

# Pioneering WEE1 Inhibition to Deliver More Convenient, Targeted Cancer Care

Corporate Presentation | August 2026

Nasdaq: ZNTL



# Forward Looking Statements and Disclaimer

Zentalis Pharmaceuticals, Inc. (“we,” “us,” “our,” “Zentalis” or the “Company”) cautions that this presentation (including oral commentary that accompanies this presentation) contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding the continued development of azenosertib; the clinical and therapeutic potential of azenosertib; the potential for azenosertib (ZN-c3) to be the first, oral, non-chemotherapy for ~50% of PROC patients and best-in-class; the Company’s development strategy and approach for azenosertib, including the Company’s strategy to focus on bringing azenosertib to patients with PROC who are Cyclin E1-positive and the potential for azenosertib to be a new treatment option for ovarian cancer patients and the potential opportunities for azenosertib as a monotherapy and in combination in other indications and in other tumor types, including in earlier lines of ovarian cancer and other tumor types; the Company’s planned strategy, vision and path forward; the market opportunity for azenosertib, including the opportunity in biomarker selected (Cyclin E1-positive) PROC patients and the potential size of the patient population; the potential for the opportunity for azenosertib to be broad/expansive; the potential for Cyclin E1 to serve as a predictive biomarker for response to azenosertib; the Company’s projected cash runway; planned clinical trials for our product candidates; the potential benefits of azenosertib, including compared to available therapies and therapies in development (not head-to-head comparisons); the potential unmet need in a particular indication and/or patient population; the timing and content of the Company’s anticipated milestones, including the completion of enrollment in all cohorts of DENALI Part 2; and the Company’s planned regulatory strategy for azenosertib and the timing thereof, including the potential for DENALI Part 2 to support an accelerated approval and the potential for ASPENOVA to support a full approval; as well as statements that include the words such as “anticipate,” “beyond,” “continue,” “design,” “estimate,” “expect,” “forward,” “intent,” “milestone,” “ongoing,” “opportunity,” “path,” “plan,” “potential,” “predictive,” “projected,” “strategy,” “support,” “vision,” “will” and similar statements of a future or forward-looking nature. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: our limited operating history, which may make it difficult to evaluate our current business and predict our future success and viability; we have and expect to continue to incur significant losses; our need for additional funding, which may not be available; our plans, including the costs thereof, of development of a companion diagnostic; the outcome of early clinical trials may not be predictive of the success of later clinical trials; failure to identify additional product candidates and develop or commercialize marketable products; potential unforeseen events during clinical trials could cause delays or other adverse consequences; risks relating to the regulatory approval process or ongoing regulatory obligations; failure to obtain U.S. or international marketing approval; azenosertib and any future product candidates may cause serious adverse side effects; the interim and preliminary data from our clinical trials may change as more patient data becomes available, and are subject to audit and verification procedures that could result in material changes in the final data; if our confirmatory trials do not verify clinical benefit, the FDA may seek to withdraw accelerated approval; our ability to establish effective sales or marketing capabilities; our reliance on third parties; the interim, initial, “topline,” and preliminary data from our clinical trials may change as more patient data becomes available, and are subject to audit and verification procedures that could result in material changes in the final data; our reliance on third parties; effects of significant competition; effects of significant competition; the possibility of system failures or security breaches; risks relating to intellectual property; our ability to attract, retain and motivate qualified personnel, and risks relating to management transitions; and significant costs as a result of operating as a public company. Other risks and uncertainties include those identified under the caption “Risk Factors” in our most recently filed periodic reports on Forms 10-K and 10-Q and subsequent filings with the U.S. Securities and Exchange Commission in the future could cause such forward-looking statements represent management’s estimates as of the date of this presentation. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. While we may elect to update these forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any law. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. Neither we nor our affiliates, advisors or representatives makes any representation as to the accuracy or completeness of that data or undertake to update such data after the date of this presentation.

Statements such as “not head-to-head,” “direct cross-study comparison not intended” and similar references indicate that no head-to-head clinical trial has been conducted evaluating azenosertib against the indicated therapies. Notable differences exist between the Company’s trial designs, conditions under study and subject characteristics as compared to the evaluated third party results and caution should be exercised when comparing data across these studies.

ZENTALIS® and its associated logos are trademarks of Zentalis and/or its affiliates. All other trademarks, trade names and service marks appearing in this presentation are the property of their respective owners. All website addresses given in this presentation are for information only and are not intended to be an active link or to incorporate any website information into this document.

Azenosertib is an investigational drug and has not yet been approved by the U.S. Food and Drug Administration or any other regulatory authority.



# A Focused Strategy to Address Critical Unmet Need in Ovarian Cancer and Beyond

---



Addressing **~20,000 Cyclin E1-positive PROC patients<sup>^</sup>** with no specifically targeted treatment options



Investigational first-in-class WEE1 inhibitor, azenosertib demonstrates compelling clinical profile as a **potential oral, non-chemo treatment** in Cyclin E1-positive PROC



**Clear development and regulatory strategy:** DENALI Part 2 topline readout expected 1H 2027 to support potential accelerated approval; ASPENOVIA Phase 3 trial enrolling, designed to support full approval

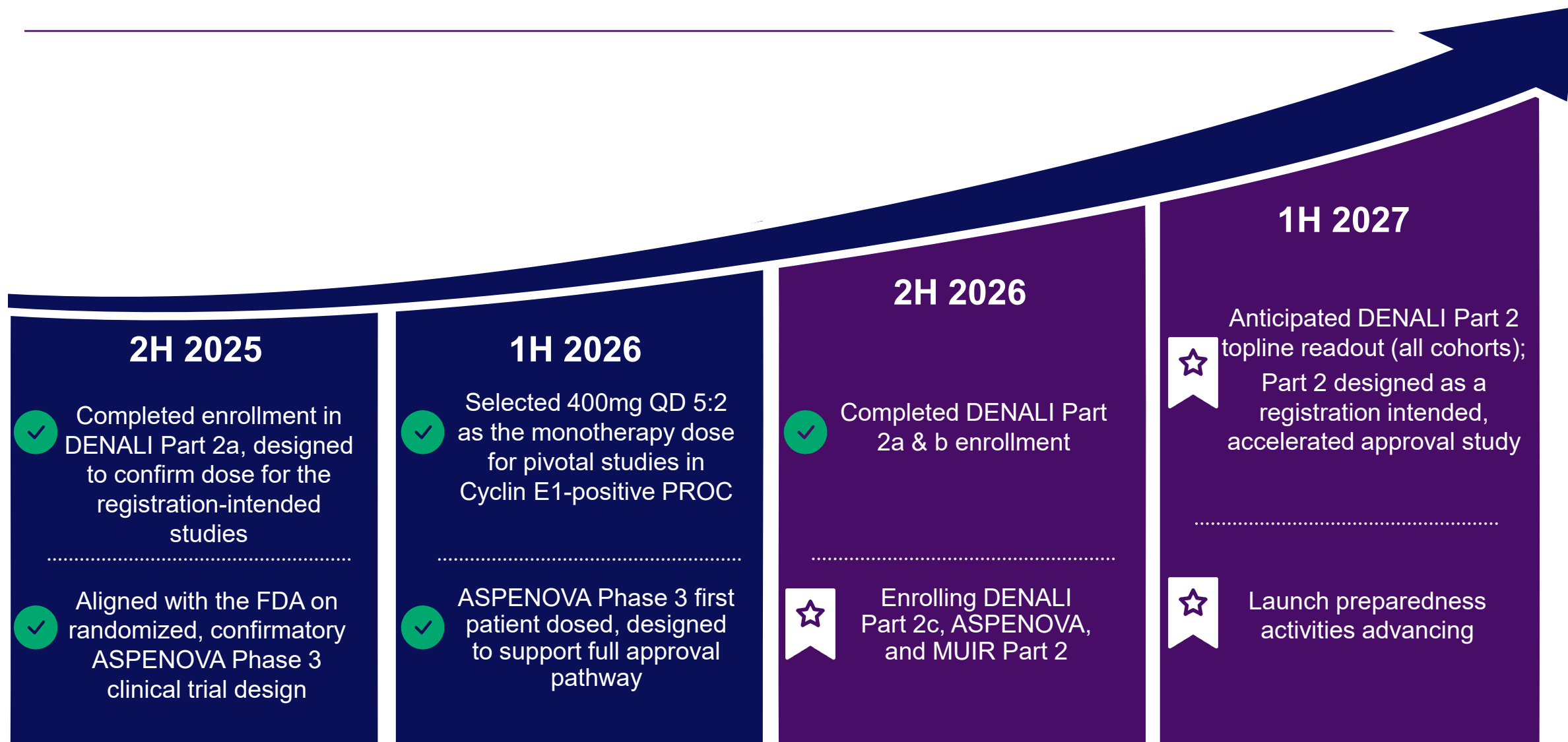


**Building azenosertib franchise** beyond PROC into earlier lines of ovarian cancer and other tumor types



Resourced to execute with **~\$175M cash<sup>†</sup>** providing runway into late 2027 and industry-leading WEE1 expertise and proven leadership

# Strong Execution Drives Momentum Towards Key Value Inflection Points



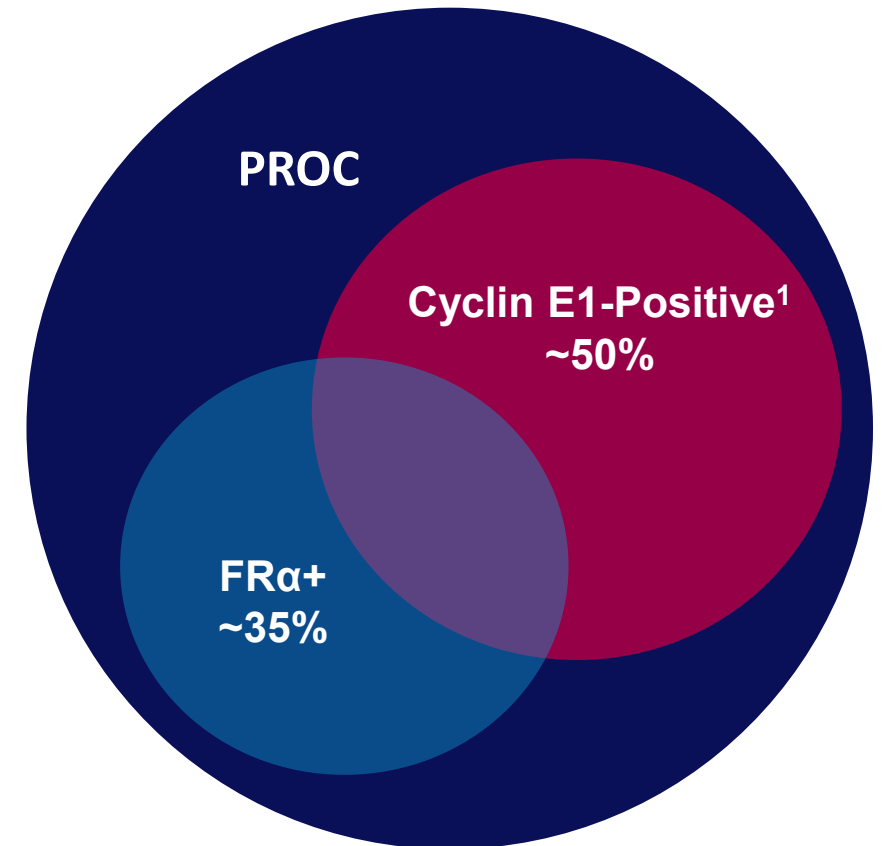
# ~50% of PROC Patients Are Cyclin E1-Positive With No Approved, Specifically Targeted Therapy

## The Unmet Need:

- ~20,000 patients with Cyclin E1-positive PROC<sup>2</sup>
- Standard-of-care single-agent chemotherapy delivers only **4-13% ORR** and **3-4 months PFS<sup>3</sup>** with high patient burden:
  - Due to safety and tolerability profiles, travel hours, and infusion time
- Cyclin E1-positivity is a biomarker of poor prognosis and low benefit from available treatments

## Proven Market Demand for Biomarker-Directed PROC Therapy:

- Elahere achieved **\$607M US sales in 2025<sup>4</sup>** in FR $\alpha$ + PROC patients
- Strong commercial potential for targeted therapies in biomarker-selected PROC populations



1. Cyclin E1-positive determined by an IHC assay and Zentalis proprietary cutoff

2. Based on 2025 Decision Resource estimates in US, EU4 (France, Germany, Italy, Spain), UK, and Japan

3. Eskander, R., et al. Front Oncol. 2023

4. Abbvie Q4 2025 Earnings

Note: Overlap between FR $\alpha$  high and Cyclin E1+ accounts for ~20% of all PROC, based on internal data

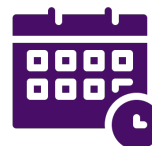
Abbreviations: PROC = platinum-resistant ovarian cancer; ORR = overall response rate; PFS = progression free survival

# Robust Clinical Foundation Supports Azenosertib as Potential First-in-Class WEE1 Inhibitor for Cyclin E1-Positive PROC



## Class-leading Clinical Experience

- **1,000+ patients treated** across multiple tumor types and dose levels in monotherapy and in combination with other agents
- Integrated learnings from ZN-c3-001, MAMMOTH and DENALI Part 1b inform registration strategy



## Optimized Dose & Schedule

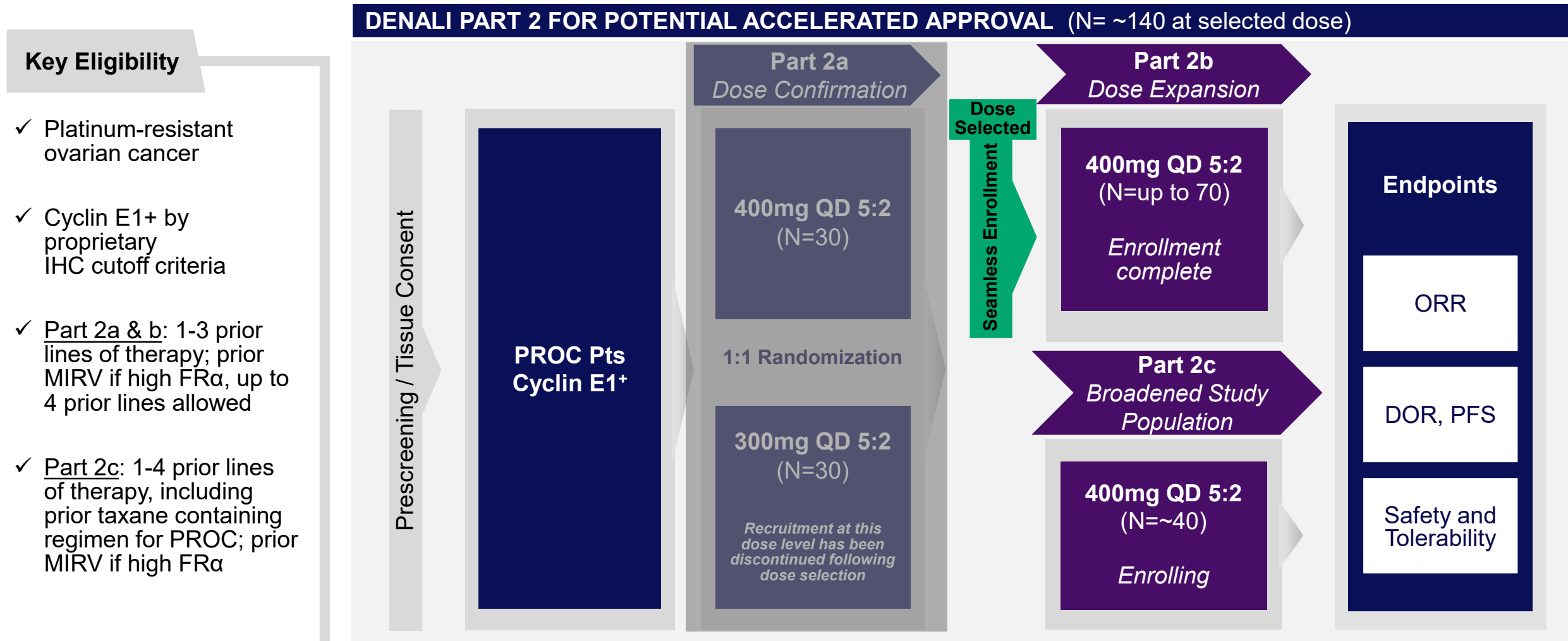
- **400mg QD 5:2** selected based on DENALI Part 2a interim analysis
- Meaningful response differentiation at 400mg vs. 300mg QD 5:2
- Key improvements in Part 2a vs. Part 1b: reported fewer discontinuations and improved select safety measures<sup>#</sup>



## Compelling Clinical Profile

- **>30% ORR and ~6 month DOR<sup>^</sup>** in Cyclin E1-positive PROC at 400mg QD 5:2
- Most common TRAEs include nausea, diarrhea, and fatigue and are clinically manageable<sup>†</sup>, supporting oral at-home dosing with appropriate monitoring

# DENALI: Phase 2 Registration-Intended Study in Cyclin E1-Positive PROC for Accelerated Approval



# ASPENOVA: Phase 3 Confirmatory Study in Cyclin E1-Positive PROC for Full Approval

## ASPENOVA RANDOMIZED TRIAL INTENDED FOR FULL APPROVAL (FDA Aligned, N= ~420)

### Key Eligibility

- ✓ Platinum-resistant ovarian cancer
- ✓ Cyclin E1+ by proprietary IHC cutoff criteria
- ✓ 1-3 prior lines of therapy
- ✓ Prior MIRV if high FR $\alpha$ , up to 4 prior lines allowed

Prescreening / Tissue Consent

PROC Pts  
Cyclin E1+

Azenosertib  
400mg QD 5:2  
(N = ~210)

1:1 Randomization

Investigator's Choice of Chemotherapy  
Paclitaxel, PLD, Gemcitabine, Topotecan  
(N = ~210)

Primary  
Endpoint

PFS

Key Secondary  
Endpoints

OS, ORR



# Focused Pipeline with Registration-Intended Cyclin E1-Positive PROC Trials

## Potential for Franchise Expansion in Earlier Lines of Ovarian Cancer and Other Tumor Types

| TRIAL                                                 | DEVELOPMENT APPROACH                                                                                                                                    | PHASE 1     | PHASE 2     | PHASE 3     | STATUS                                                                                                   |
|-------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|-------------|-------------|----------------------------------------------------------------------------------------------------------|
| Cyclin E1-Positive PROC Monotherapy (lead indication) |                                                                                                                                                         |             |             |             |                                                                                                          |
| DENALI                                                | <b>DENALI Part 1b</b><br>Demonstrated Cyclin E1 overexpression as biomarker predicting response to azenosertib                                          | <div></div> |             |             | In Long-term Follow-up Only                                                                              |
|                                                       | <b>DENALI Part 2a + 2b + 2c</b><br>Registration-intended Cyclin E1-Positive<br><i>FDA Fast Track Designation</i>                                        | <div></div> | <div></div> | <div></div> | Topline Readout Expected 1H2027<br><i>Parts 2a&amp;b enrollment complete</i><br><i>Part 2c enrolling</i> |
| ASPENOVA                                              | <b>Azenosertib vs. SOC chemo</b><br>Randomized, confirmatory trial<br>Cyclin E1-Positive                                                                | <div></div> |             |             | First Patient Dosed Q2 2026<br><i>Enrolling</i>                                                          |
| Ovarian Cancer Combination Therapy                    |                                                                                                                                                         |             |             |             |                                                                                                          |
| MUIR*                                                 | <b>Part 2:</b> Azenosertib + bevacizumab (1L/2L PSOC maintenance therapy)<br><b>Part 1:</b> Azenosertib + multiple chemo backbones (in PROC, completed) | <div></div> | <div></div> | <div></div> | Ongoing<br><i>Part 2 Enrolling</i>                                                                       |

Abbreviations: PROC = platinum-resistant ovarian cancer; SOC = standard-of-care; 1L = first line; 2L = second line; PSOC = platinum-sensitive ovarian cancer  
\* Also known as ZN-c3-002

# **Cyclin E1-Positive PROC Patients Face Poor Prognosis with No Specifically Targeted Treatment Options**

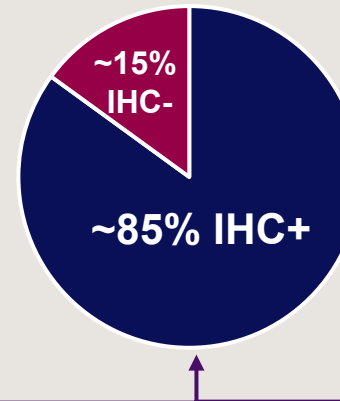


# Cyclin E1 Protein Overexpression is the Key Biomarker Identifying PROC Patients Who may Benefit from Azenosertib Monotherapy

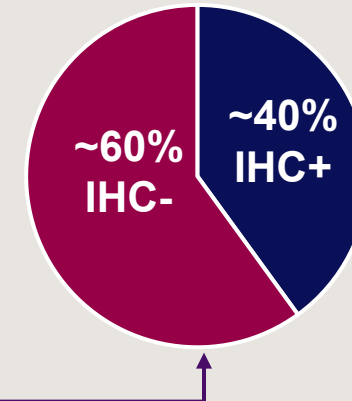
All PROC Patients Should Be Screened by IHC Regardless of CCNE1 Gene Amplification Status

~50% of PROC patients estimated to be Cyclin E1 IHC+\*, more than doubling the CCNE1 amplification population

CCNE1 Amplified  
(~20% of PROC)



CCNE1 Non-Amplified  
(~80% of PROC)



Multiple mechanisms drive Cyclin E1 protein overexpression<sup>1</sup>, including:

- CCNE1 gene amplification
- Increased gene transcription
- Reduced protein degradation

IHC testing on archival tissues to identify Cyclin E1-positive patients

- Zentalis' proprietary IHC cutoff determined through results from multiple early clinical trials
- Same cutoff being validated in registration-intended trials
- CDx registration and market development under way

\*Cyclin E1 IHC+ based on Zentalis proprietary IHC cutoff and Cyclin E1 IHC assay developed from multiple early clinical trials; Cyclin E1 IHC+% based on literature and the unbiased CCNE1 amp & Cyclin E1 overlapping data generated from Zentalis clinical trial samples

1. Kim, D., et al. Cyclin E1/CDK2 activation defines a key vulnerability to WEE1 kinase inhibition in gynecological cancers, npj Precis. Onc. 9, 3 (2025).

Abbreviations: IHC = immunohistochemistry; CDx = companion diagnostic

# Cyclin E1-Positive Patients Experience Significantly Worse Outcomes with Current Treatments

|                                                | Tempus Lens Real World Data <sup>^†</sup><br>(N=193) | Prior Tx Data from Patients Enrolled in Azenosertib Clinical Trials <sup>^</sup><br>(N=79) |
|------------------------------------------------|------------------------------------------------------|--------------------------------------------------------------------------------------------|
| Cyclin E1 Status                               | 1L OC mPFS                                           | 1L OC mTTNT                                                                                |
| Cyclin E1-positive with CCNE1 amplification    | 13.6 months                                          | 13.2 months                                                                                |
| Cyclin E1-positive without CCNE1 amplification | 13.5 months                                          | 14.9 months                                                                                |
| Cyclin E1-negative                             | 18.9 months                                          | 19.5 months                                                                                |
| P-value                                        | 0.18                                                 | 0.002                                                                                      |

- Cyclin E1-positive ovarian cancer patients show **consistently poor outcomes across two independent cohorts** and worse prognosis independent of CCNE1 gene amplification status
- **Trend toward reduced clinical benefit from available PROC therapies** in Cyclin E1-positive patients<sup>^</sup>

*Worse outcome of Cyclin E1-positive ovarian cancer patients highlights critical unmet need for targeted therapies in this population*

# Standard-of-Care\* Single-Agent Chemotherapy Delivers Limited Benefits to PROC Patients

| Study                                             | Study Population                                                | Chemotherapy Arm               | ORR, % | mPFS, mo | mOS, mo |
|---------------------------------------------------|-----------------------------------------------------------------|--------------------------------|--------|----------|---------|
| <b>JAVELIN Ovarian 200<sup>1</sup></b><br>(n=190) | ≤3 priors, 75% PROC and 25% Platinum refractory (28% prior bev) | PLD                            | 4      | 3.5      | 15.7    |
| <b>FORWARD I re-read<sup>2</sup></b><br>(n=61)    | PROC 1–3 priors high FRα (33% prior bev)                        | Paclitaxel or PLD or topotecan | 6      | 3.2      | 12      |
| <b>CORAIL<sup>3</sup></b><br>(n=199)              | PROC ≤3 priors (46% prior bev)                                  | PLD or topotecan               | 12     | 3.6      | 11      |
| <b>NINJA<sup>4</sup></b><br>(n=159)               | PROC 77% >2 prior                                               | Gemcitabine or PLD             | 13     | 3.8      | 12.1    |
| <b>AURELIA<sup>5</sup></b><br>(n=182)             | PROC ≤2 priors; 25% platinum refractory (8% prior bev)          | Paclitaxel or PLD or topotecan | 13     | 3.4      | 13.3    |

***SOC with limited benefits and high patient burden (time toxicity from IV, hair loss, and neuropathy) highlights the urgent unmet needs in PROC***

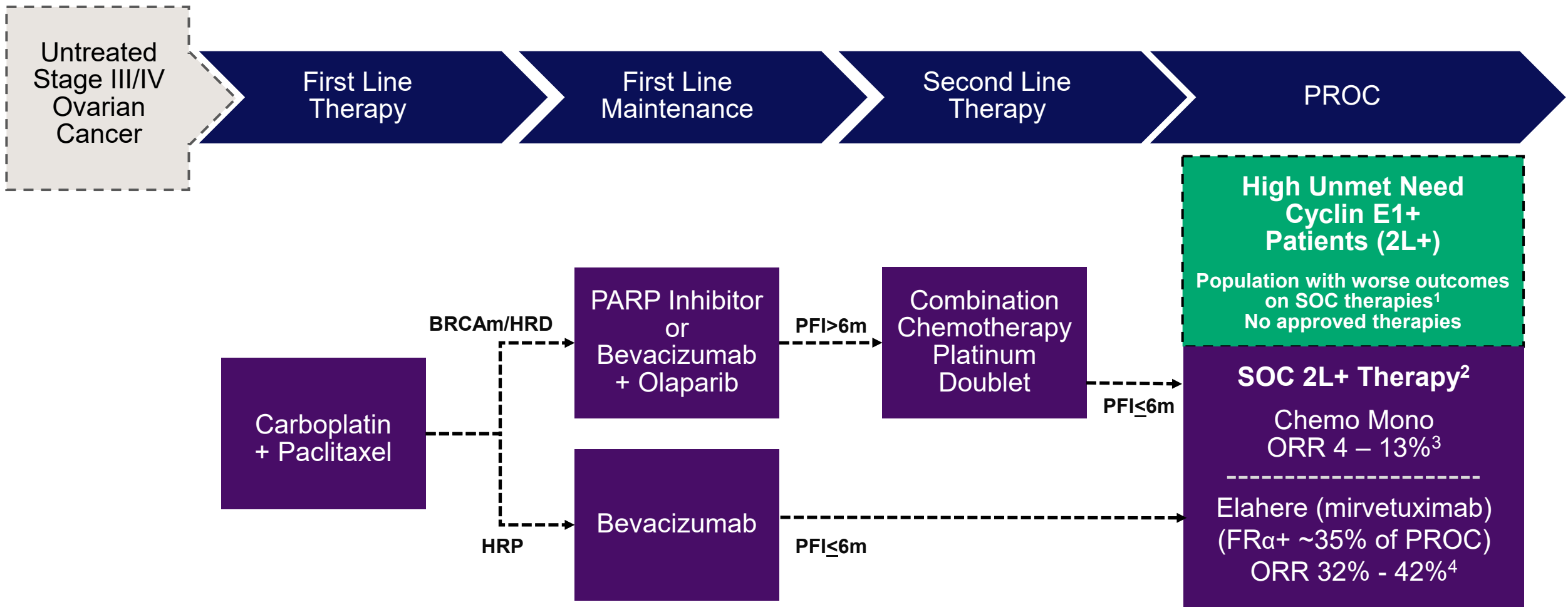
Direct cross-study comparison of results from independently conducted clinical trials is not intended on this slide. \* Excludes recently approved taxane combo regimens

Abbreviations: bev, bevacizumab; FRα, folate receptor alpha; IV, intravenous administration; mo, months; ORR, objective response rate; PFS, progression-free survival; PLD, pegylated liposomal doxorubicin; PROC, platinum-resistant ovarian cancer; mPFS = median progression-free survival; mOS = median overall survival

1. Pujade Lauraine E et al. *Lancet Oncol.* 2021;22(7):1034-1046, 2. Moore KN et al. ESMO 2019, 3. Gaillard SL et al. ESMO 2018, 4. Omatsu K ESMO 2020, 5. Pujade-Lauraine E et al. *J Clin Oncol.* 2014;32(13):1302–1308.

# Azenosertib May Address Critical Gap in Cyclin E1-Positive PROC Treatment Landscape\*

No approved therapies specifically for Cyclin E1+ PROC presents opportunity for azenosertib as potentially first, oral, non-chemotherapy for ~50% of PROC patients



\*If successful in clinical testing and approved by regulators

Abbreviations: PROC = platinum-resistant ovarian cancer; FRα = Folate Receptor alpha

<sup>1</sup>Jeong et al., AACR 2026, Poster #1708; <sup>2</sup> Excludes recently approved taxane combo regimens; <sup>3</sup> Eskander, R., et al. Overcoming the Challenges in Drug Development, Front Oncol. 2023 Oct 17; 13:1258228;

<sup>4</sup> Clinical Trial SORAYA ORR 32%, MIRASOL ORR 42%;



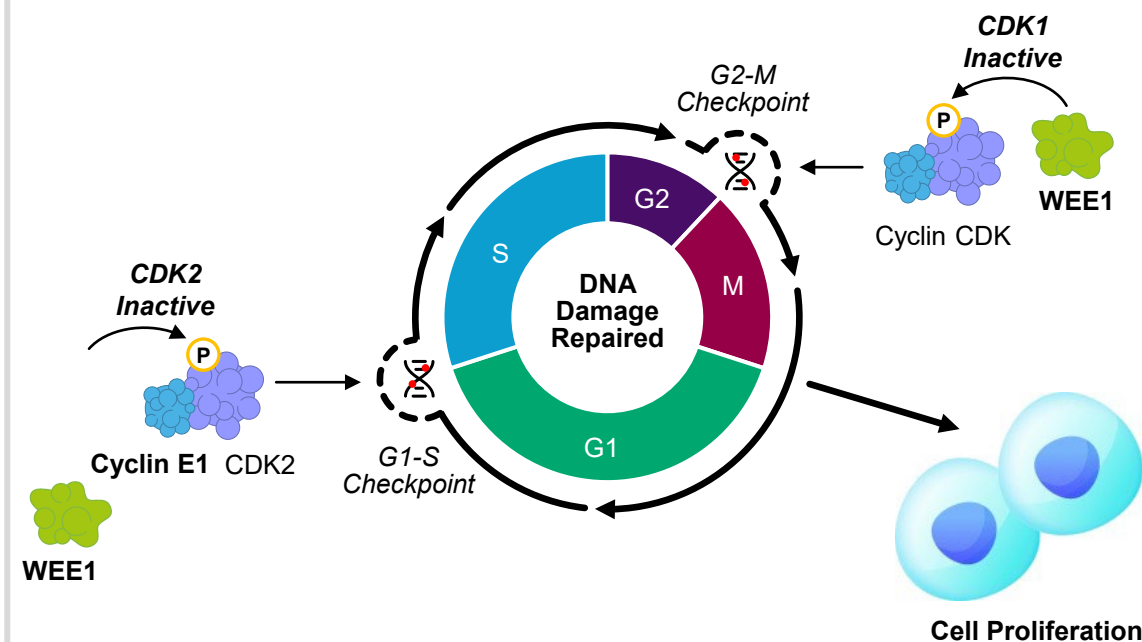
# Compelling Clinical Profile Across Multiple Studies Supports Cyclin E1-Positive PROC Registration Strategy



# Azenosertib: A Differentiated, Potentially First-in-Class WEE1 Inhibitor

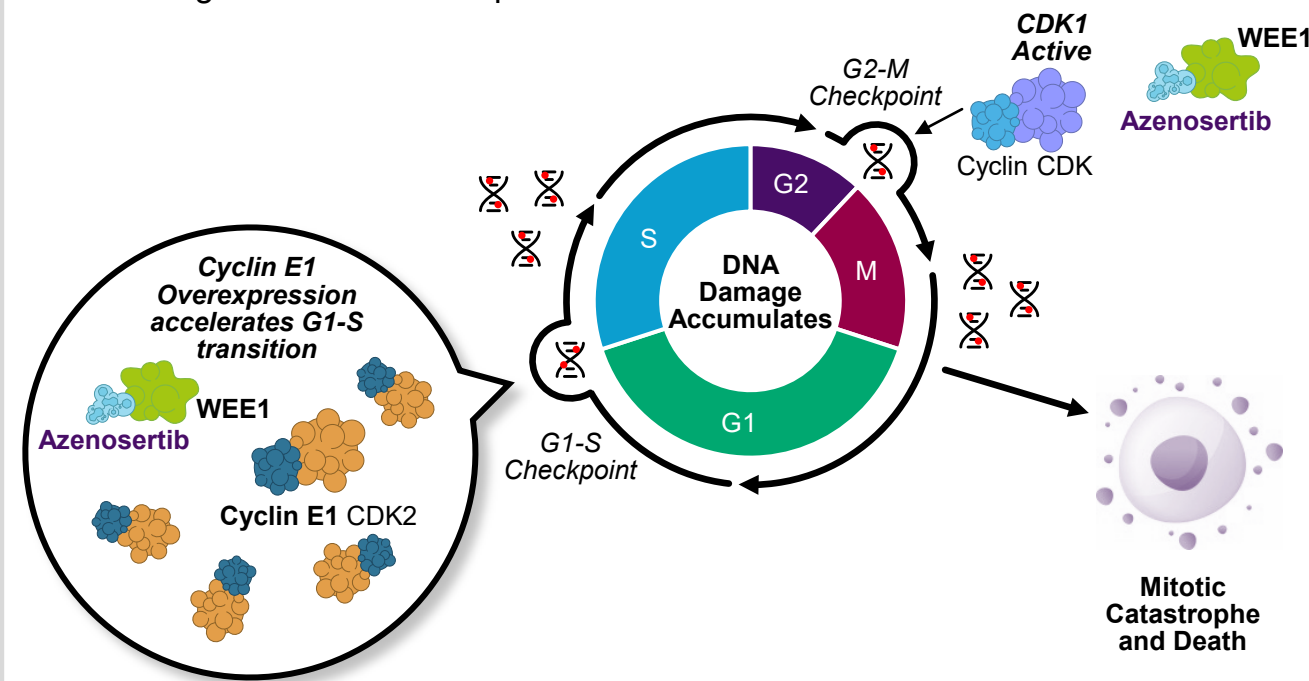
## Normal Cell Cycle Regulation

- CDKs and their cyclin binding partners promote progression through the cell cycle
- Following DNA damage, WEE1 kinase inactivates Cyclin/CDK complexes at both G1-S and G2-M checkpoints to halt the cell cycle and allow for repair
- Upon DNA repair, cells progress through the cell cycle and proliferate



## Cancer Cell and Azenosertib

- Cyclin E1 overexpression increases CDK2 activity and accelerates G1-S transition, rendering cells more dependent on the DNA repair at the G2-M checkpoint
- Inhibition of WEE1 activates CDKs, accelerates G1-S and G2-M transitions, and increases DNA damage to intolerable levels, resulting in mitotic catastrophe and cell death



**P** Phosphorylation, causing inactivation of CDK1/2

**⚡** DNA damage



# Integrated Data Across Multiple Early Clinical Studies Demonstrate Compelling Benefit-Risk Profile for Azenosertib Monotherapy in PROC

Learnings from ZN-c3-001, MAMMOTH, and DENALI Part 1b Inform Registration Strategy in Cyclin E1+ PROC

## ZN-c3-001

First-in-human, solid tumors  
N=40 (PROC, intermittent dosing)  
300mg & 400mg QD 5:2  
✓ *Therapeutic window established in PROC with intermittent dosing*

## MAMMOTH

PARPi-resistant PROC  
N=61  
300mg & 400mg QD 5:2  
✓ *Activity confirmed in heavily pre-treated, PARPi-resistant population*

## DENALI Part 1b

PROC, All-comers  
N=102  
400mg QD 5:2  
✓ *Retrospective analysis demonstrated Cyclin E1 as predictive biomarker*

### Integrated Efficacy Analysis of Cyclin E1-positive PROC Patients

400mg QD 5:2 (N=73)

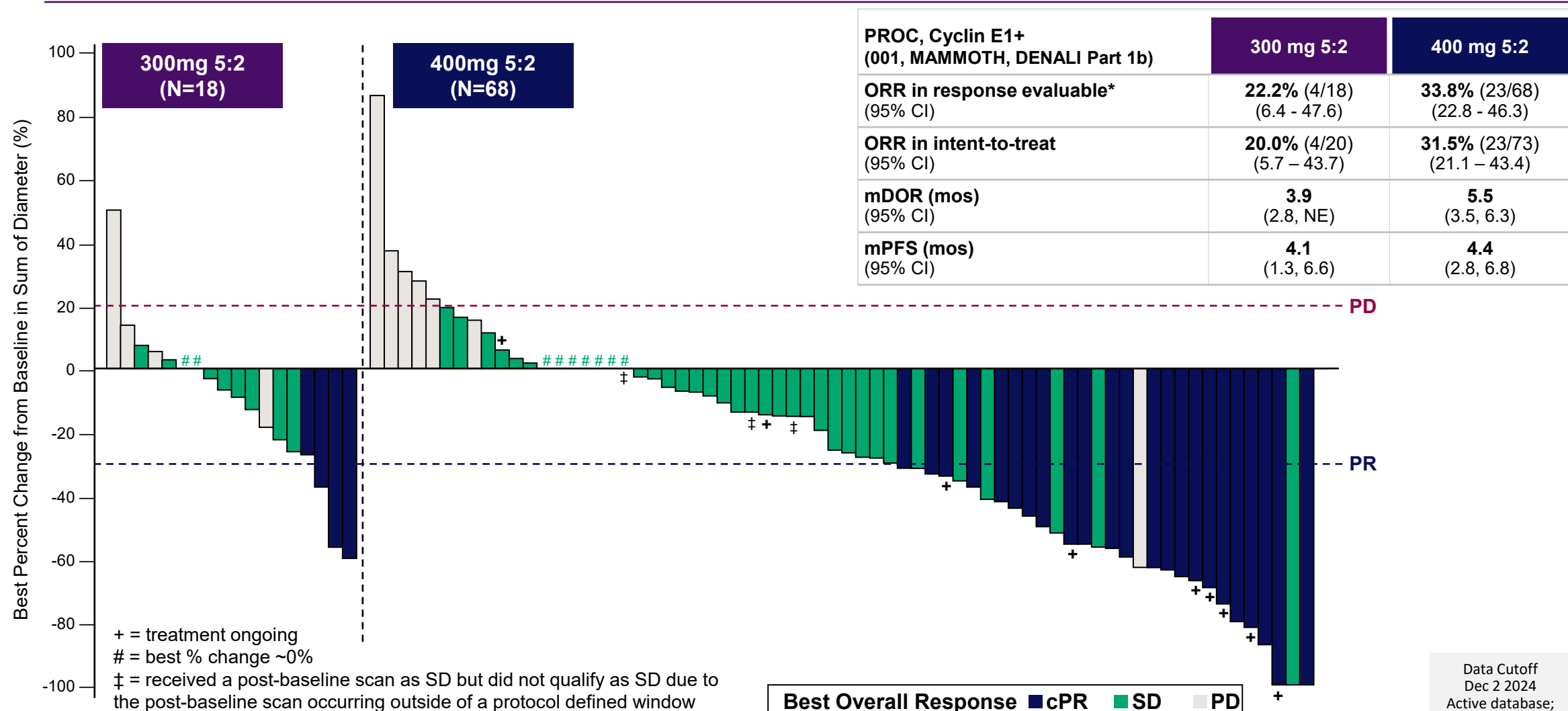
300mg QD 5:2 (N=20)

### Integrated Safety Analysis of PROC Patients

400mg QD 5:2 (N=165)

300mg QD 5:2 (N=38)

# 400mg QD 5:2 Shows >30% ORR and ~6 Month Duration in Cyclin E1-Positive PROC



Data Cutoff  
Dec 2 2024  
Active database;  
subject to further  
change

# Safety and Tolerability at 300mg and 400mg QD 5:2 Broadly Comparable

## Monotherapy Safety Profiles in PROC Patients from Integrated Analysis (001, MAMMOTH, DENALI Part 1b)

| Treatment-related AEs*, N (%) | 300mg (N=38) |          | 400mg (N=165) |            | Treatment-related AEs, N (%)                                                                                                                                                                                                                                   | 300mg (N=38) | 400mg (N=165) |
|-------------------------------|--------------|----------|---------------|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|---------------|
|                               | All Grade    | Grade 3+ | All Grade     | Grade 3+   |                                                                                                                                                                                                                                                                |              |               |
| <b>Gastrointestinal</b>       |              |          |               |            |                                                                                                                                                                                                                                                                |              |               |
| Decreased appetite            | 8 (21.1%)    | 1 (2.6%) | 40 (24.2%)    | 2 (1.2%)   | Treatment-Related SAE                                                                                                                                                                                                                                          | 6 (15.8%)    | 31 (18.8%)    |
| Diarrhea                      | 18 (47.4%)   | 1 (2.6%) | 86 (52.1%)    | 12 (7.3%)  | TRAE leading to dose reduction                                                                                                                                                                                                                                 | 13 (34.2%)   | 69 (41.8%)    |
| Nausea                        | 23 (60.5%)   | 0        | 101 (61.2%)   | 6 (3.6%)   | TRAE leading to dose interruption                                                                                                                                                                                                                              | 16 (42.1%)   | 89 (53.9%)    |
| Vomiting                      | 3 (7.9%)     | 0        | 17 (10.3%)    | 3 (1.8%)   | TRAE leading to discontinuation                                                                                                                                                                                                                                | 5 (13.2%)    | 26 (15.8%)    |
| Dehydration                   | 1 (2.6%)     | 0        | 14 (8.5%)     | 1 (0.6%)   | TRAE leading to death                                                                                                                                                                                                                                          | 0            | 3 (1.8%)      |
| <b>Fatigue</b>                | 14 (36.8%)   | 2 (5.3%) | 90 (54.5%)    | 20 (12.1%) | <ul style="list-style-type: none"> <li>• While numerically different, broadly comparable safety profiles at 300mg and 400mg 5:2</li> <li>• Low frequency of G3+ febrile neutropenia, sepsis, and previously reported G5 TRAEs observed at 400mg 5:2</li> </ul> |              |               |
| <b>Sepsis</b>                 | 0            | 0        | 4 (2.4%)      | 4 (2.4%)   |                                                                                                                                                                                                                                                                |              |               |
| <b>Hematologic</b>            |              |          |               |            |                                                                                                                                                                                                                                                                |              |               |
| Anemia                        | 13 (34.2%)   | 3 (7.9%) | 53 (32.1%)    | 20 (12.1%) |                                                                                                                                                                                                                                                                |              |               |
| Thrombocytopenia              | 13 (34.2%)   | 2 (5.3%) | 36 (21.8%)    | 8 (4.8%)   |                                                                                                                                                                                                                                                                |              |               |
| Neutropenia                   | 4 (10.5%)    | 3 (7.9%) | 30 (18.2%)    | 21 (12.7%) |                                                                                                                                                                                                                                                                |              |               |
| Febrile Neutropenia           | 0            | 0        | 4 (2.4%)      | 4 (2.4%)   |                                                                                                                                                                                                                                                                |              |               |

\* TRAEs listed here represent adverse events of special interest and adverse events of clinical significance for azenosertib and this class of molecules

# DENALI Part 1b Patient Characteristics: Heavily Pre-Treated PROC Population

~50% of Patients Identified with Cyclin E1 Overexpression per IHC Retrospectively

| Characteristics <sup>a</sup> (N=102) |            |
|--------------------------------------|------------|
| Median age (range), years            | 66 (34-82) |
| Race, n (%)                          |            |
| White                                | 70 (69)    |
| Black/African American               | 6 (6)      |
| Asian                                | 3 (3)      |
| Other <sup>b</sup>                   | 1 (1)      |
| Not reported                         | 22 (21)    |
| ECOG PS, n (%)                       |            |
| 0                                    | 53 (52)    |
| 1                                    | 49 (48)    |
| Prior lines of treatment             |            |
| Median (range)                       | 3 (1-5)    |
| 1-2, n (%)                           | 35 (34)    |
| 3-4, n (%)                           | 57 (56)    |
| 5, n (%)                             | 10 (10)    |

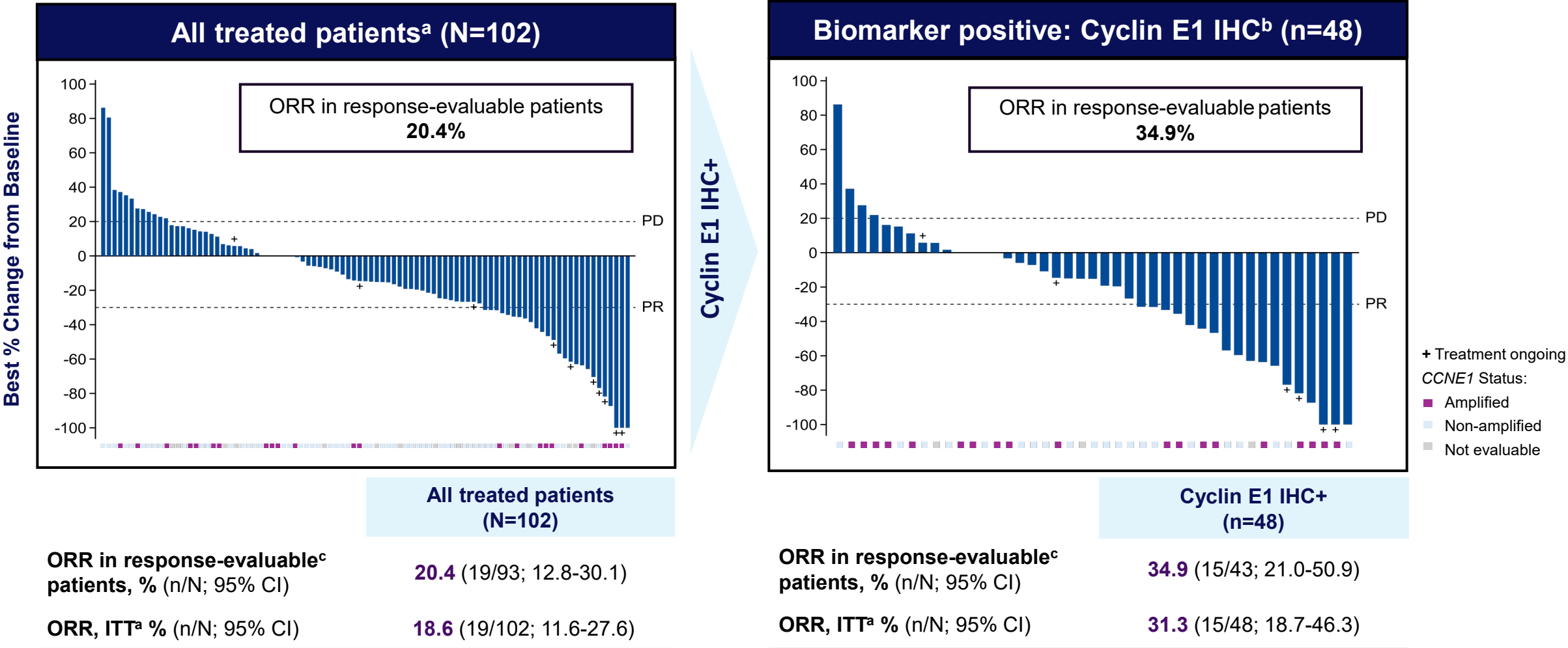
| Characteristics <sup>a</sup> (N=102) |         |
|--------------------------------------|---------|
| Prior therapy, n (%)                 |         |
| Bevacizumab                          | 93 (91) |
| PARPi                                | 57 (56) |
| Mirvetuximab                         | 15 (15) |
| CCNE1 amplification, <sup>c</sup>    |         |
| Evaluable, n                         | 88      |
| Amplified, n (%)                     | 27 (31) |
| Cyclin E1 status by IHC              |         |
| Evaluable, n                         | 94      |
| IHC+, n (%)                          | 48 (51) |

***DENALI Part 1b enrolled patients with 1-5 prior lines of therapy (>65% had 3+ prior lines)***

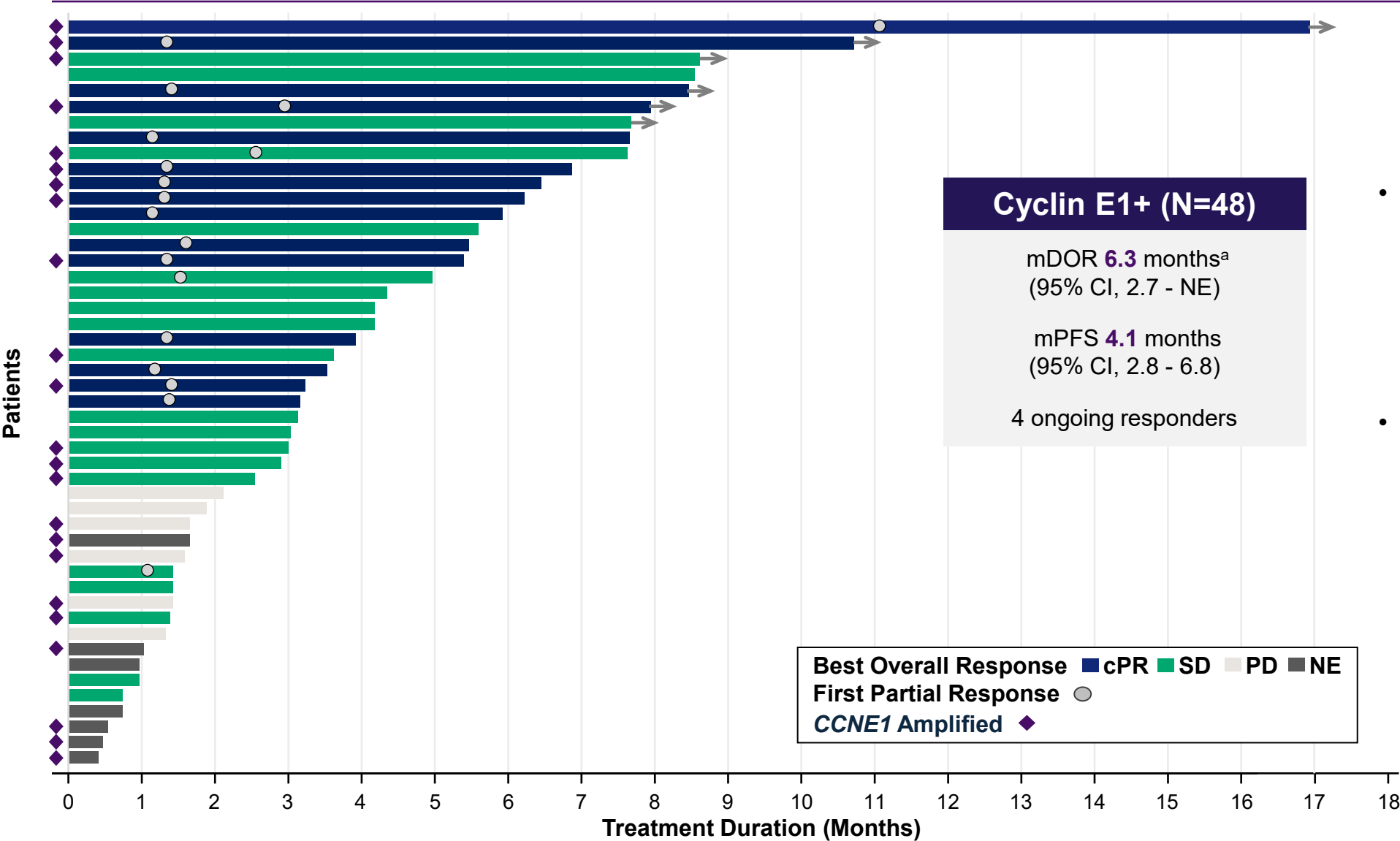
Data cutoff date: January 13, 2025. <sup>a</sup>Full analysis set: all treated patients. Biomarker dataset: all treated patients with evaluable tissue and Cyclin E1 IHC status. <sup>b</sup>Hispanic. <sup>c</sup>85% (23/27) of patients with CCNE1-amplified tumors were also Cyclin E1+ by IHC. Amp, amplified; CCNE1 amplification defined as Copy Number ratio ≥3 with genomic ploidy correction as per Foundation Medicine. ECOG PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry; PARPi, poly(ADP-ribose) polymerase inhibitor.

# DENALI Part 1b Demonstrated Cyclin E1 as Predictive Biomarker for Response to Azenosertib

34.9% ORR in Cyclin E1-Positive Patients vs 20.4% in All-Comers



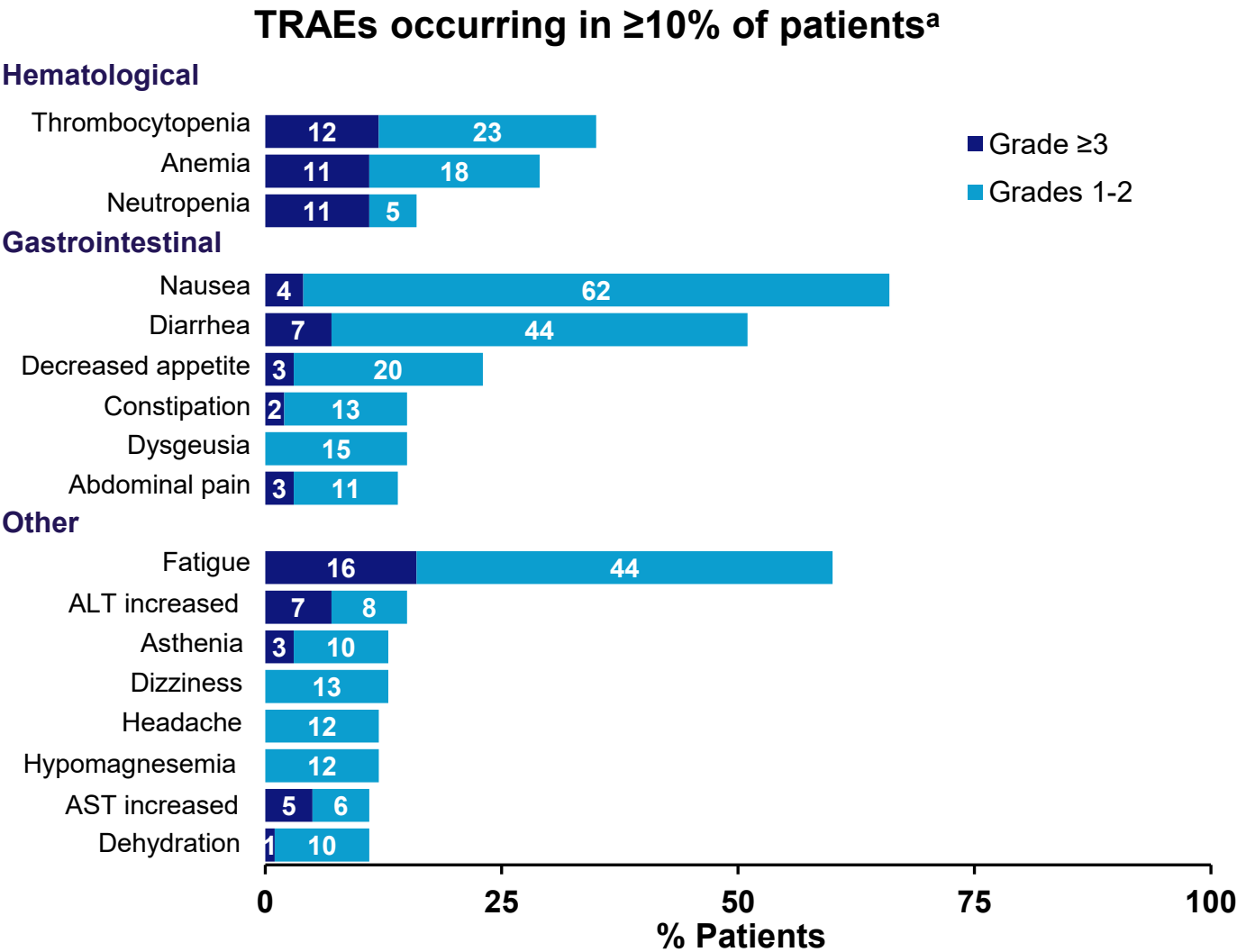
# Durable Responses Observed in Cyclin E1-Positive PROC Patients



- Durable responses observed regardless of **CCNE1 amplification status**, reinforcing Cyclin E1 IHC as the predictive biomarker
- Supports potential for **sustained clinical benefit** in biomarker-selected PROC population with limited treatment options



# DENALI Part 1b Safety and Tolerability Summary



| TRAEs, n (%)                 |                      |
|------------------------------|----------------------|
| Leading to dose reduction    | 44 (43.1)            |
| Leading to dose interruption | 59 (57.8)            |
| Leading to discontinuation   | 22 (21.6)            |
| Leading to death             | 2 (2.0) <sup>b</sup> |
| Serious TRAEs                | 22 (21.6)            |

- **Part 1b informed enhanced trial management and supportive care protocols** for registration-intended DENALI Part 2
- **Part 2a showed ~50% reduction in discontinuation rate and no treatment-related deaths**, validating trial management & supportive care optimizations

Data cutoff date: January 13, 2025

<sup>a</sup>If a patient had multiple grades of the same adverse event, The worse grade was reported <sup>b</sup>One patient had sepsis, and one patient had pancytopenia.  
ALT, alanine aminotransferase; AST, aspartate aminotransferase; TRAE, treatment-related adverse event.

# Building Azenosertib Franchise in Ovarian Cancer and Beyond



# MUIR: Ongoing Phase 1b, **Part 2** Study of Azenosertib in Combination with Bevacizumab Focused on Platinum Sensitive Ovarian Cancer

## Key Eligibility

- ✓ Advanced ovarian, peritoneal, or fallopian tube cancer
- ✓ Part 1: 1-2 prior lines of therapy; platinum-resistant
- ✓ Part 2 Dose Escalation: 1L maintenance or platinum-sensitive 2L maintenance
- ✓ Part 2 Dose Expansion: Platinum-sensitive 2L maintenance; progressed while on a PARPi for 1L maintenance

## Part 1 *Azenosertib + Chemo Combo in PROC*

Azenosertib +  
Carboplatin,  
Gemcitabine,  
Pegylated liposomal  
doxorubicin, or  
Paclitaxel

### Primary Endpoints

Safety and Tolerability

### Key Secondary Endpoints

ORR, DOR, PFS

Completed

## Part 2 *Azenosertib + Bevacizumab as 1L/2L PSOC Maintenance Therapy*

### Dose Escalation

Assess safety and  
recommended dose of  
azenosertib + bevacizumab

### Dose Expansion

Evaluate azenosertib at  
recommended dose in  
combination with  
bevacizumab

### Primary Endpoints

Safety and Tolerability

### Key Secondary Endpoint

PFS

Enrolling

Open for enrollment

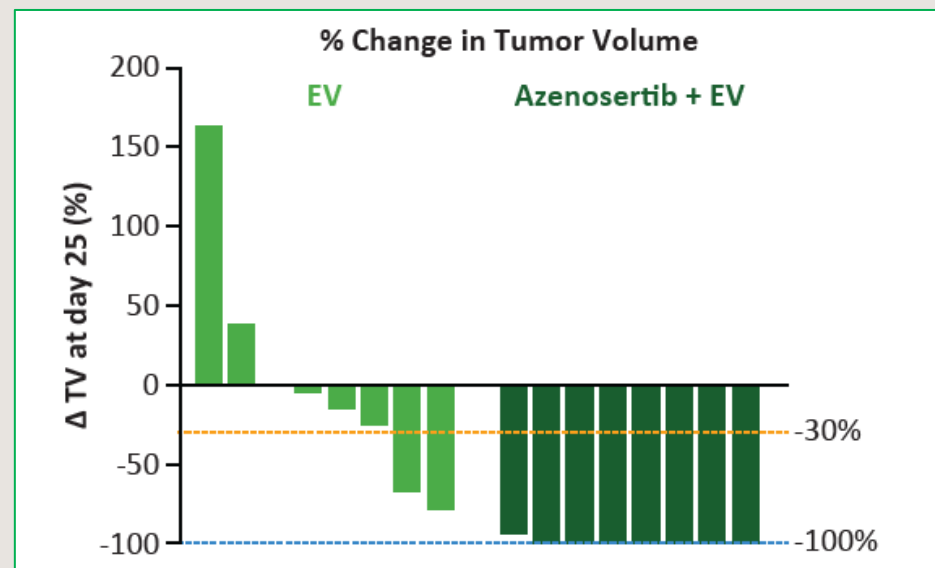


# Azenosertib Combinations Demonstrate Compelling Activity in Preclinical ADC-Resistant Triple-Negative Breast Cancer Models

## TNBC Exhibits High Cyclin E1 Expression and Sensitivity to WEE1 Inhibition

- As ADCs advance toward first-line use in TNBC, **post-ADC resistance represents a growing unmet need** that azenosertib combinations may be uniquely positioned to address
- Azenosertib may address ADC resistance through **multiple mechanisms: resensitizing tumors to chemotherapy, enhancing ADC responses, and extending duration of response**

### Azenosertib + EV Induces Complete Responses in TOPO1i ADC-Resistant TNBC Model



Percent change in tumor volume for individual mice on last day of treatment. Orange dashed line = partial response threshold (-30%); Blue dashed line = complete response threshold (-100%)

| Treatment Group  | PR at Day 25 | CR at Day 25 |
|------------------|--------------|--------------|
| EV               | 2/8 (25%)    | 0/8 (0%)     |
| Azenosertib + EV | 1/8 (12.5%)  | 7/8 (87.5%)  |

**87.5% CR rate (7/8 mice) with Azenosertib + EV vs. 0% CR with EV alone**

# **Pioneering WEE1 Inhibition to Deliver More Convenient, Targeted Cancer Care for Patients with Cyclin E1-Positive Ovarian Cancer and Beyond**

# Our Mission: Delivering a More Convenient, Targeted Approach to Cancer Care

---



- First investigational oral, non-chemo targeted therapy for Cyclin E1-positive PROC patients with no specifically targeted treatment options
- Compelling azenosertib clinical profile: >30% ORR and ~6 month mDOR\* in biomarker-selected population at 400mg QD 5:2
- Clear development and regulatory strategy: DENALI Part 2 topline readout expected 1H 2027 to support potential accelerated approval; ASPENOVA confirmatory Phase 3 trial enrolling
- Franchise expansion opportunities: in earlier lines of ovarian cancer and other tumor types
- Resourced to execute: ~\$175M cash\*\* with runway into late 2027

\* Integrated analysis across 001, MAMMOTH and DENALI Part 1b at 400mg QD 5:2

\*\* Cash, cash equivalents and marketable securities as of 6/30/26

Abbreviations: PROC = platinum-resistant ovarian cancer; ORR = overall response rate; mDOR = median duration of response; 5:2 schedule = 5 days once-daily administration of azenosertib, followed by 2 days without azenosertib



Julie Eastland

Chief Executive Officer  
[jeastland@zentalis.com](mailto:jeastland@zentalis.com)

Haibo Wang

Chief Business Officer  
[hwang@zentalis.com](mailto:hwang@zentalis.com)

Aron Feingold

VP, IR and Corporate Communications  
[afeingold@zentalis.com](mailto:afeingold@zentalis.com)