celgene. AUGMENT study results. Leonard, et. Al, J Clin Oncol 37, no. 14 (May 10, 2019) 1188-1199.

R^2, rituximab + lenalidomide; R2, Revlimid + rituximab is a registered trademark of Celgene Corporation, a Bristol Myers Squibb company. R/R, relapsed or refractory; 2L, second line, FL, follicular lymphoma; POD24, progression of disease within 24 months.

VIOLA: Proposed Natural History Study Design

Methodology

- Identify patients who meet the inclusion criteria of the SYMPHONY-1 safety run-in study
- Conduct chart review of the defined population with R^2

Study Endpoints

- *Primary Endpoint:*
  - ORR
- *Secondary End Point:*
  - DOR @ time points
  - PFS @ time points
  - OS
  - Safety

Statistical Analysis

- Comparative evaluation of patient population using propensity score
- Utilize datasets of R^2 outcomes (synthetic control arm) to compare with SYMPHONY-1 Phase 1b datapoints

R^2, rituximab + lenalidomide; ORR, overall response rate; PFS, progression-free survival; DOR, duration of response; OS, overall survival.
R^2, Revlimid + rituximab is a registered trademark of Celgene Corporation, a Bristol Myers Squibb company.

LYSA/LYSARC: Rationale for Expanding Study of Tazemetostat + R-CHOP in Front-Line FL & DLBCL

Background

- High unmet need for patients in front-line, high-risk FL and DLBCL
- Patients often have a poor prognosis

Approach

- Phase 1 data*, published in *Clinical Cancer Research,* of tazemetostat + R-CHOP in high-risk, front-line DLBCL was encouraging
- Serves as foundation for Phase 2 study, expanded to include high-risk, front-line FL

Goal

- Demonstrate activity in front-line, high-risk FL and DLBCL
- Enrollment nearly complete with top-line data anticipated in 2H 2022

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*Source: Sarkozy C et al A LYSA Phase Ib Study of Tazemetostat (EPZ-6438) plus R-CHOP in Patients with Newly Diagnosed Diffuse Large B-Cell Lymphoma (DLBCL) with Poor Prognosis Features. Clin Cancer Res. 2020 Jul 1;26(13):3145-3153. doi: 10.1158/1078-0432.CCR-19-3741. Epub 2020 Mar 2. PMID: 32122924.
FL, follicular lymphoma; DLBCL, diffuse large B-cell lymphoma; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone.

LYSA/LYSARC (Epi-RCHOP): Phase 1b/2 Study Evaluating High-Risk, Front-Line FL And DLBCL Patients

Objective:

Phase 1b: determine RP2D for tazemetostat in combination with R-CHOP

Phase 2: Determine the safety and the efficacy of tazemetostat in high-risk, front-line DLBCL and FL patients

Phase 2 Primary Endpoints:

- DLBCL: CRR by Central Review, ORR, PFS, DoR, OS, BOR
- FL: PET CRR, ORR, PFS, EFS, OS, DoR, BOR
- Safety

RP2D: tazemetostat 800 mg BID in combination with R-CHOP

Phase 2 Portion of Study

Targeted Enrollment

n = 184

n = 62 FL patients
(FL enrollment complete)

n = 122 DLBCL patients

DLBCL: R-CHOP (induction by 6 cycles + 2 cycles R, every 21 days)
+
Tazemetostat (800 mg BID) for ~6 months

FL: R-CHOP (induction by 6 cycles + 2 cycles R, every 21 days)
+
Tazemetostat (800 mg BID) for ~6 months

Maintenance (FL arm)
Tazemetostat: 6 months
Rituximab: 24 months

Tumor Assessment

- Clinical examination, laboratory test
- Abdomen and chest scan, PET and CT-scans
- Bone marrow and lymph node biopsy

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Note: LYSA is an independent clinical lymphoma research network, and LYSARC is the EU academic structure dedicated to lymphoma research operations.
FL, follicular lymphoma; DLBCL, diffuse large B-cell lymphoma; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone; RP2D, recommended Phase 2 dose; CRR, complete response rate, ORR, overall response rate, PFS, progression-free survival, DoR, duration of response, OS, overall survival, BOR, best overall response.

CELLO-1 Study: Randomized Phase 2 in mCRPC
Phase 2 Portion of Study is 85% Enrolled

Primary Endpoint:
Radiographic Progression-Free Survival (rPFS)

Secondary Endpoints:
- PSA50, TTPP, time to first SRE, ORR and BOR, DCR, time to new treatment
- Safety, PK
- FACT-P, FWB and PCS subscales and TDD

Intensive Biomarker Program

RP2D: tazemetostat 1200 mg BID plus enzalutamide 160 mg DAILY

Safety Run-in Complete
Updated data expected in 2H 2022

Randomized Phase 2 Portion Ongoing
Interim data expected in 2H 2022

Tazemetostat RP2D for Enzalutamide combination
(1200 mg BID)

Randomization

Tazemetostat (1200 mg BID) + Enzalutamide (160 mg QD)
N=40

VS

Enzalutamide (160 mg QD)
N=40

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PSA50, prostate-specific antigen 50; TTPP, time to pain progression; SRE; ORR, overall response rate; BOR, best overall response; DCR, disease control rate; PK, pharmacokinetic; FACT-P, functional assessment of cancer therapy, prostate; FWB, functional well-being; PCS, prostate cancer subscale; TDD, time to definitive deterioration; RP2D, recommended phase 2 dose; BID, twice daily.

CELLO-1 Study: Phase 1b in mCRPC
Safety Run-in & Activity Data

Updated Phase 1b safety run-in results demonstrated that combination of tazemetostat + enzalutamide was generally safe and well tolerated, with no DLTs

Patients With a TEAE, n (%)	TAZ+A/P (n=7)	TAZ+E (n=14)	Total (N=21)
Any TEAE	7 (100)	14 (100)	21 (100)
Grade 3 or 4 TEAE	3 (42.9)	7 (50)	10 (47.6)
TEAE leading to dose reduction	1 (14.3)	1 (7.1)	2 (9.5)
TEAE leading to study drug interruption	2 (28.6)	4 (28.6)	6 (28.6)
TEAE leading to study drug discontinuation	0	1 (7.1)	1 (4.8)
TEAE leading to study withdrawal	0	0	0
Any TESAE	2 (28.6)	2 (14.3)	4 (19)
Any treatment-related TESAE	1 (14.3)	0	1 (4.8)

- Low rate of Grade ≥3 AEs
- No DLTs observed
- Low rate of dose interruptions / modifications
- No new safety signals
- Most common TEAEs were fatigue, constipation, arthralgia, hypertension, and diarrhea

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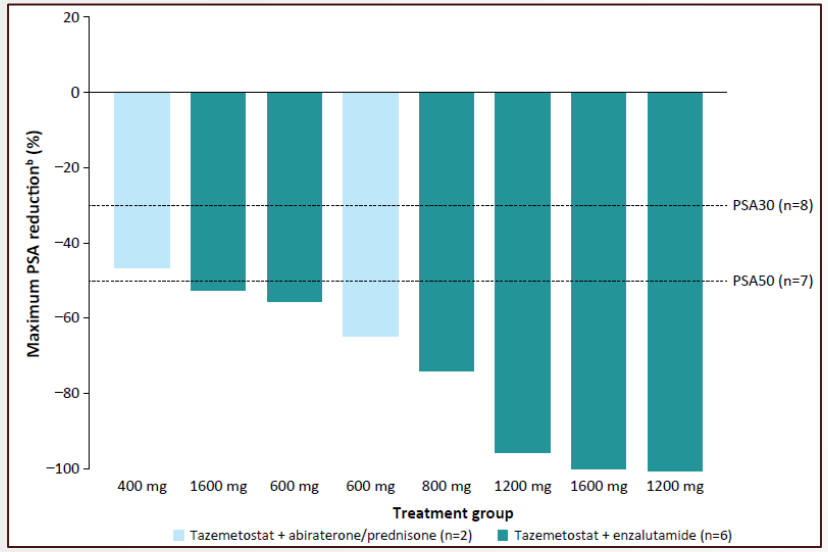
As of the July 22, 2021 data cutoff date. Preliminary data presented at the European Society of Medical Oncology (ESMO) Virtual Congress, September 2021.
DLTs: dose-limiting toxicities; A/P: abiraterone/prednisone; E: enzalutamide; TEAE: treatment-emergent adverse event; TESAE: treatment-emergent serious adverse event.

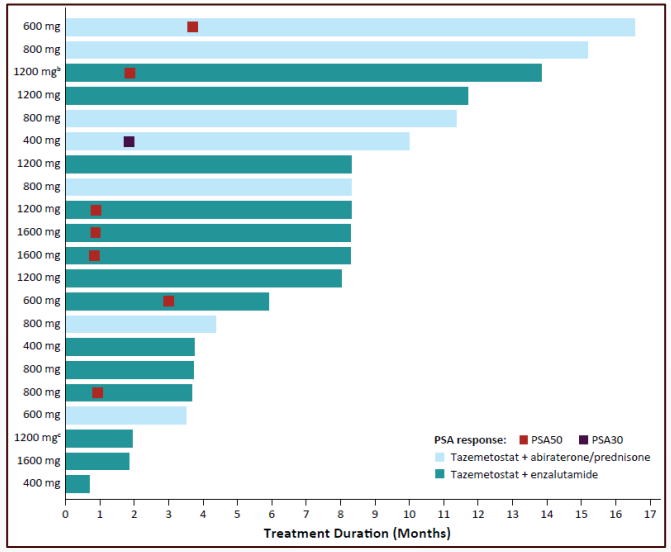
CELLO-1 Study: Phase 1b in mCRPC
Safety Run-in Data (continued)

Preliminary activity of tazemetostat + enzalutamide show durable reductions in PSA

Patients with ≥30% Decline in PSA Levels[a]



Treatment Duration and Patient PSA Response[b,c]



- **Median PFS not reached at cutoff for TAZ+E arm; six-month PFS was 61.7%**
- **Preliminary activity of TAZ+E show durable reductions in PSA; 33% of patients achieved PSA50**
- **11/21 patients experienced decrease in PSA from baseline; 1 patient with ≥30% PSA; and 7/21 patients with ≥50% PSA. Of those 7:**
  - **6 of PSA50 were in TAZ+E cohort**
  - **1 was in TAZ+A/E cohort**
- **One patient with PSA50 achieved a radiographic partial response**

As of the July 22, 2021 data cutoff date. Preliminary data presented at the European Society of Medical Oncology (ESMO) Virtual Congress, September 2021.
PSA: prostate-specific antigens; PFS, progression-free survival; A/P: abiraterone/prednisone; E: enzalutamide.
a PSA30, 30% decline in PSA level; PSA50: 50% decline in PSA level
b Best overall response was partial response. c Patient is AR-V7 positive.

Tazemetostat Projected Publication & Data Dissemination 2022-2024

	1H 2022	2H 2022	2023 – 2024*
Tazemetostat	**SYMPHONY-1 FL** Updated Phase 1b Data	**SYMPHONY-1 FL** Updated Phase 1b Data **LYSA FL/DLBCL** Top-line Phase 2 Data **CELLO-1 mCRPC** Updated Phase 1b Safety Run-in and Interim Phase 2 Data	**SYMPHONY-1 FL** • Ongoing Phase 1b Cohort DOR/PFS (2023) • Phase 3 1st Interim Futility Outcome (2023) **VIOLA FL –** R2 Natural History Study Publication **LYSA FL/DLBCL** Final Phase 2 Study Results **ARIA/EZH-1501** Heme Basket Preliminary Data & Final Study Results **CELLO-1 mCRPC** Final Phase 2 Study Results **Other Studies** including ISTs and other collaborations

*Actual timeframes dependent on clinical trial accruals and data maturity.
DOR, duration of response; PFS, progression free survival; IST, investigator-sponsored trial.

Our Vision to Expand Tazemetostat's Utility

Maximize Monotherapy

- Accelerated Approvals in Jan 2020 (ES) and June 2020 (R/R FL)
- Making targeted investments to enhance TAVERIK adoption and commercial effectiveness

Leverage Initial Combination Data

- Upcoming FL and prostate data readouts (SYMPHONY-1 and CELLO-1)
- LYSA/LYSARC collaboration in 1L High Risk FL and DLBCL readout anticipated in 2H 2022
- Initial data from ongoing heme basket trial and ISTs could support further trials

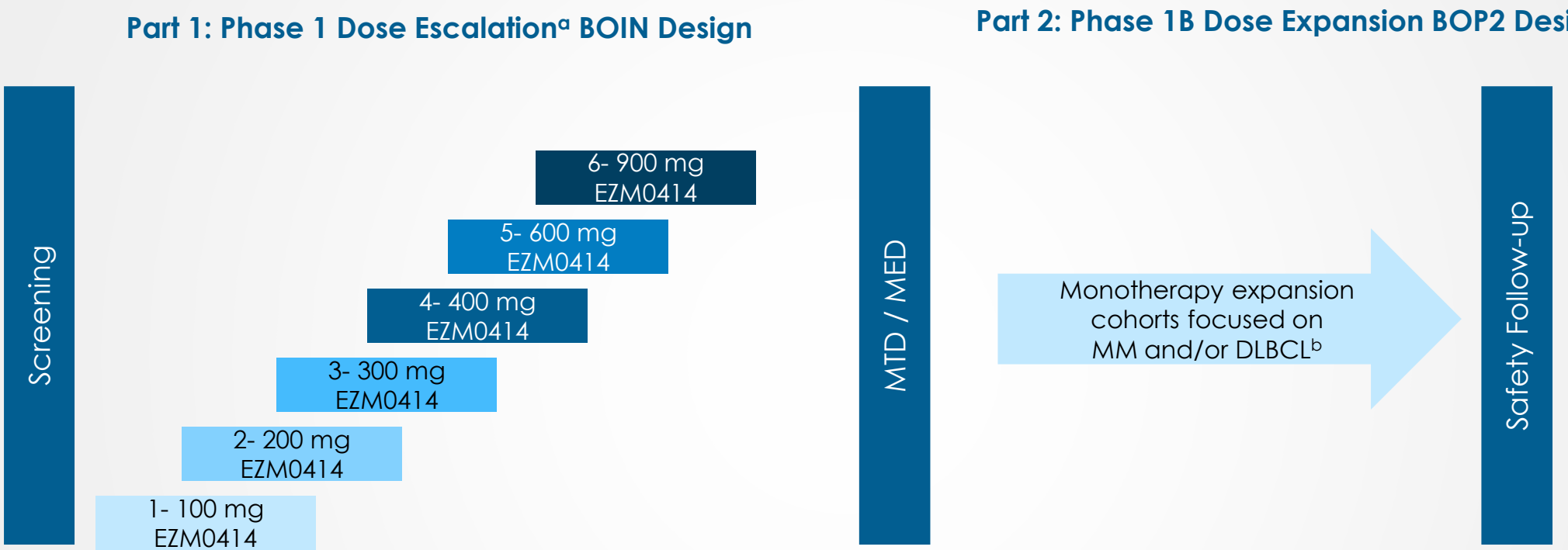
Potential Broad Combination Use in Solid Tumors and Heme Malignancies

- Potential to become backbone therapy in FL and DLBCL, combining with other active agents
- Potential to become significant treatment option in combination with androgen inhibition in mCRPC, proof of concept achieved in CELLO-1 study with enzalutamide
- Potential to explore combination opportunities with emerging active agents in heme and solid tumors

We believe TAZVERIK is well-positioned, due to its novel mode of action and safety profile, to become a backbone therapy in FL and to be utilized in combination with active agents in other hematological malignancies like DLBCL and solid tumors like mCRPC.

Expanding Epizyme's Epigenetic Pipeline

SET-101: Phase 1/1b Study of EZM0414 in R/R MM and R/R DLBCL



Primary Endpoints:

Phase 1: maximum tolerated dose (MTD) / maximum efficacious dose (MED) of EZM0414 QD

Phase 1b: Safety

Patient Enrollment:

- ~30-36 relapsed/refractory patients to be enrolled in dose escalation
- ~8 t(4;14) and ~8 non-t(4;14) MM, and ~8 R/R DLBCL, plus 10 additional patients of any type at MTD or MED

[a] Patients who are treated at the MTD in the phase 1 dose escalation AND who do not experience any DLTs will be rolled over to the phase 1b dose expansion and receive treatment until disease progression, occurrence of unacceptable toxicity, or withdrawal of consent.
[b] expansion cohorts dependent on data obtained in dose escalation phase.
BOIN, Bayesian optimal interval design; BOP2, Bayesian optimal phase 2; DLBCL, diffuse large B-cell lymphoma; MM, multiple myeloma; QD, once daily; R/R, relapsed or refractory.

Multiple Potential Opportunities for Epizyme's SETD2 Inhibitor Drug Candidate, EZM0414

t(4;14) MM Monotherapy and synergy with MM therapies	• Specific therapy for t(4;14) MM • Explore monotherapy and combination with standard of care and/or emerging pipeline agents
Non-t(4;14) MM Synergy with MM therapies	• Therapy for non-t(4;14) MM • Explore combination with standard of care and/or emerging pipeline agents
DLBCL Synergy with DLBCL therapies	• Explore combination with standard of care and/or emerging pipeline agents • Potential for biomarkers: e.g., mutant H1, SETD2, or MMSET
Other Cancers (incl. Solid Tumors)	• Explore combination in other heme malignancies or cancers, including solids (e.g., lung) • Potential for biomarker: H3K36me2 overexpression or dysregulation

MM, multiple myeloma; DLBCL, diffuse large B-cell lymphoma.

Collaborate To Expand Patient Reach And Build Value

STRATEGIC COLLABORATIONS FOR TAZEMETOSTAT

Partner	Date	Scope	Territory
Eisai	2015*	• Eisai has development and commercialization rights to tazemetostat in Japan, including the right to manufacture tazemetostat in Japan	• Japan
Roche	2012**	• Eisai and Epizyme entered into a companion diagnostics agreement with Roche Molecular to develop a companion diagnostic to identify patients with activating mutations in EZH2	• Major Markets
HUTCHMED	2021***	• Development, manufacture, and commercialization of tazemetostat either as a monotherapy or in combination with other therapies, including HutchMed proprietary compounds	• Greater China

*Amended and restated 2015, original contract signed in 2011.
** Amended in concert with Eisai re-negotiation in 2015.
*** Amended in May 2022.

2022 Projected Clinical Development Milestones

SYMPHONY-1	Continue to screen and enroll patients in the Phase 3 portion of the global trial in R/R FL patients; additional follow-up data on 40 patients enrolled in Phase 1b safety run-in portion to be presented at ASCO; plans to present additional updated Phase 1b data later this year
CELLO-1	Complete enrollment in Phase 2 portion of the trial in mCRPC patients; 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
LYSA Study	Complete enrollment in Phase 2 trial in front-line, high-risk FL and DLBCL during 1H 2022; LYSA and Epizyme, in collaboration, anticipate presenting top-line results from the Phase 2 portion of the study in the second half of the year
ARIA	Dose first patient and continue to enroll patients in hematological malignancy Phase 1b/2 basket study (EZH-1501); plans to provide preliminary data in the second half of 2022
SET-101	Dose first patient and continue to enroll patients in dose escalation portion of Phase 1/1b trial of EZM0414; plans to provide updates on this program in the second half of 2022
VIOLA	Initiate natural history study of R^2 in 2L+ FL, including patients who are rituximab-refractory or POD24

Note: Continue to advance additional studies evaluating tazemetostat, including FDA post-marketing commitments; preclinical development on differentiated epigenetic assets to supplement pipeline

Epizyme®

R/R, relapsed/refractory; FL, follicular lymphoma; mCRPC, metastatic castration resistant prostate cancer; DLBCL, diffuse large B-cell lymphoma; MTD, maximum tolerated dose; MED, maximum efficacious dose; 2L+, second-line plus; POD24, progression of disease within 24 months.

FDA-Approved For Treatment of Multiple Cancers

INDICATED FOR

- 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 2 prior systemic therapies
- Adult patients with relapsed or refractory follicular lymphoma who have no satisfactory alternative treatment options

TAZVERIK®
(tazemetostat) tablets
200 mg

FIRST AND ONLY APPROVED
EZH2 INHIBITOR

DURABLE RESPONSES
WITH POTENTIAL FOR EXTENDED TREATMENT DURATION

GENERALLY SAFE AND WELL-TOLERATED WITH NO BLACK BOX WARNINGS
OR CONTRAINDICATIONS; NO REMS

ORAL, AT-HOME
ADMINISTRATION

TAZVERIK® (tazemetostat) tablets 200 mg

Important 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