Epizyme

# *Rewriting Treatments for People with Cancer and Other Serious Diseases*

May 6, 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 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 NOW EXECUTING AS A FULLY INTEGRATED COMMERCIAL ENTERPRISE

TAZVERIK™ (tazemetostat) tablets

## APPROVED FOR 2 INDICATIONS

accelerated approval granted in epithelioid sarcoma (ES) Jan 2020

accelerated approval granted in follicular lymphoma (FL) June 2020

## MULTI-BILLION DOLLAR

GLOBAL MARKET OPPORTUNITY

## CONFIRMATORY TRIALS REMAIN ON TRACK

INITIAL DATA EXPECTED 2021

## HIGH-VALUE RESEARCH PIPELINE

ADVANCING TOWARD CLINIC

## WELL-CAPITALIZED

CASH RUNWAY INTO 2023



Full prescribing information is available at www.TAZVERIK.com

# TAZVERIK™ (tazemetostat) tablets

**NOVEL MECHANISM OF ACTION**

**POTENTIAL FOR EXTENDED TREATMENT DURATION**

**ACTIVITY DEMONSTRATED IN MULTIPLE CANCERS**

**BROAD THERAPEUTIC POTENTIAL IN SOLID TUMORS AND HEME MALIGNANCIES**

**GENERALY WELL-TOLERATED; LOW DISCONTINUATION RATES**

**COMBINATION OPPORTUNITIES WITH SOC TREATMENTS**

# TAZVERIK Approvals and Launch Execution

TAZVERIK™ (tazemetostat) tablets

Accelerated approval granted in **epithelioid sarcoma (ES)** Jan 2020

Accelerated approval granted in **follicular lymphoma (FL)** June 2020

**100%** of Top Tier FL accounts reached[1]

**68%** of Top Tier FL accounts prescribing[1]

**96%** Post-approval awareness among target physicians[2]

**38%** Increase in new accounts prescribing TAZVERIK in 1Q 21[3]

## NCCN GUIDELINES

Adapted to support TAZVERIK use in both ES and R/R FL

**>90%** Lives covered in both indications[1]

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Not for promotional use. TAZVERIK approved for treatment of R/R FL on June 18, 2020; Full prescribing information is available at www.TAZVERIK.com.
[1] Epizyme Internal Data. [2]Epizyme Message Recall Study Fielded Oct-December 2020. N= 151. [3]Ipsos US Oncology Monitor (October-December 2020), Participating doctors were primary treaters and saw a minimum number of patients per month.) Data © Ipsos 2020, all rights reserved

# Our Vision to Fuel Long-term Growth


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

# Multiple Value Driving Milestones Expected in 2021

- Continue to expand the commercial adoption of TAZVERIK® (tazemetostat) in FL and ES
- Phase 1b safety run-in data from EZH-301 clinical trial of TAZVERIK plus Doxorubicin in ES at ASCO
- Preclinical data for SETD2 at EHA; IND submission mid-2021
- Follow-up data from Phase 1b safety run-ins for EZH-302 in FL and EZH-1101 in mCRPC 2H 2021
- Advance to the efficacy stages of our ES, FL, and prostate cancer clinical programs
- Initiate novel basket trials in both hematological malignancies and solid tumors in 2H 2021
- Anticipated alignment with EMA on registration path for TAZVERIK in Europe

# TAZVERIK Development Strategy

# The Next EPIsode:
## Rewriting Oncology Treatment with Epigenetics

TAZVERIK™ (tazemetostat) tablets

## Executing a Multi-year Vision to Bring the Benefits of TAZVERIK to Patients in Need

1. Approval of tazemetostat to treat patients with ES and FL
2. Bring tazemetostat benefits to earlier lines of ES and FL therapy
3. Bring tazemetostat to patients beyond ES and FL as monotherapy and in combination

# Broad Development Approach for TAZVERIK: Initiating Basket Studies in Heme and Solid Tumors to Maximize Signal Finding Efficiency Across Multiple Tumors

| | |
|---|---|
| **Maximize signal-finding potential** | Basket trials for heme and solid tumors offer an **efficient signal finding mechanism** while producing a wide and consistent flow of new data |
| **Combo with SoC and novel therapies** | Internal and collaboration combination development efforts will ***prioritize both standard-of-care (SoC) therapies and new mechanism-of-action (MOAs)*** to solidify placement of TAZVERIK in the treatment paradigm |
| **Accelerate clinical timelines** | The basket design optimizes ***shorter clinical development timelines*** anticipated to broaden TAZVERIK label and ***expand available patient populations for TAZVERIK*** |

# Ongoing Heme Studies

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

**2021 Follicular Lymphoma Epidemiology**
~13,700 Patients Diagnosed Annually

**TAZVERIK + R-CHOP**
High-risk FL Patients
IST Enrolling

**TAZVERIK + BR**
IST Approved

**1st Line**
**~11,000**

**TAZVERIK + R²**
Confirmatory Phase 1b/3 trial (EZH-302)
Safety run-in complete | Efficacy portion initiated

**2nd Line**
**~6,000**

TAZVERIK™ (tazemetostat) tablets

**TAZVERIK + Rituximab**
Phase 2 (EZH-1401) Enrolling

**TAZVERIK + Other Combinations**
Multiple ISTs Ongoing

**3L+**
**~5,000**

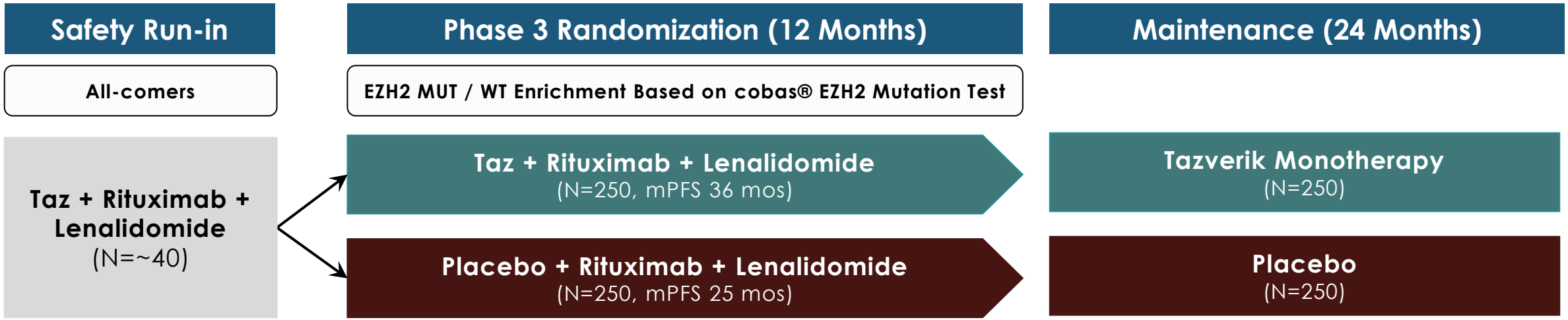
**2L+ Supported by Current Label**

Source: internal drug-treated estimates.

R² = Revlimid® in combination with a rituxmab product is indicated for the treatment of adult patients with previously treated follicular lymphoma
[1] Freedman et al. *American Journal of* Hematology; Volume 87, Issue 10.

# EZH-302 Phase 1b/3 Tazemetostat in Combination with R$^2$ in Patients with R/R FL

| | |
|---|---|
| **Population** | Patients with relapsed / rituximab refractory FL who have been treated with at least one prior systemic therapy. |
| **Key Objectives** | **Phase 1b (safety run-in)**<br>Safety, pharmacokinetics, anti-tumor activity<br><br>**Phase 3 (efficacy)**<br>Primary: PFS as determined by Investigator; interim analyses for futility<br>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.*

# EZH302: Study of Tazemetostat + $R^2$ in 2nd Line+ Follicular Lymphoma
## Rationale for Success in Phase 3 Confirmatory Study

- ✓ Pre-clinical evidence suggesting synergy between tazemetostat + lenalidomide and tazemetostat + rituximab, the two components of the $R^2$ regimen
- ✓ Preliminary clinical activity with rituximab in Phase 1b study of R-CHOP + tazemetostat previously presented
- ✓ Unique clinical trial design for EZH-302
  - Inclusion of patients who initially failed rituximab (real world population)
  - Inclusion of tazemetostat maintenance treatment period to extend treatment benefit
  - Adaptive study design allows adjustment of Phase 3 trial based on 2 interim assessments
  - 2nd interim analysis includes efficacy evaluation once 65% progression free survival (PFS) events have occurred
- ✓ TAZVERIK safety characteristics allows for extended treatment with high treatment compliance

# EZH-302 Safety Summary

**Safety of tazemetostat** (400, 600, 800 mg BID) **+ rituximab** (375 mg/m2) **+ lenalidomide** (10, 20 mg) **evaluated in 13 patients**

**NO** DLTs reported for patients evaluated during first cycle

**Only 4** patients had treatment-related AEs that were Grade 3 or 4

**Only 1** patient had at least 1 treatment-related emergent SAE

**NO** patients discontinued study treatment due to an AE

**NO** special interest adverse events were reported

**Tazemetostat well tolerated up to 800 mg BID in combination with $R^2$**

*In-line with highest dose level for tazemetostat approved as monotherapy*

# Seven of 13 Patients Treated with Tazemetostat + R$^2$ to Date Were Evaluable for Response; All Seven Patients Responded to Treatment

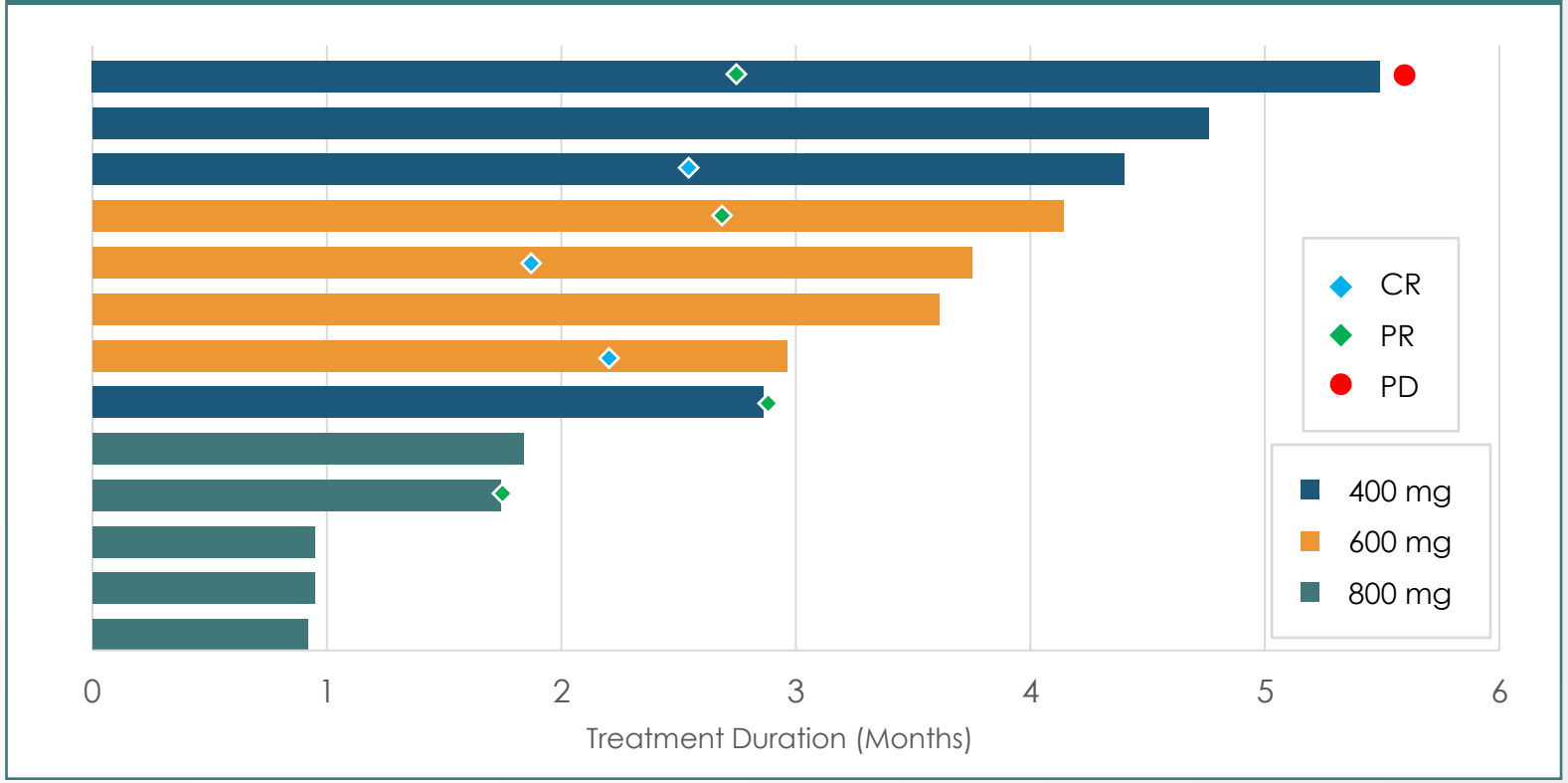
## TAZEMETOSTAT + Lenalidomide/Rituximab

**Best Overall Tumor Response**
*Evaluable Population**

| | |
|---|---|
| Complete Response (CR) | 3 (43%) |
| Partial Response (PR) | 4 (57%) |
| Stable Disease (SD) | 0 |
| Progressive Disease (PD) | 0 |
| **Objective Response Rate (ORR)** | **7 (100%)** |

***Six patients not yet evaluable due to no post-baseline scan data yet***
***Data cut mid-February 2021***

## TAZEMETOSTAT + R$^2$ Treatment Duration and Patient Response to Investigator Assessment (iTT Population)




**All but one patient remain on therapy**

# CR in Rituximab Refractory Patient with Extensive Extranodal Disease (600 mg Cohort)

**Patient Background:**
Female in 50s with follicular lymphoma, predom grade 1-2 (80%) with focal grade 3A (20%), stage IVA (subcutaneous nodules, extensive left axillary / subpectoral adenopathy, and diffuse LA). Markedly FDG-avid bulky axillary LA concerning for transformation, bx confirmed FL grade 1-2 (no e/o transformation).

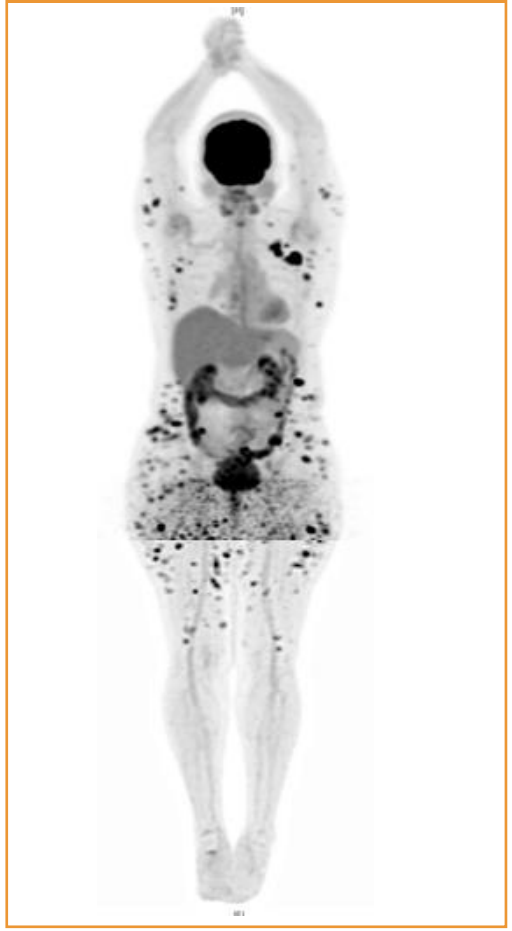
**Genetics:** EZH2 unknown

**Tx #1:** R-CHOP x 6, CR in 2015, s/p rituximab maintenance completed 2017. Relapse 2018 (<12 mo from last Rituximab dose).
- Multiple PET and lymph node biopsy confirm FL grade 1-2, disease focal area with FL3A

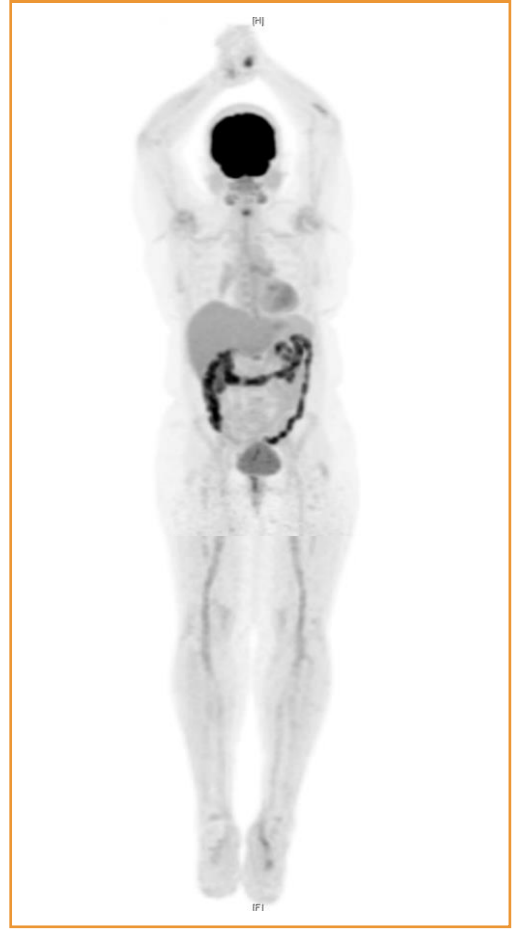
**Tx #2:** Single-agent Rituximab x 4, completed 2020 with PR. Continued progression summer 2020

**Tx #3: Tazemetostat 600mg BID + $R^2$, initiated tx on 9/8/20, CR to treatment**

**Before**



**After**
*1st Restaging*



**Case courtesy of Dr. Connie Batlevi**

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# CR in Elderly Patient with Early POD24 (800 mg Cohort)

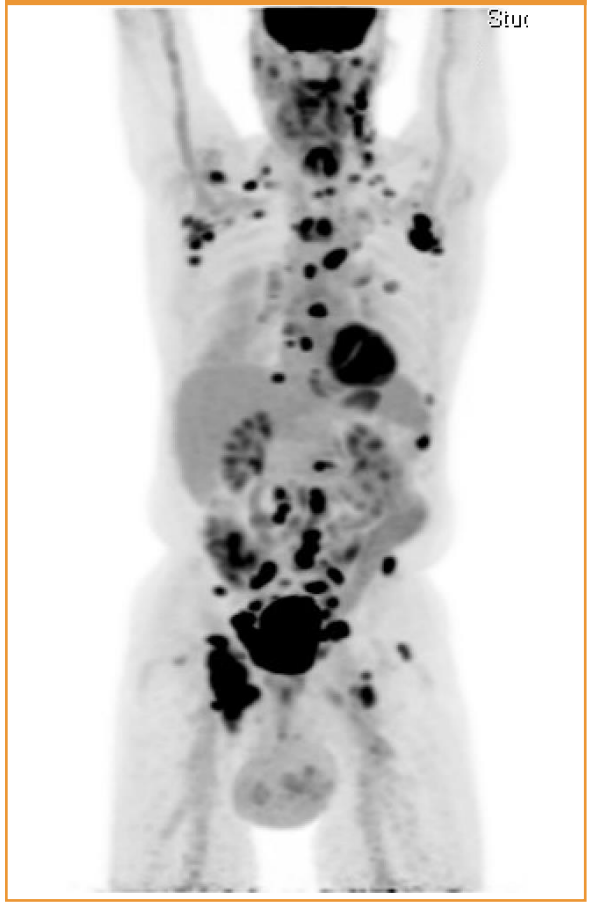
**Patient Background:**
Male in 80s with stage IV FL grade 2, diagnosed with multiple extranodal sites in gallbladder, bone and >4 nodal sites. **EZH2 WT**

**Tx#1:** R-Bendamustine x 6 completed on 2019 complicated by cytopenias, CR at end of treatment

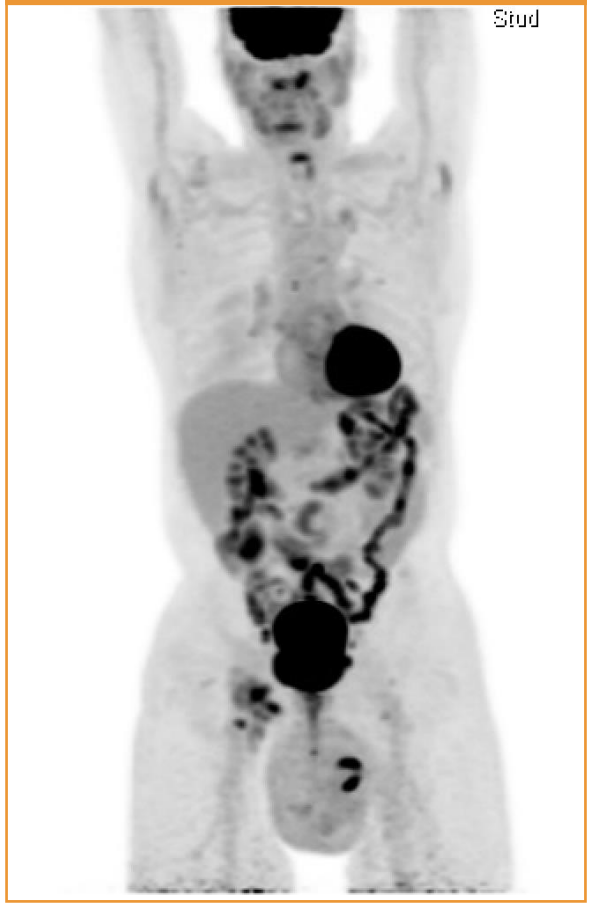
- Relapse <12 months from end of treatment

**Tx #2: Tazemetostat 800mg BID +R2, initiated tx on 11/12/20 in CR**

**Before**



**After**
*1st Restaging*



**Case courtesy of Dr. Connie Batlevi**

# EZH-302 Phase 1b Safety Run-in Summary

**Safety profile observed with tazemetostat (800mg BID) + $R^2$ is consistent with that described in the respective reference safety information documents**

- No patients discontinued study treatment due to an AE

**Seven of seven evaluable patients responded to treatment with tazemetostat + $R^2$**

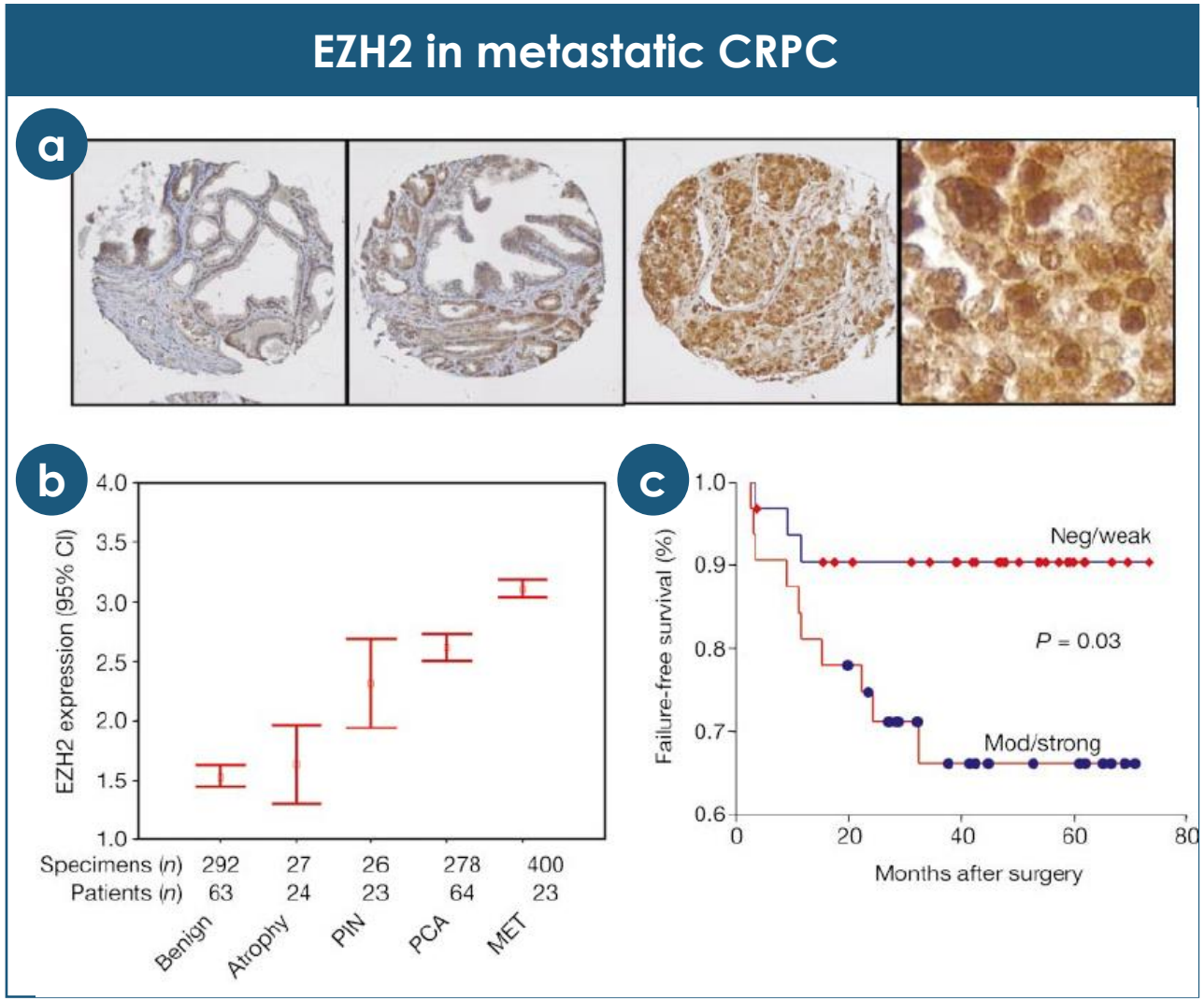
- 3 complete responses and 4 partial responses

**Phase 1b portion of the study to include a minimum of 15 patients in the cohorts of 600 and 800 mg BID to help inform selection of the Phase 3 dose**

# Ongoing Solid Tumor Studies

# Targeting EZH2 in mCRPC with Tazemetostat: Clinical Hypotheses

## EZH2 in metastatic CRPC




Varambally et al. 2002 Nature. 419:624

EZH2 cooperates with the androgen receptor during oncogenic transformation, leading to epigenetic silencing of many tumor suppressors and regulators of differentiation

In combination experiments, EZH2 inhibition resensitizes both mCRPC cultured cells and xenograft tumor models to androgen signaling inhibitor (ASI) therapy

**a, b:** EZH2 protein expression correlates with advancing disease progression

**c.** Moderate to high EZH2 expression associated with worse failure-free survival

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# EZH-1101 Phase 1b Prostate Cancer Safety Overview

## All 8 cohorts (5 enzalutamide, 3 abiraterone/prednisone) dosed without DLTs

| Patients With a TEAE, n (%) | TAZ+A/P (n=7) | TAZ+E (n=14) | Total (N=21) |
|---|---|---|---|
| Any TEAE | 7 (100) | 12 (85.7) | 19 (90.5) |
| Grade 3 or 4 TEAE | 2 (28.6) | 5 (35.7) | 7 (33.3) |
| TEAE leading to dose reduction | 1 (14.3) | 1 (7.1) | 2 (9.5) |
| TEAE leading to study drug interruption | 2 (28.6) | 3 (21.4) | 5 (23.8) |
| TEAE leading to study drug discontinuation | 0 | 1 (7.1) | 1 (4.8) |
| TEAE leading to study withdrawal | 0 | 0 | 0 |

- Low rate of Grade ≥3 AEs
- Low rate of dose interruptions / modifications
- No new safety signals

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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.

# To Date, We've Already Observed PSA50 Responses Across Dosing Cohorts

**PSA reduction of ≥50% in 7/21 patients treated, across all cohorts**

- 6 patients receiving taz/enza PSA50
- 1 on taz/abi/pred PSA50
- 10 patients remain on therapy with potential to exhibit response
- 1 additional patient with PSA decrease of **≥35%**

**All responses were in ARV7- patients**

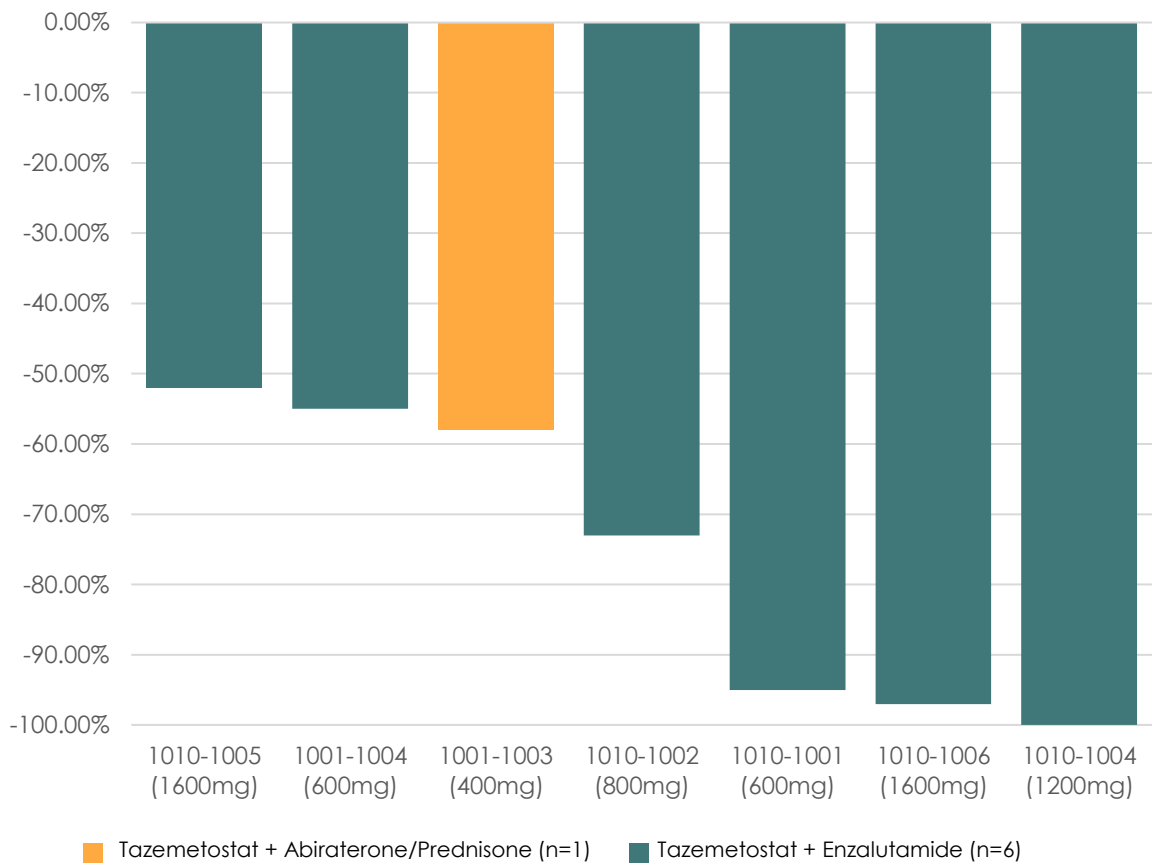
- 85 to 90% of prostate cancer patients are ARV7-
- Only one ARV7+ patient enrolled in safety run-in portion of the study

**47% disease control rate to date**

- Longest patient continuation since January 2020

*Data cut mid-February 2021

## EZH-1101: Maximum PSA Reduction To Date



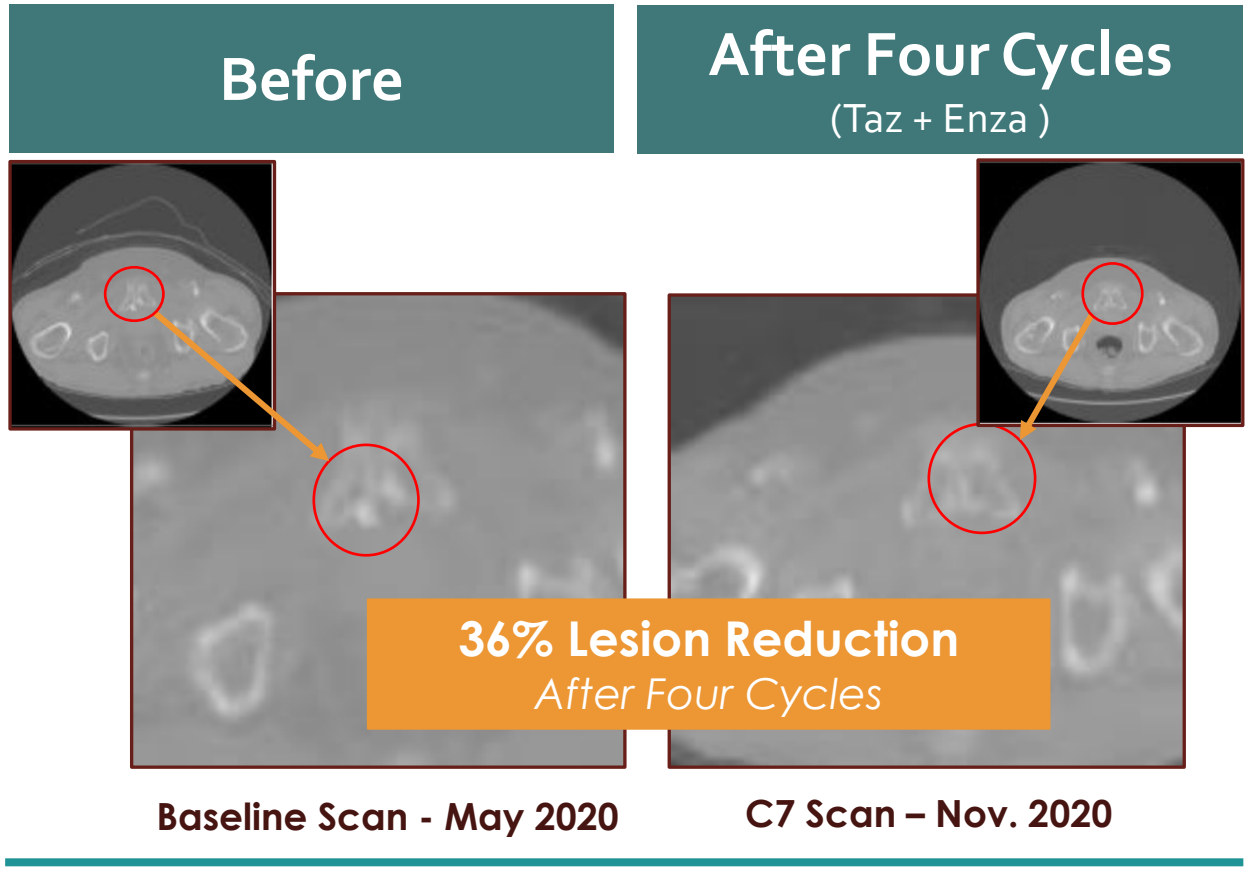
# Signs of Early Response to Treatment with Tazemetostat + Enzalutamide in Prostate Cancer Patient

- 77-year-old male with mCRPC progressing on Lupron and Zytiga/prednisone
- Lesions at left apex and mid gland of the prostate
- Patient treated with tazemetostat 600mg BID and enzalutamide 160mg DAILY

**After 2 Cycles:**
**24% reduction** in diameter of the target lesion

**After 3 Cycles:**
**32% reduction** (PR)

| Baseline (May 2020) | RECIST response |
|---|---|
| C3 JUL2020 | -24% |
| C5 SEP2020 | -32% |
| C7 Nov2020 | -36% |




Note: scan is performed at the end of a cycle and before the start of the next cycle, e.g., at C3D1 scan the patient has received 2 cycles of treatment

# Randomized Portion of Phase 2 EZH-1101 Trial Ongoing

**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 1200mg BID plus enzalutamide 160mg DAILY

**Safety Run-in Complete**
*10 of 21 Patients Remain on Therapy*

**Randomized Efficacy Portion Ongoing**

**Tazemetostat RP2D for Enzalutamide combination**
(1200mg BID)

***Randomization***

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

*VS*

**Enzalutamide (160 mg QD)**
N=40

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# Planned Activities

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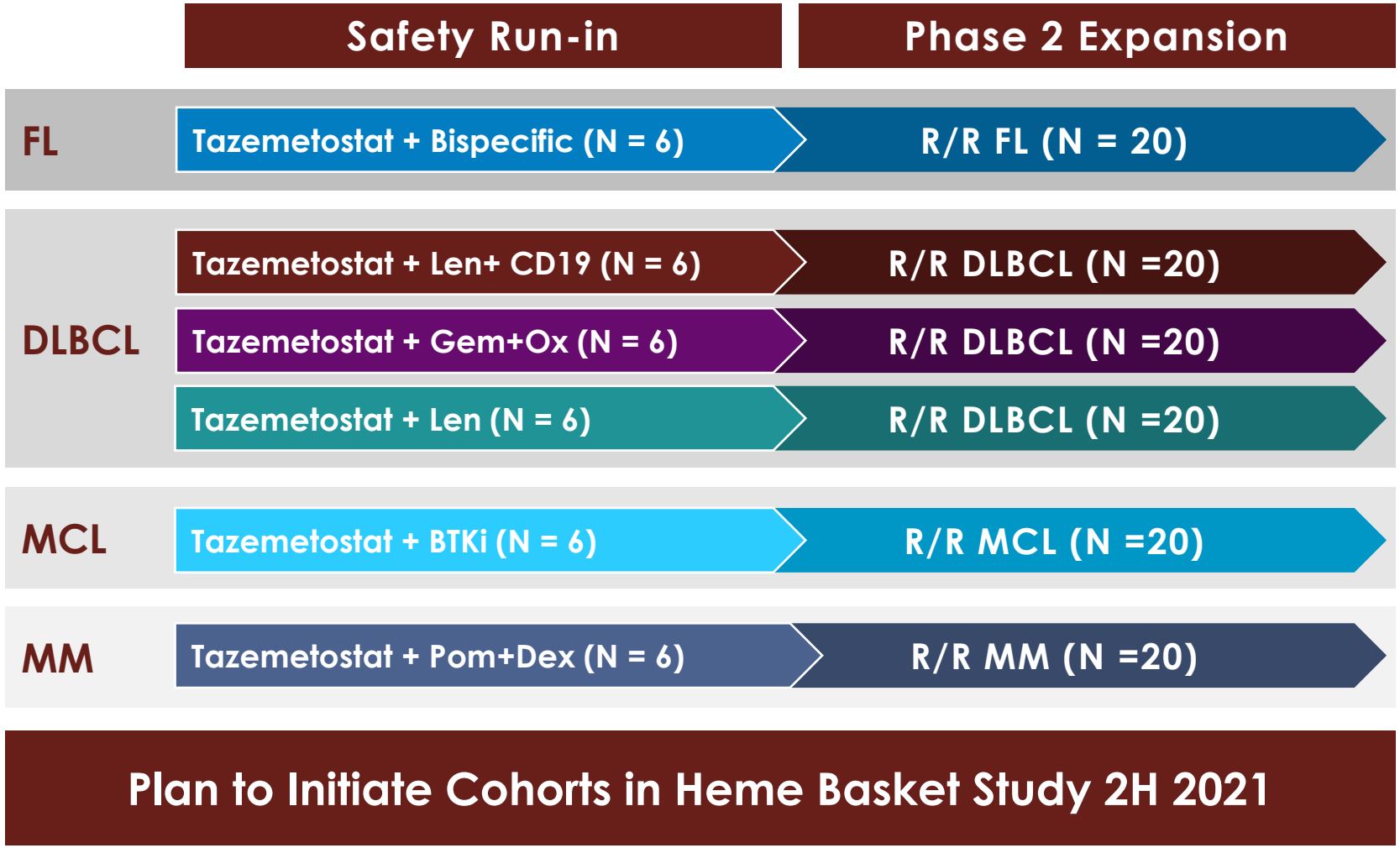
# A Phase 1/2 Open-Label Bayesian Basket Trial of Tazemetostat with Multiple Combinations in Hematological Malignancies

**Basket trial provides an efficient signal finding mechanism while producing a wide and consistent set of new data**

**Adaptive study design leveraging Bayesian continuous monitoring based on predictive probability**

*Objective response (CR or PR) and Biomarker PD will determine go/no-go*




**Plan to Initiate Cohorts in Heme Basket Study 2H 2021**

# A Phase 2 Open-Label Bayesian Basket Trial of Tazemetostat with a PARP inhibitor or IO in Patients with Solid Tumors

**Study evaluating patients previously treated with a PARP inhibitor or chemotherapy ineligible**

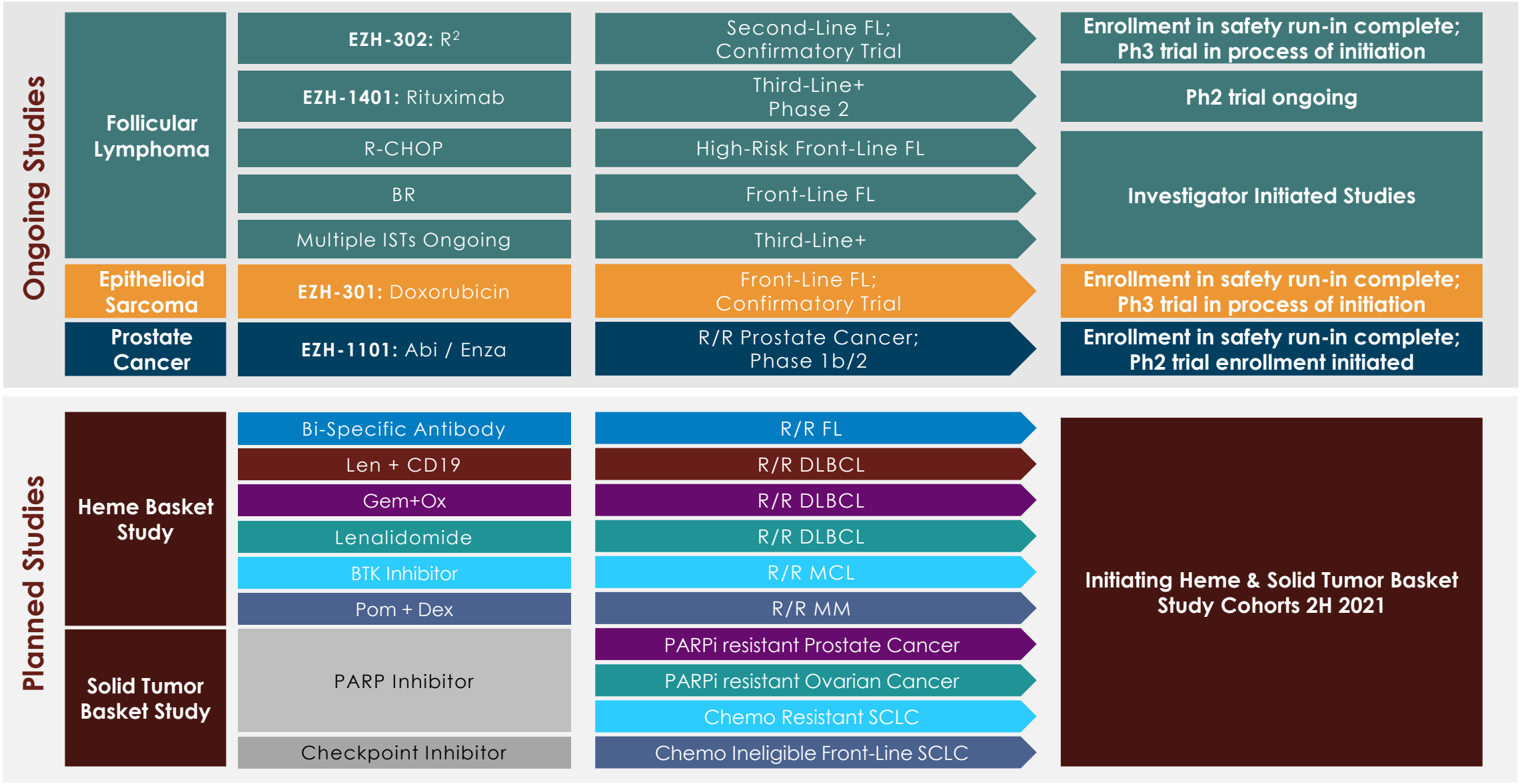
**Adaptive study design leveraging Bayesian continuous monitoring based on predictive probability**

*Objective response (CR or PR) and Biomarker PD will determine go/no-go*

| Safety Run-in | Phase 2 Expansion |
|---|---|
| **Tazemetostat + PARP inhibitor** (N=6)<br>*Advanced stage, metastatic cancer, progressed on PARPi* | **PARPi resistant Prostate Cancer** (N=20)<br>**PARPi resistant Ovarian Cancer** (N=20)<br>**Chemo resistant SCLC** (N=20) |
| **Tazemetostat + CP inhibitor** (N=6)<br>*Advanced stage, metastatic SCLC chemotherapy resistant* | **Chemo ineligible front-line SCLC** (N=20) |

**Plan to Initiate Cohorts in Solid Tumor Basket Study 2H 2021**

# Robust Tazemetostat Development Program Will Produce a Stream of New Data Over the Next 5 Years



# Partial List of Active Studies & Approved IST Concepts for Tazemetostat in Hematologic Malignancies

| | | |
|---|---|---|
| **TKI-resistant CML** *+TKI* | **1L DLBCL** *+R-CHOP* | **1L FL** *+BR* |
| **r/r FL** *+venetoclax* | **r/r NHL** *+venetoclax* | **3L GCB-DLBCL** *+axi-cel* |
| **R/R FL** *+ ubi/umbra* | **r/r FL/PTCL** *+belinostat* | **DH/TH DLBCL** *+DA-EPOCH-R* |

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Active Stage | Protocol Approved | Protocol Pending | Concept Stage

# Partial List of Active Studies & Approved IST Concepts for Tazemetostat in Solid Tumors

| | | | |
|---|---|---|---|
| **Urothelial** *+pembro* | **Pediatric MATCH** | **Ovarian** | **CAIRE** *+durvalumab* |
| **IO res SCCHN** *+pembro* | **IO resistant Lung** *+pembro* | **ATRT** *+nivo/ipi* | **1L Meso** *+cis/pem* |
| **BRAF-m Melanoma** *+DT* | **mCRPC** *+talazoparib* | **SCLC/NSCLC** *Topo+pembro* | **Solid Tumors with EZH2 Mutation** |

| | | | | |
|---|---|---|---|---|
| **MPNST** | **ARID1AMT in Solid Tumors** | **Advanced Triple Negative BC** *+atezo* | **INI 1 loss Sarcoma** *+doxo/ifosfamide* | **SCCHN** *+ nivo* |

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**Active Stage** | **Protocol Approved** | **Protocol Pending**

# Key Takeaways

TAZVERIK™ (tazemetostat) tablets

1. Broad expansion plan for TAZVERIK in multiple indications of interest, supported by preclinical data and biological rationale
2. Several ongoing clinical trials evaluating TAZVERIK combinations advancing; steady stream of data expected over next five years
3. Objective Responses demonstrated in EZH-302 Phase 1b safety run-in study of TAZ+R2 with no new safety signals; advancing to Phase 3 randomization trial
4. PSA50 and Objective Response demonstrated in EZH-1101 Phase 1 safety run-in study in combination with Abiraterone or Enzalutamide in mCRPC; advancing to Phase 2 portion in combination with Enzalutamide
5. Heme basket trial evaluating 7 combinations across 4 indications & solid tumor basket trial evaluating 4 combinations across 3 indications on track to initiate 2H21
6. Over 30 active or approved IST concepts across heme and solid tumors, supporting broad interest in TAZVERIK combinations

# Research Platform

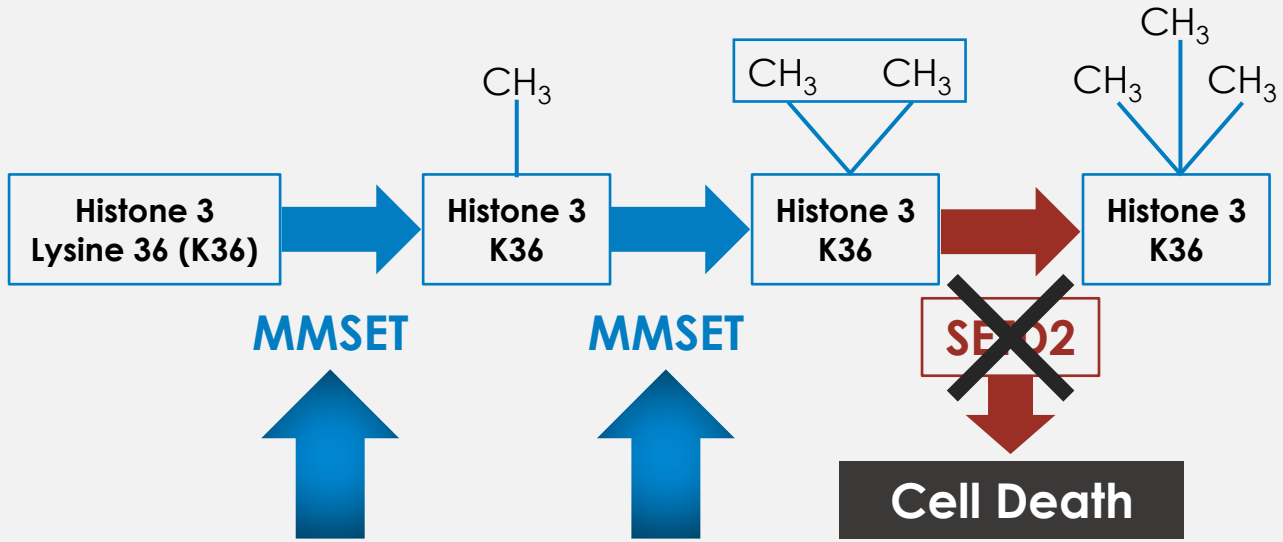
# Robust Discovery Pipeline Across 3 Important Epigenetic Target Families

| PROGRAM | POTENTIAL INDICATIONS | TARGET VALIDATION | LEAD DISCOVERY | LEAD OPTIMIZATION | DEVELOPMENT CANDIDATE | IND-ENABLING |
|---|---|---|---|---|---|---|
| HMT INHIBITORS | | | | | | |
| SETD2 | Heme Malignancies | | | | | |
| HMT2 | Heme & Solid Malignancies | | | | | |
| HMT3 | Heme Malignancies | | | | | |
| HAT INHIBITORS | | | | | | |
| HAT1 | Heme & Solid Malignancies | | | | | |
| HAT2 | Solid Malignancies | | | | | |
| HELICASE INHIBITORS | | | | | | |
| HEL1 | Solid Malignancies | | | | | |
| HEL2 | Heme and Solid Malignancies | | | | | |
| HEL3 | Solid Malignancies | | | | | |
| HEL4 | Solid Malignancies | | | | | |
| HEL5 | Solid Malignancies | | | | | |
| HEL6 | Solid Malignancies | | | | | |

# SETD2 is a Therapeutic Target, Particularly in MM with (4;14) Translocation

- t(4;14) juxtaposes IgH control elements with multiple myeloma SET domain (MMSET) gene leading to its overexpression
- MMSET scientifically confirmed as driver in t(4;14) pathogenesis (Mirabella et al Blood Canc J 2013), but MMSET remains undruggable
- Over-expression of MMSET results in ubiquitous H3K36me2 in t(4;14) MM, which is the substrate for HMT SETD2

**Does the overexpression of MMSET and subsequent increase in H3K36me2 in t(4;14) MM lead to a dependency on SETD2 for MM cell growth and survival ?**




t(4;14) drives high levels of MMSET and, therefore, H3K36me2

# Epizyme has Discovered a Potent and Selective, Oral Inhibitor of SETD2

**MOLECULE TARGETING SETD2** was discovered from Epizyme's large internal library of compounds and significant structure activity relationship analysis

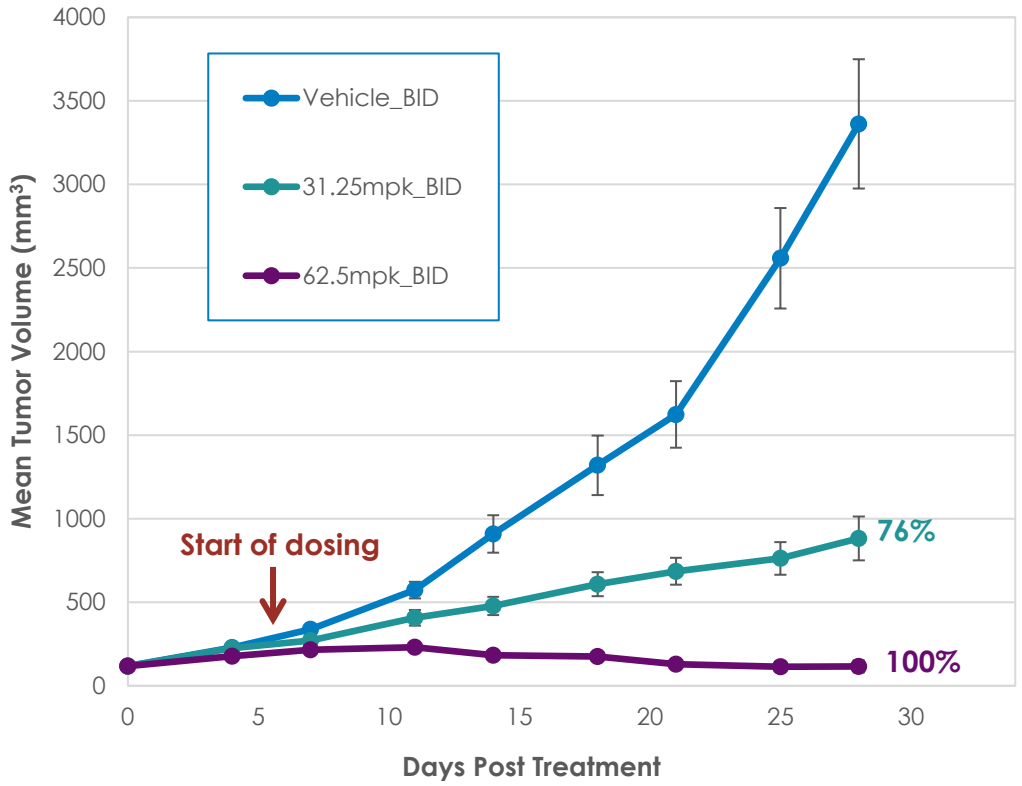
**POTENT** – low nanomolar inhibitor of enzymatic activity

**SELECTIVE** - >11,000-fold selectivity over other HMTs

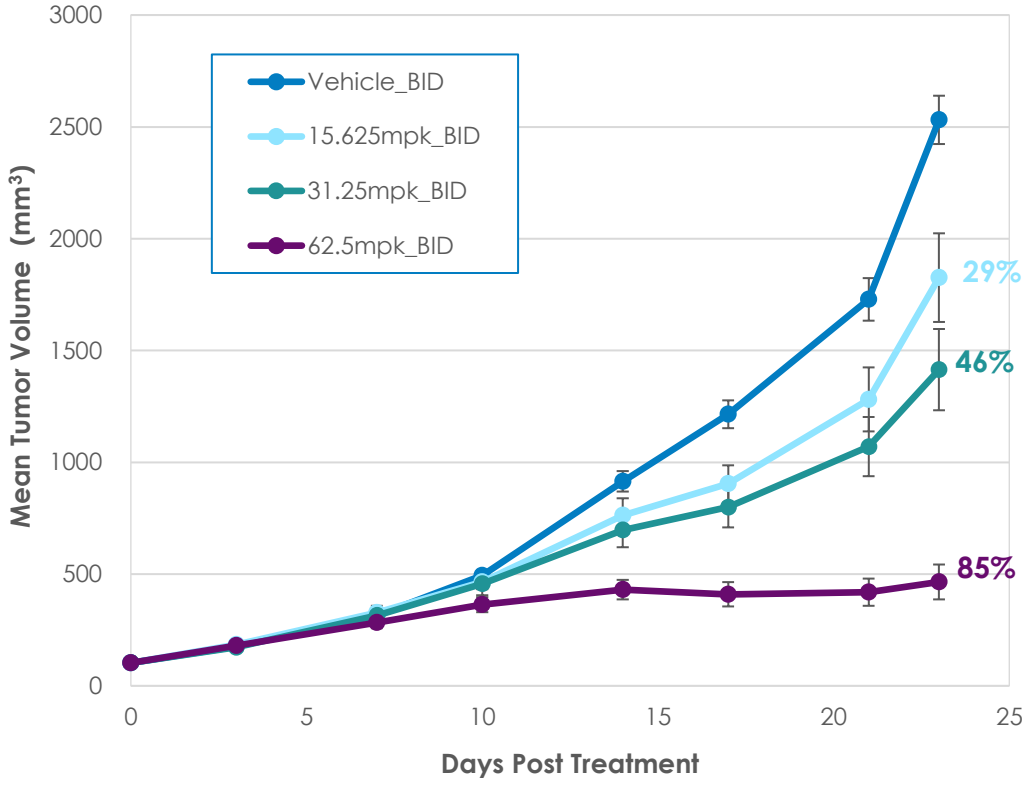
**EXCELLENT DRUG-LIKE PROPERTIES** – potential for oral administration

# SETD2 Inhibition Elicited Robust Tumor Inhibition/Regressions in a t(4;14) and Non-t(4;14) Multiple Myeloma Xenograft Models

## t(4;14) MM model

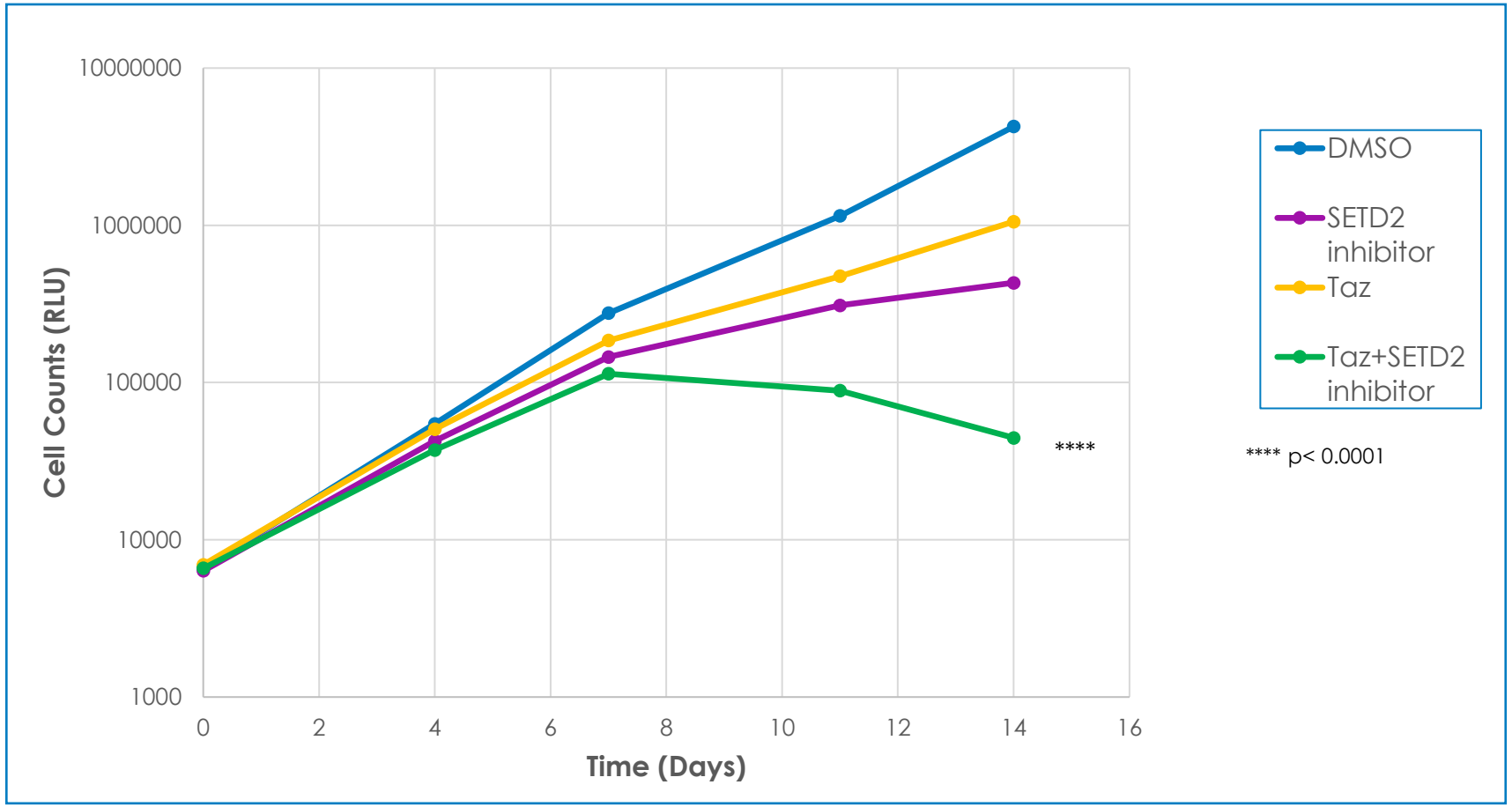



## Non-t(4;14) MM model




Epizyme

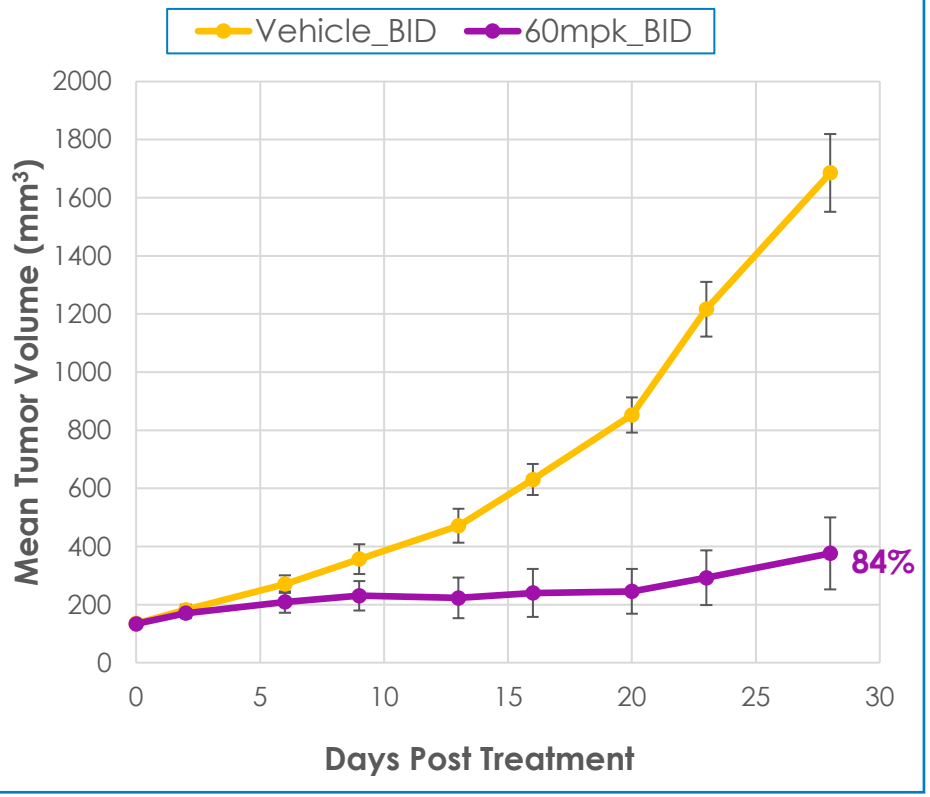
# Enhanced Anti-Proliferative Activity With Combination of SETD2 Inhibitor and Tazemetostat in t(4;14) Myeloma Cell Line Compared to Single Agents



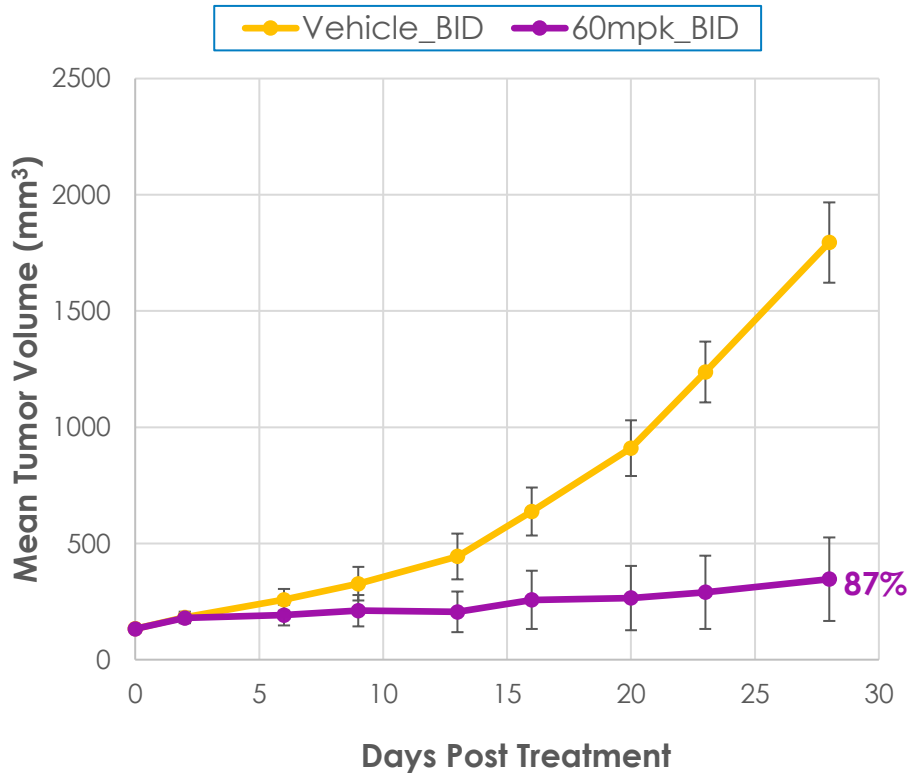

*P values derived from one-way ANOVA with Tukey's Multiple Comparisons of treatment compared to each of the dual combinations.*

# SETD2 Inhibitor Elicited Robust Tumor Inhibition in DLBCL *In Vivo* Models

## Germinal Center Cell type DLBCL




## Activated B Cell type DLBCL



# SETD2 Inhibitor Summary and Milestones

**Preclinical data to support rationale for investigating SETD2 in:**

**t(4;14) MM and non – t(4;14) MM**
as a single agent

**t(4;14) MM**
Synergy with tazemetostat

**t(4;14) MM and non – t(4;14) MM**
Synergy with existing MM therapies

**B-cell malignancies**
as a single agent

**Key Milestone for SETD2 inhibitor in 2021**

- IND filing planned mid-year

# Summary

# EPIZYME OVER THE NEXT 5 YEARS

THE NEXT EPIsode
REWRITING ONCOLOGY TREATMENT WITH EPIGENETICS

| | |
|---|---|
| 1 MAXIMIZE COMMERCIAL EFFECTIVENESS | TAZVERIK adopted as backbone therapy for FL<br>TAZVERIK utilized in multiple combination regimens |
| 2 BUILD ON TAVZERIK'S PIPELINE-IN-A-DRUG POTENTIAL | TAZVERIK approved in additional heme and solid tumor indications<br>Robust flow of data read-outs |
| 3 EXPAND PIPELINE & PORTFOLIO TO OVERCOME UNDRUGGABLE TARGETS | Five new clinical-stage programs<br>Evolving oncology portfolio company |
| 4 COLLABORATE TO EXPAND PATIENT REACH & BUILD VALUE | TAZVERIK partnered to reach ex-US markets<br>Multiple clinical and scientific collaborations |

# Multiple Value Driving Milestones Expected in 2021

- Continue to expand the commercial adoption of TAZVERIK® (tazemetostat) in FL and ES
- Phase 1b safety run-in data from EZH-301 clinical trial of TAZVERIK plus Doxorubicin in ES at ASCO
- Preclinical data for SETD2 at EHA; IND submission mid-2021
- Follow-up data from Phase 1b safety run-ins for EZH-302 in FL and EZH-1101 in mCRPC 2H 2021
- Advance to the efficacy stages of our ES, FL, and prostate cancer clinical programs
- Initiate novel basket trials in both hematological malignancies and solid tumors in 2H 2021
- Anticipated alignment with EMA on registration path for TAZVERIK in Europe

# 1Q 2021 FINANCIAL RESULTS

| Statement of Operations | Three Months Ended March 31 | |
|---|---|---|
| | **2021** | **2020** |
| **Total Revenue** | **$7.6M** | **$1.4M** |
| TAZVERIK Net Sales | $6.2M | $1.3M |
| Collaboration Revenue | $1.4M | $0.1M |
| **Total Operating Expenses** | **$72.0M** | **$52.7M** |
| Cost of Product Revenue | $2.9M | $0.6M |
| Research and Development | $32.7M | $25.2M |
| Selling, General and Administrative | $36.4M | $26.9M |
| **Net Loss Attributable to Common Stockholders** | $70.3M ($0.69 per share) | $50.9M ($0.51 per share) |

# BALANCE SHEET AND 2021 FINANCIAL GUIDANCE

| Balance Sheet | March 31, 2021 | December 31, 2020 |
|---|---|---|
| Cash, Cash Equivalents, and Marketable Securities | $298.9M | $373.6M |

- Full year 2021 non-GAAP adjusted cash expenses anticipated to be between $235 - $255M
- Cash runway expected to be sufficient to fund operations into 2023