zentalis®

Corporate Presentation

April 2026

Nasdaq: ZNTL

Forward Looking Statements and Disclaimer

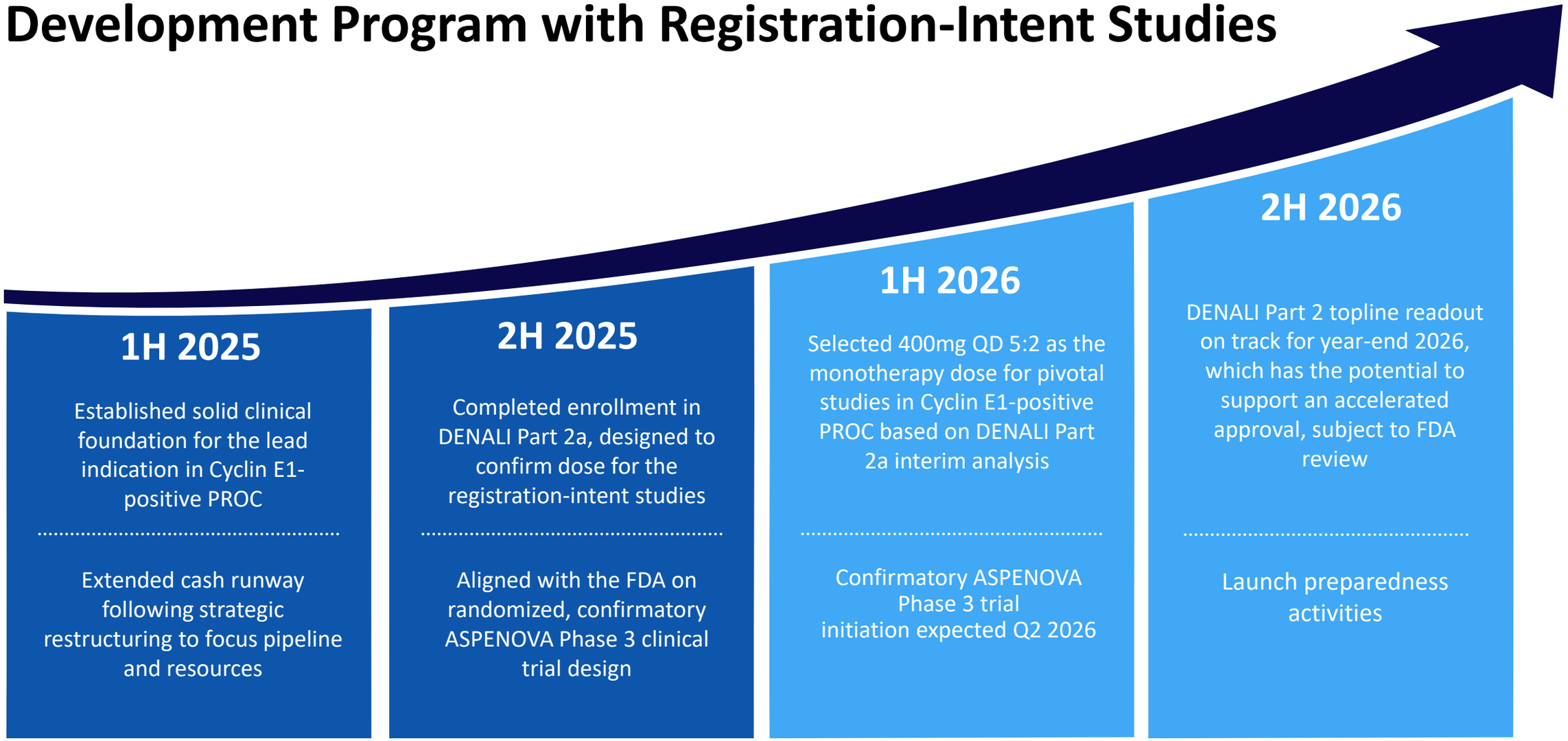
Zentalis Pharmaceuticals, Inc. (“we,” “us,” “our,” “Zentalis” or the “Company”) cautions that this presentation (including oral commentary that accompanies this presentation) contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. All statements 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 first-in-class and best-in-class; the potential regulatory strategy, approach and pathway for azenosertib, including the potential for FDA accelerated approval of azenosertib in Cyclin E1-positive PROC and the potential for studies to be registrational or intended for registration; our development strategy and approach for azenosertib, including our 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; our 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; existing data being supportive of the go-forward azenosertib development strategy; the potential for the opportunity for azenosertib to be broad/expansive; 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 potential for Cyclin E1 to serve as a predictive biomarker for response to azenosertib; the opportunity to improve outcomes in the next stage of development, including via close monitoring; our projected cash runway; planned clinical trials for our product candidates, including the initiation of our DENALI Part 2c trial and our ASPENOVA Phase 3 confirmatory trial of azenosertib in Cyclin E1-positive PROC; the potential of azenosertib to address a significant unmet need in patients with PROC who are Cyclin E1-positive; 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 our anticipated milestones, including the completion of enrollment in all cohorts of DENALI Part 2 and the topline readout from DENALI Part 2; our planned regulatory strategy for azenosertib and the timing thereof, including the potential for DENALI Part 2 to support an accelerated approval; and our launch preparedness activities; 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; 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.

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

Momentum Expected to Continue in 2026 for Azenosertib Development Program with Registration-Intent Studies



$245.9M cash, cash equivalents and marketable securities as of Dec 31, 2025 supports expected milestones with anticipated runway into late 2027

Abbreviations: PROC = platinum-resistant ovarian cancer; 5:2 schedule = 5 days once-daily administration of azenosertib, followed by 2 days without azenosertib

Extensive Data Support Azenosertib as Potential Best-in-Class, Orally Available, Non-Chemo Therapy for Patients with Cyclin E1-Positive Platinum-Resistant Ovarian Cancer (PROC)

>30% ORR, ~6 mos mDOR‡

in Cyclin E1-positive PROC patients at monotherapy dose of 400mg QD 5:2

- Cyclin E1 protein overexpression is a biomarker of poor prognosis and low benefit from standard-of-care (SOC) single-agent chemotherapy in PROC[1]
  - 4-13% ORR for SOC mono chemo in PROC reported in literature[2†]

Manageable safety profile

800+ patients treated with azenosertib in clinical trials*

Most common TRAEs include nausea, diarrhea, and fatigue and are clinically manageable**

400mg QD 5:2 monotherapy regimen selected as pivotal trial dose

A prespecified interim analysis from DENALI Part 2a showed:

- A meaningful and clearly differentiated response rate at 400mg QD 5:2 over 300mg QD 5:2 dose
- Comparable safety profiles across the two dose groups and observed improvements in several key measures, such as:
  - A discontinuation rate due to adverse events at approximately half of the rate reported in DENALI Part 1b
  - No treatment-related deaths

‡ As of Jan. 13, 2025 data cutoff in DENALI Part 1b, mDOR subject to change; † Not a head-to-head comparison; * 800+ patients treated with azenosertib across all tumor types; ** Most common TRAE represents all grade TRAEs ≥ 50%

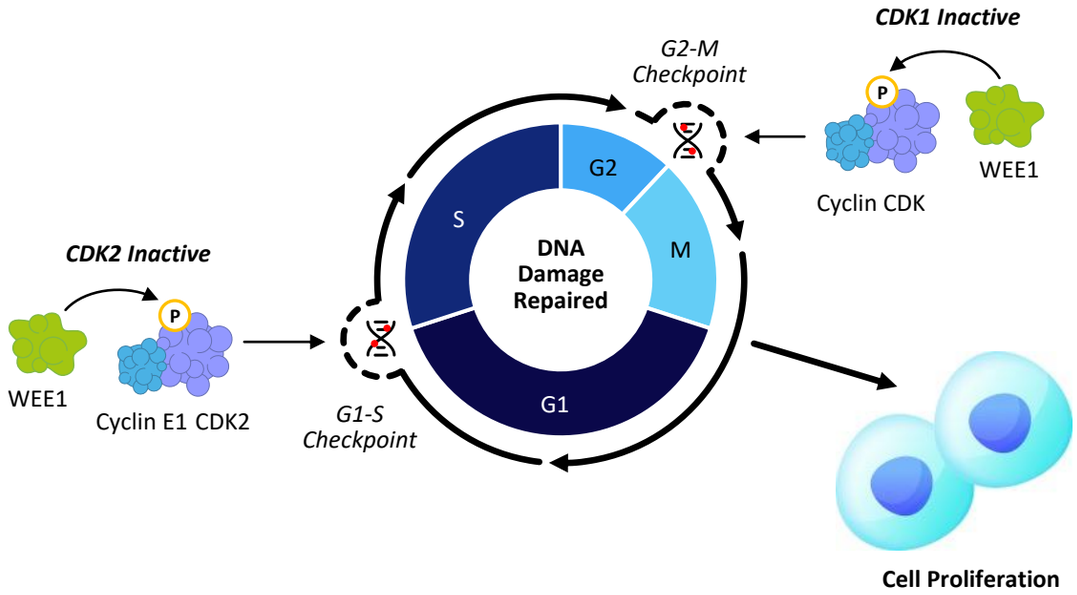
1. Kang EY, et al. *Cancer.* 2023;129:697-713
2. Eskander, R., et al. Overcoming the Challenges in Drug Development, Front Oncol. 2023 Oct 17; 13:1258228

Abbreviations: ORR = objective response rate; mDOR = median duration of response; TRAEs = treatment-related adverse events; 5:2 schedule = 5 days once-daily administration of azenosertib, followed by 2 days without azenosertib

Cyclin E1 Overexpression Sensitizes Cancer Cells to Azenosertib

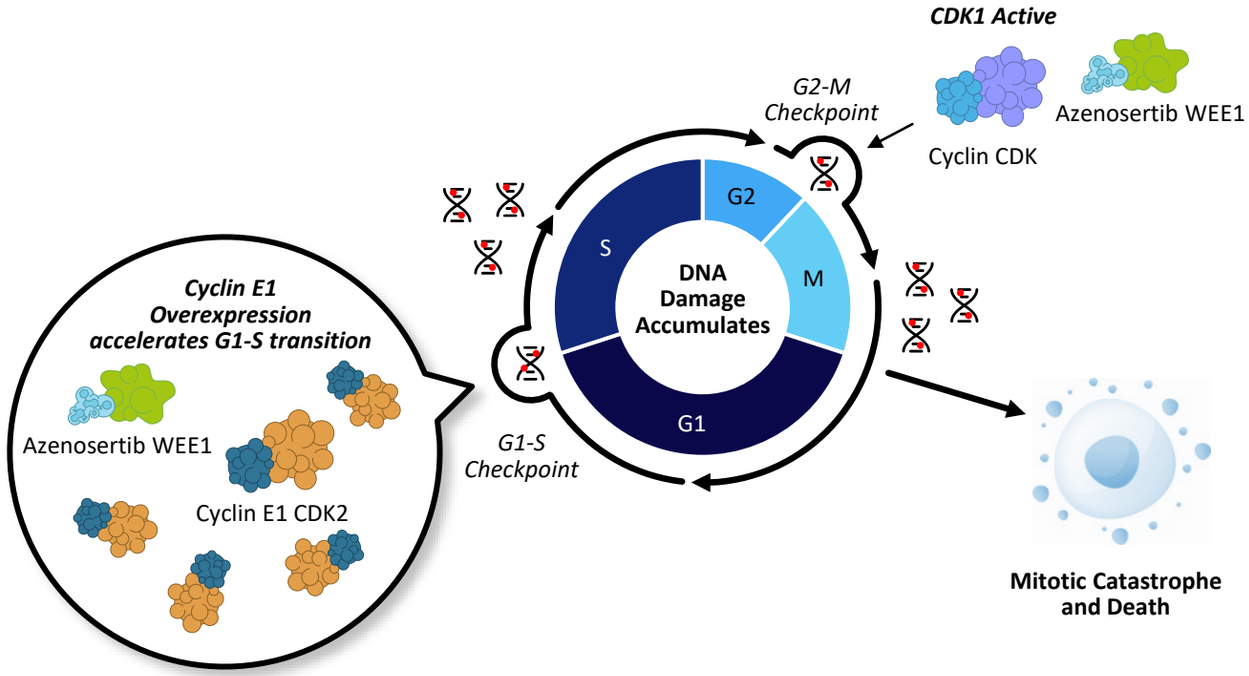
Normal Cell Cycle Regulation

- 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

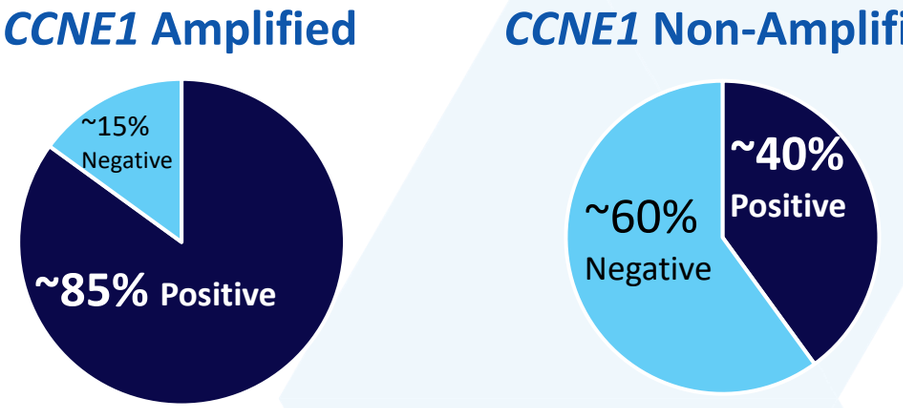
Multiple Drivers of Cyclin E1 Protein Overexpression

Companion diagnostic ready for use in registration-intent studies to identify Cyclin E1-Positive patients, ~50% of PROC patient population†

Cyclin E1 overexpression driven by different mechanisms[1], including:

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

Cyclin E1-Positivity more than doubles the eligible patient population beyond *CCNE1* gene amplified:



Predicted Cyclin E1 IHC*

All PROC patients, regardless of* CCNE1 *amplification status, should be screened for Cyclin E1 overexpression

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). https://doi.org/10.1038/s41698-024-00787-4

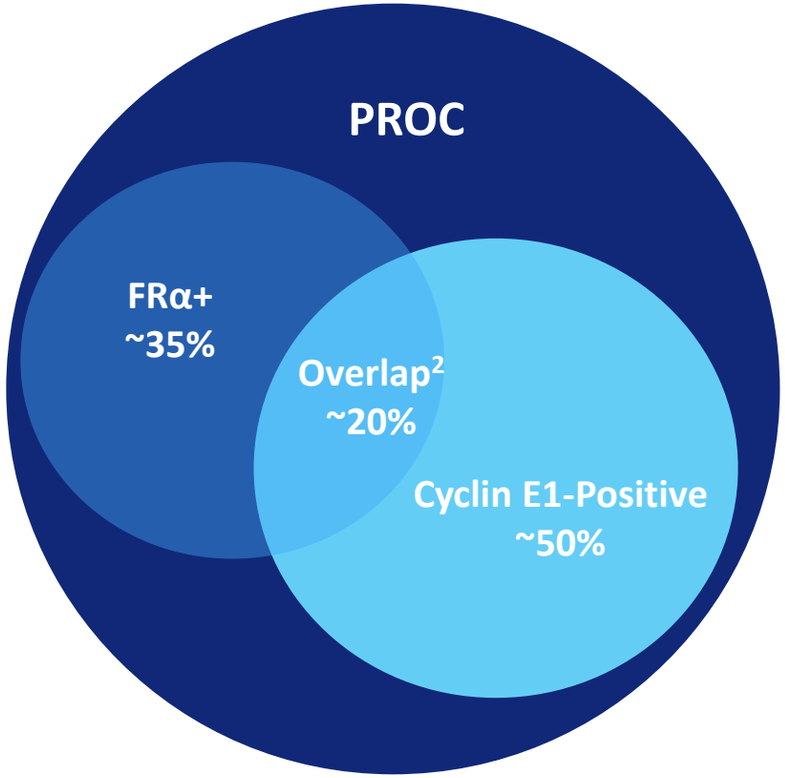
* Cyclin E1 IHC+ based on Zentalis proprietary IHC cutoff and Cyclin E1 IHC assay developed from the existing clinical data

† Cyclin E1 IHC+% based on literature and the unbiased CCNE1 amp & Cyclin E1 overlapping data generated from Zentalis clinical trial samples

IHC - immunohistochemistry

Significant Market Opportunity in High Unmet Need Cyclin E1-Positive PROC

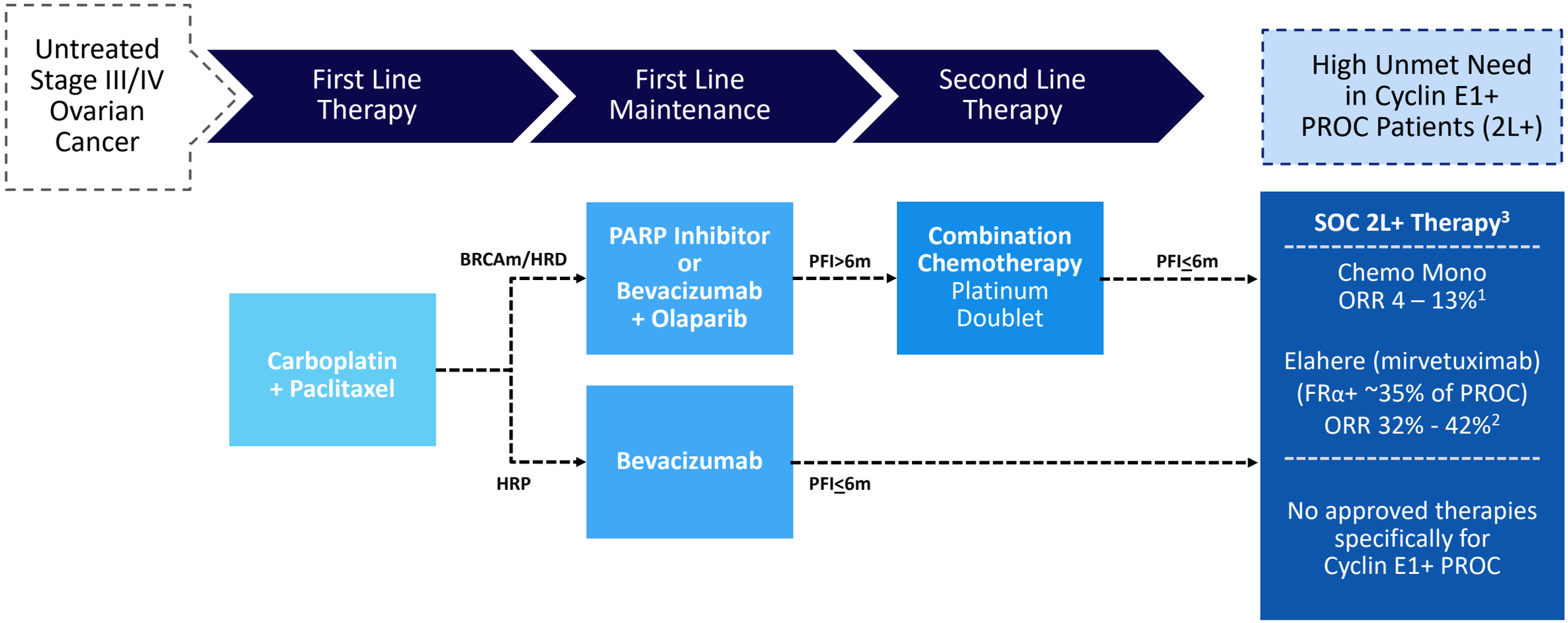
- **No approved treatment option** specifically for this biomarker selected PROC population
- **~21,500** Cyclin E1-Positive PROC patients* (~50% of PROC population)
- Elahere (mirvetuximab soravtansine) approved for biomarker selected FRα+ PROC population; US sales in 2025 were $607 million[1]
  - Underscores demand for biomarker-directed therapies for PROC patients
- Additional opportunities in earlier lines of ovarian cancer and other tumor types



* Based on 2024 annual estimates in US and EU4 (France, Germany, Italy, Spain) + UK

1. Abbvie Q4 2025 Earnings: https://news.abbvie.com/2026-02-04-AbbVie-Reports-Full-Year-and-Fourth-Quarter-2025-Financial-Results
2. ~20% of all PROC; based on internal data

Platinum Resistant Ovarian Cancer: High Unmet Need Provides Opportunity for Azenosertib Monotherapy



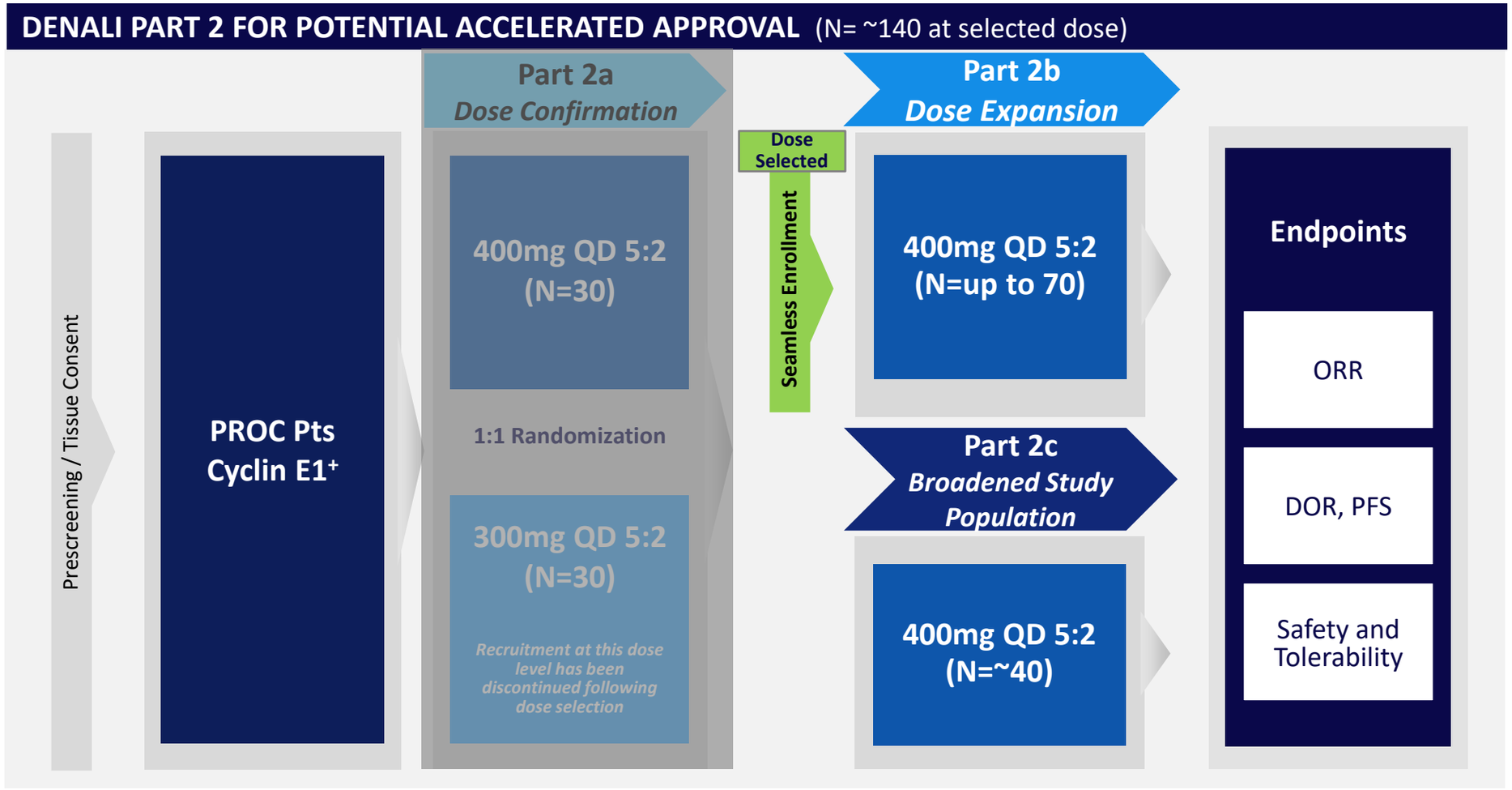
PROC, platinum-resistant ovarian cancer; FRα, Folate Receptor alpha

1 Eskander, R., et al. Overcoming the Challenges in Drug Development, Front Oncol. 2023 Oct 17; 13:1258228; 2 Clinical Trial SORAYA ORR 32%, MIRASOL ORR 42%; 3 Excludes recently approved taxane combo regimens

DENALI – Phase 2 Registration-Intent Study for Accelerated Approval of Azenosertib Monotherapy in Cyclin E1+ PROC Patients

Key Eligibility

- ✓ **Platinum-resistant ovarian cancer**
- ✓ **Cyclin E1+ by proprietary IHC cutoff criteria**
- ✓ **Part 2a & b: 1-3 prior lines of therapy; prior MIRV if high FRα, up to 4 prior lines allowed**
- ✓ **Part 2c: 1-4 prior lines of therapy, including prior taxane containing regimen for PROC; prior MIRV if high FRα**



Abbreviations: 5:2 schedule = 5 days once-daily administration of azenosertib, followed by 2 days without azenosertib; IHC= immunohistochemistry; MIRV=mirvetuximab soravtansine; PROC=platinum resistant ovarian cancer; DOR=duration of response; ORR=overall response rate; PFS=progression free survival.

ASPENOVA – Phase 3 Registration-Intent, Confirmatory Study for Full Approval of Azenosertib Monotherapy in Cyclin E1+ PROC Patients

Key Eligibility

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

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

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

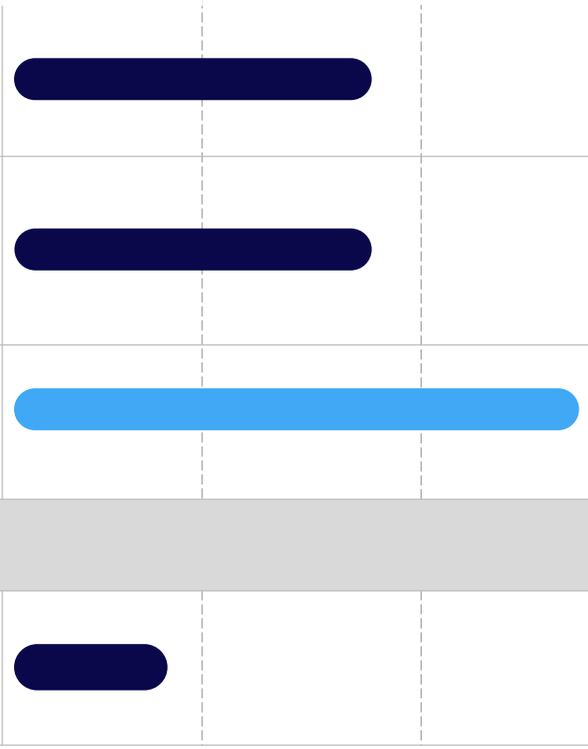
Key Secondary Endpoints
OS, ORR

Trial Initiation Expected in Q2 2026

Abbreviations: 5:2 schedule = 5 days once-daily administration of azenosertib, followed by 2 days without azenosertib; IHC= immunohistochemistry; MIRV=mirvetuximab soravtansine; PROC=platinum resistant ovarian cancer; PLD=pegylated liposomal doxorubicin; OS=overall survival; ORR=overall response rate; PFS=progression free survival

Azenosertib has the Potential to be a First-in-Class and Best-in-Class WEE1 Inhibitor for Patients with Ovarian Cancer and Other Tumor Types

TRIAL NAME	DEVELOPMENT APPROACH	PHASE 1	PHASE 2	PHASE 3	STUDY STATUS
Cyclin E1-Positive PROC Monotherapy (lead indication)					
DENALI	**DENALI Part 1b** Demonstrated Cyclin E1 protein overexpression as biomarker predicting response to azenosertib				Ongoing In Long-term Follow-up Only
	DENALI Part 2a + Part 2b + Part 2c Registration-intent Cyclin E1+ *FDA Fast Track Designation*				Topline Readout Expected YE 2026 Ongoing Study
ASPENOVA	**Azenosertib vs. SOC chemo** Randomized, confirmatory trial Cyclin E1+				Initiation Expected Q2 2026 Planned Study
Ovarian Cancer Combination Therapy					
MUIR*	**Part 2: Azenosertib + bevacizumab (in earlier lines of OC)** **Part 1: Azenosertib + multiple chemo backbones (in PROC, completed)**				Currently Enrolling Part 2 Ongoing Study



zentalis

* Also known as ZN-c3-002

Integrated Data of ZN-c3-001, MAMMOTH, and DENALI Part 1b

Standard of Care* Single-Agent Chemotherapy has Low Efficacy in PROC

New Options with Greater Efficacy Needed

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

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

bev, bevacizumab; FRα, folate receptor alpha; mo, months; ORR, objective response rate; PFS, progression-free survival; PLD, pegylated liposomal doxorubicin; PROC, platinum-resistant ovarian cancer.

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.

Integrated Safety Analysis in All Patients Total Daily Dose ≥300mg (N=356)

Monotherapy Safety Profiles in 001, MAMMOTH, DENALI Part 1b

Treatment Related AEs*, N (%)	All Grade	Grade 3+
Gastrointestinal		
Decreased appetite	93 (26.1)	6 (1.7)
Diarrhea	181 (50.8)	26 (7.3)
Nausea	218 (61.2)	13 (3.7)
Vomiting	63 (17.7)	5 (1.4)
Dehydration	33 (9.3)	2 (0.6)
Hematologic		
Anemia	113 (31.7)	42 (11.8)
Thrombocytopenia	108 (30.3)	39 (11.0)
Neutropenia	57 (16.0)	44 (12.4)
Febrile Neutropenia	6 (1.7)	6 (1.7)
Pancytopenia	2 (0.6)	2 (0.6)
Fatigue	191 (53.7)	44 (12.4)
Sepsis	4 (1.1)	4 (1.1)

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

Treatment Related AEs, N (%)	
TRAE leading to dose reduction	145 (40.7)
TRAE leading to dose interruption	163 (45.8)
TRAE leading to discontinuation	38 (10.7)
TRAE leading to death	4 (1.1)
Treatment related SAE	52 (14.6)

- Well characterized, manageable safety profile in relatively large sample size
- All Grade 5 TRAEs previously reported

Neutropenia: Neutropenia, neutrophil count decreased, neutrophil percentage decreased; Thrombocytopenia: platelet count decreased and thrombocytopenia; Anemia: haematocrit decreased, haemoglobin decreased, RBC count decreased

Abbreviations: AE, adverse event; TRAE, treatment related adverse event. SAE, serious adverse event.

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

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

Monotherapy Safety Profiles in PROC Patients in 001, MAMMOTH, DENALI Part 1b

Treatment-related AEs*, N (%)	300mg (N=38)		400mg (N=165)	
	All Grade	Grade 3+	All Grade	Grade 3+
Gastrointestinal				
Decreased appetite	8 (21.1%)	1 (2.6%)	40 (24.2%)	2 (1.2%)
Diarrhea	18 (47.4%)	1 (2.6%)	86 (52.1%)	12 (7.3%)
Nausea	23 (60.5%)	0	101 (61.2%)	6 (3.6%)
Vomiting	3 (7.9%)	0	17 (10.3%)	3 (1.8%)
Dehydration	1 (2.6%)	0	14 (8.5%)	1 (0.6%)
Fatigue	14 (36.8%)	2 (5.3%)	90 (54.5%)	20 (12.1%)
Sepsis	0	0	4 (2.4%)	4 (2.4%)
Hematologic				
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%)

Treatment-related AEs, N (%)	300mg (N=38)	400mg (N=165)
Treatment-Related SAE	6 (15.8%)	31 (18.8%)
TRAE leading to dose reduction	13 (34.2%)	69 (41.8%)
TRAE leading to dose interruption	16 (42.1%)	89 (53.9%)
TRAE leading to discontinuation	5 (13.2%)	26 (15.8%)
TRAE leading to death	0	3 (1.8%)

- While numerically different, broadly comparable safety profiles at 300mg and 400mg 5:2
- Low frequency of previously reported G5 TRAEs, G3+ febrile neutropenia and sepsis observed at 400mg 5:2

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

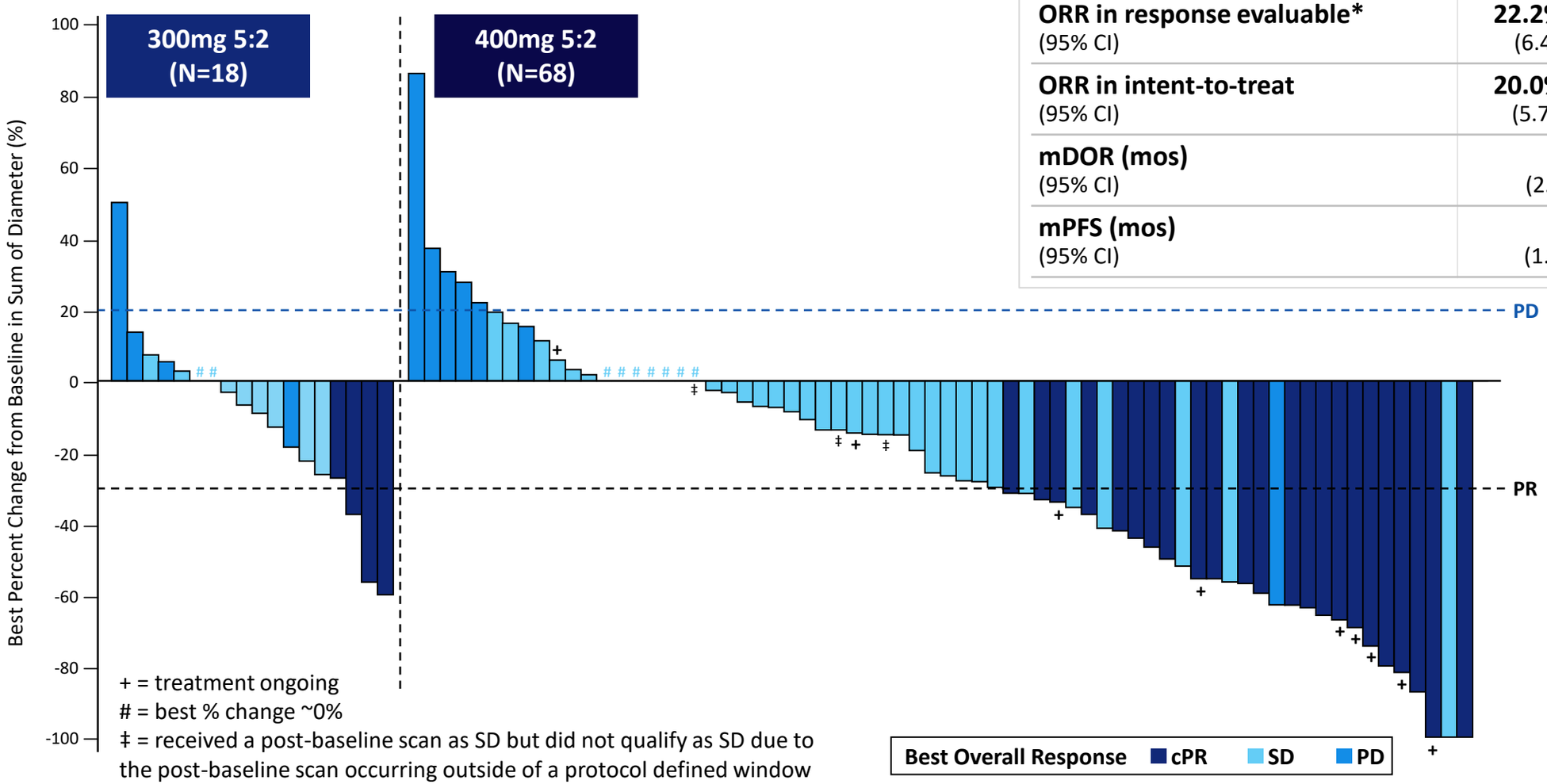
zentalis

Neutropenia: Neutropenia, neutrophil count decreased, neutrophil percentage decreased; Thrombocytopenia: platelet count decreased and thrombocytopenia; Anemia: hematocrit decreased, hemoglobin decreased, RBC count decreased
Abbreviations: AE, adverse event; TRAE, treatment related adverse event. SAE, serious adverse event.

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

400mg 5:2 Shows Meaningful Response Rates >30% and mDOR >5 mos

PROC, Cyclin E1+ (001, MAMMOTH, DENALI Part 1b)	300 mg 5:2	400 mg 5:2
ORR in response evaluable* (95% CI)	**22.2%** (4/18) (6.4 - 47.6)	**33.8%** (23/68) (22.8 - 46.3)
ORR in intent-to-treat (95% CI)	**20.0%** (4/20) (5.7 – 43.7)	**31.5%** (23/73) (21.1 – 43.4)
mDOR (mos) (95% CI)	**3.9** (2.8, NE)	**5.5** (3.5, 6.3)
mPFS (mos) (95% CI)	**4.1** (1.3, 6.6)	**4.4** (2.8, 6.8)



*Includes patients who received at least one post-treatment scan

Abbreviations: CI, confidence interval; cPR, confirmed partial response; mDOR, median duration of response; PD, progressive disease; SD, stable disease; NE, not estimable due to small number of subjects and events.

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

Higher Response Rates and Longer PFS with Fewer Prior Lines of Therapy

Subgroup Analysis by Prior Line of Therapy
Cyclin E1+ PROC patients treated at 400mg QD 5:2 in 001, MAMMOTH and DENALI Part 1b

	Overall	1-3 PLoT	4+ PLoT
ORR in response evaluable* (95% CI)	**33.8%** (23/68) (22.8 – 46.3)	**40.0%** (16/40) (24.9 – 56.7)	**25.0%** (7/28) (10.7 – 44.9)
ORR in intent-to-treat (95% CI)	**31.5%** (23/73) (21.1 – 43.4)	**36.4%** (16/44) (22.4 – 52.2)	**24.1%** (7/29) (10.3 – 43.5)
mDOR (mos) (95% CI)	**5.5** (3.5 – 6.3)	**5.5** (3.5 – 6.3)	**NE** (2.7 – NE)
mPFS (mos) (95% CI)	**4.4** (2.8 – 6.8)	**5.4** (2.8 – 6.8)	**4.1** (2.6 – 8.5)

*Includes patients who received at least one post-treatment scan
Abbreviations: CI, confidence interval; mDOR, median duration of response; mPFS, median progression free survival; NE, not estimable due to small number of subjects and events; PLoT, prior line of therapy

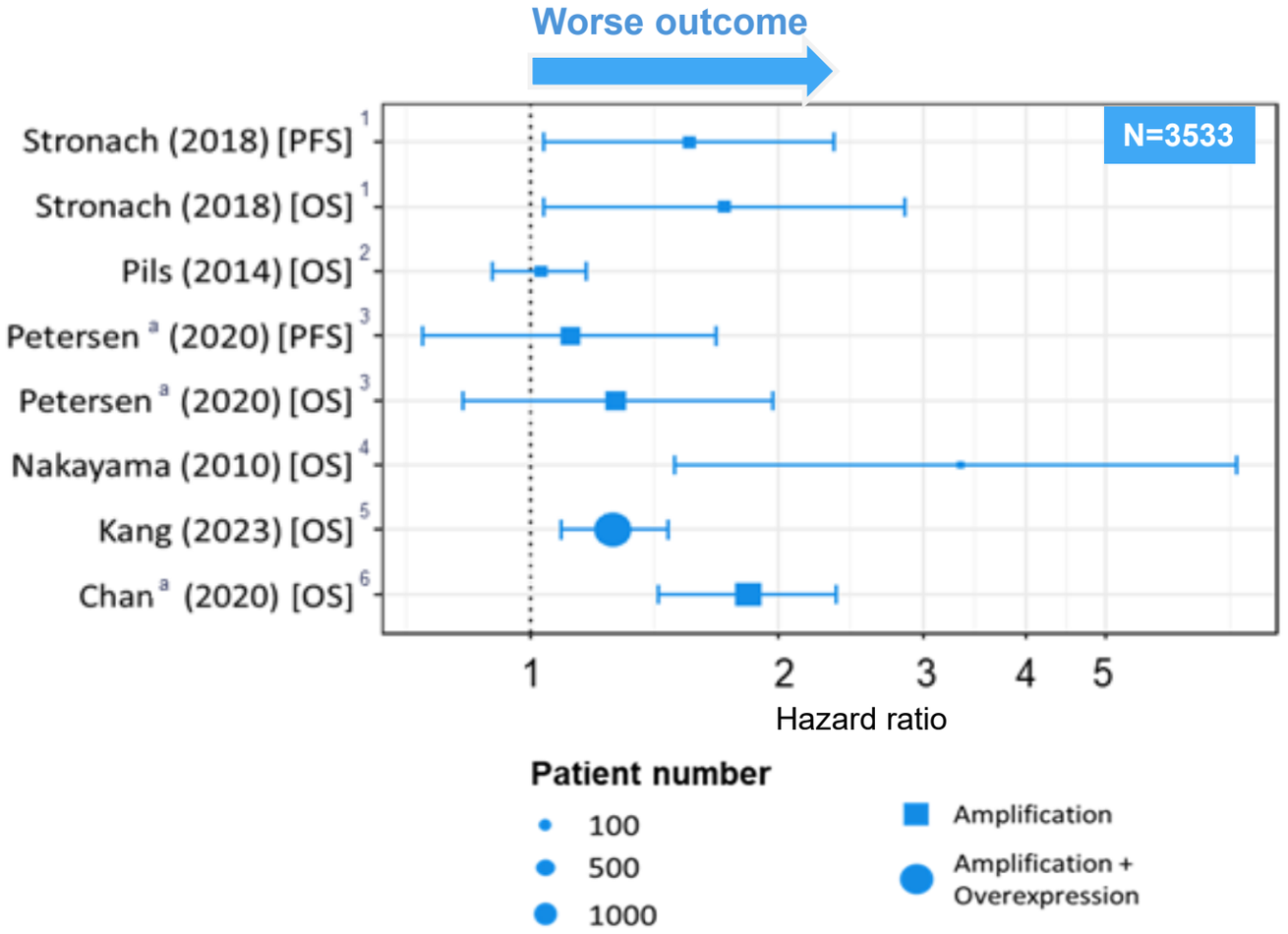
Data Cutoff
Dec 2 2024
Active database; subject to further change

DENALI Part 1b (ZN-c3-005)

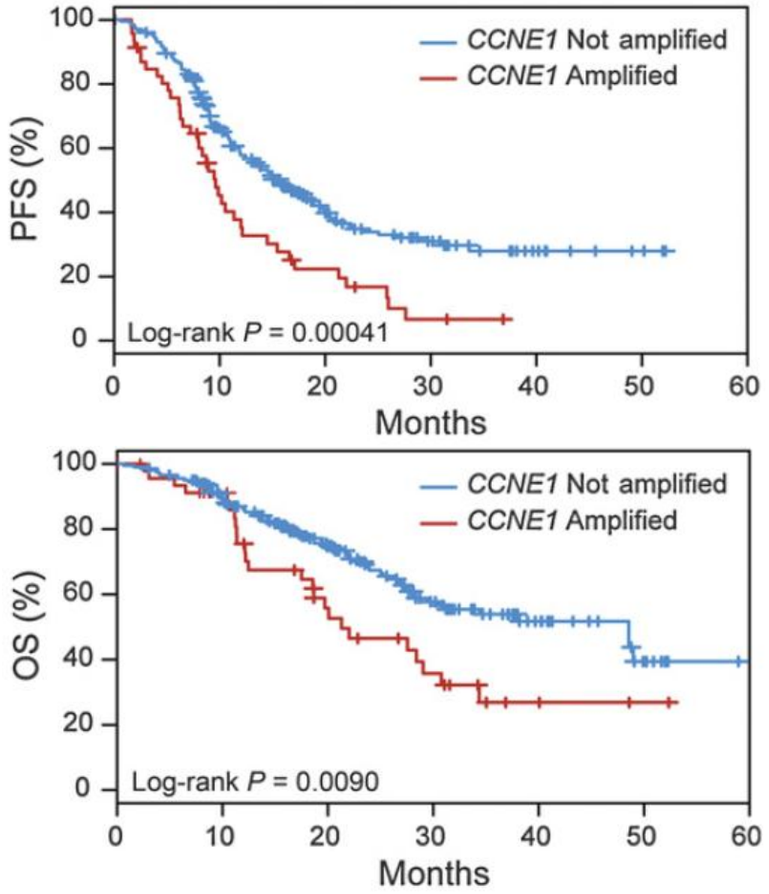
NCT05198804

Updated data at SGO 2025, Data cutoff January 13, 2025

Ovarian Cancer Patients With Cyclin E1 Overexpression and/or *CCNE1* Amplified Ovarian Cancers Have Worse Outcomes



Survival according to *CCNE1* amplification status[1]



[a]Timing of tissue collection was not disclosed. OS, overall survival; PFS, progression-free survival. **1.** Stronach EA, et al. *Mol Cancer Res.* 2018;16:1103-1111. **2.** Pils D, et al. *Eur J Cancer.* 2014;50:99-110. **3.** Peterson S, et al. *Gynecol Oncol.* 2020;157:405-410. **4.** Nakayama N, et al. *Cancer.* 2010;116:2621-2634. **5.** Kang EY, et al. *Cancer.* 2023;129:697-713. **6.** Chan AM, et al. *J Pathol Clin Res.* 2020;6:252-262.

DENALI Part 1b Evaluated 400mg 5:2 QD and Confirmed Cyclin E1 Biomarker

Study Design

Key Eligibility

- ✓ Platinum-resistant ovarian cancer
- ✓ 1-5 prior lines of therapy
- ✓ Tissue mandatory for biomarker assessment

Enrollment
(N=102)

Azenosertib monotherapy
400 mg QD 5:2

Endpoints

- ORR, DOR
- PFS
- Safety and Tolerability

Status Part 1b Enrollment Complete

Abbreviations: QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; DOR, duration of response; PFS, progression-free survival

DENALI Part 1b: Patient Baseline Characteristics

Characteristics[a] (N=102)	
Median age (range), years	66 (34-82)
Race, n (%)	
White	70 (69)
Black/African American	6 (6)
Asian	3 (3)
Other[b]	1 (1)
Not reported	22 (22)
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)

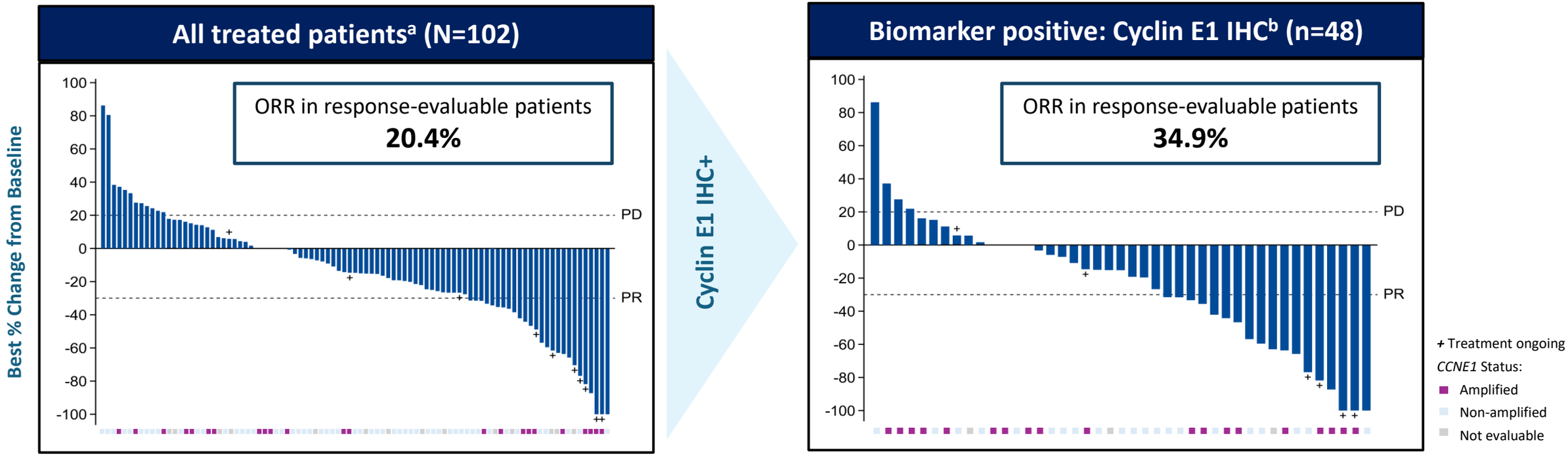
Characteristics[a] (N=102)	
Prior therapy, n (%)	
Bevacizumab	93 (91)
PARPi	57 (56)
Mirvetuximab	15 (15)
***CCNE1* amplification,[c]**	
Evaluable, n	88
Amplified, n (%)	27 (31)
Cyclin E1 status by IHC	
Evaluable, n	94
IHC+, n (%)	48 (51)

- **Heavily pre-treated population: >65% with 3+ lines of therapy**
- **~50% of patients identified with Cyclin E1 overexpression per Zentalis IHC assay**

Data cutoff date: January 13, 2025. [a]Full analysis set: all treated patients. Biomarker dataset: all treated patients with evaluable tissue and Cyclin E1 IHC status. [b]Hispanic. [c]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.

Cyclin E1+ by IHC is a Biomarker Predicting Response to Azenosertib

SGO ANNUAL MEETING ON WOMEN'S CANCER SEATTLE, WA • 2025

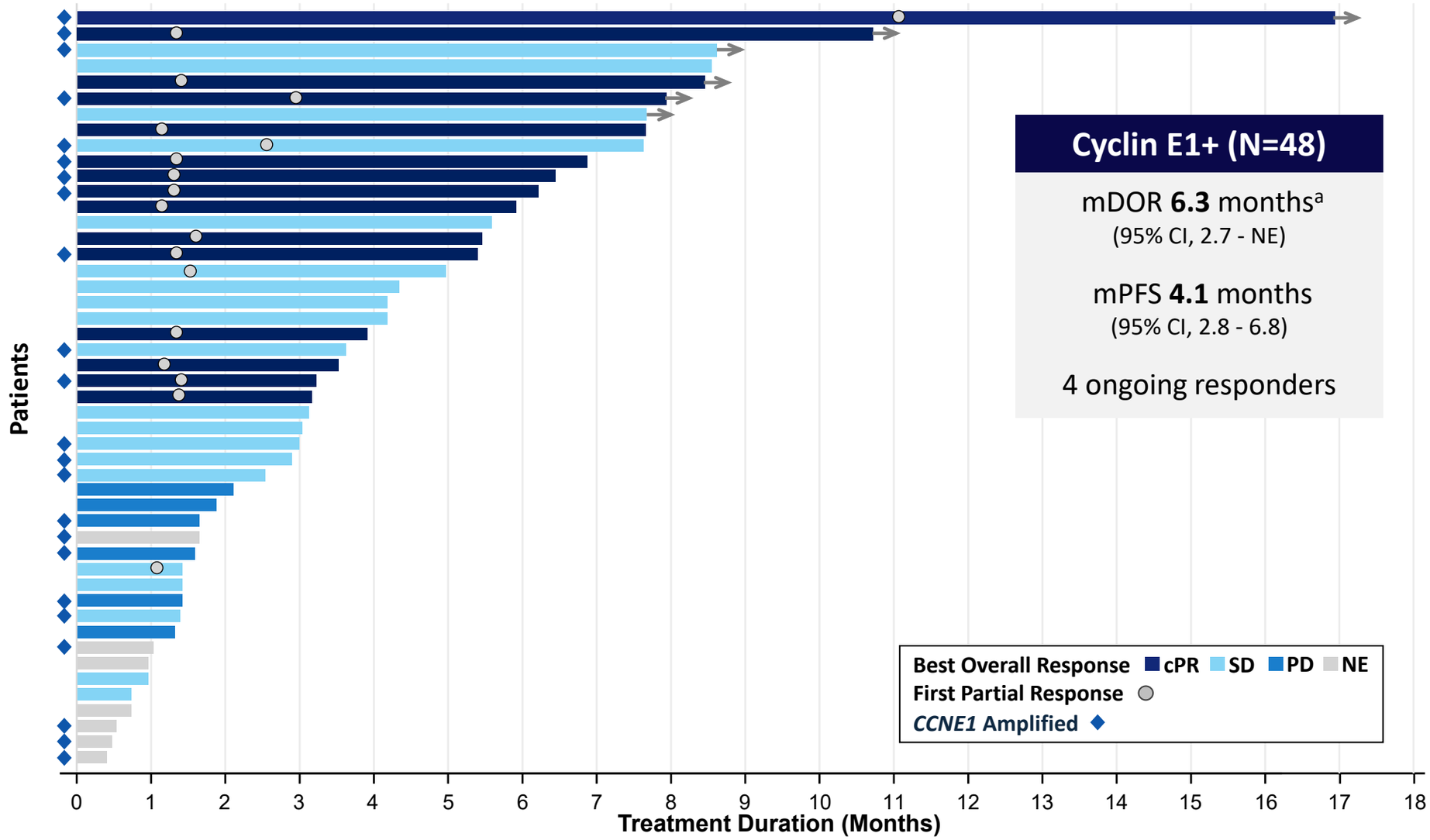


	All treated patients (N=102)	Cyclin E1 IHC+ (n=48)
ORR in response-evaluable[c] patients, % (n/N; 95% CI)	**20.4** (19/93; 12.8-30.1)	**34.9** (15/43; 21.0-50.9)
ORR, ITT[a] % (n/N; 95% CI)	**18.6** (19/102; 11.6-27.6)	**31.3** (15/48; 18.7-46.3)

Data cutoff date: Jan 13, 2025. [a]Intent to treat/Full analysis set: all treated patients. [b]Biomarker dataset: all treated patients with evaluable tissue and Cyclin E1 IHC status. [c]Includes patients who received at least one post-treatment scan.
Amp, amplified; IHC, immunohistochemistry; ITT, Intent to treat population; ORR, objective response rate; PD, progressive disease; PR, partial response.

DENALI Part 1b: Duration of Response in Cyclin E1 IHC+ Ovarian Cancer

SGO ANNUAL MEETING ON WOMEN'S CANCER SEATTLE, WA • 2025

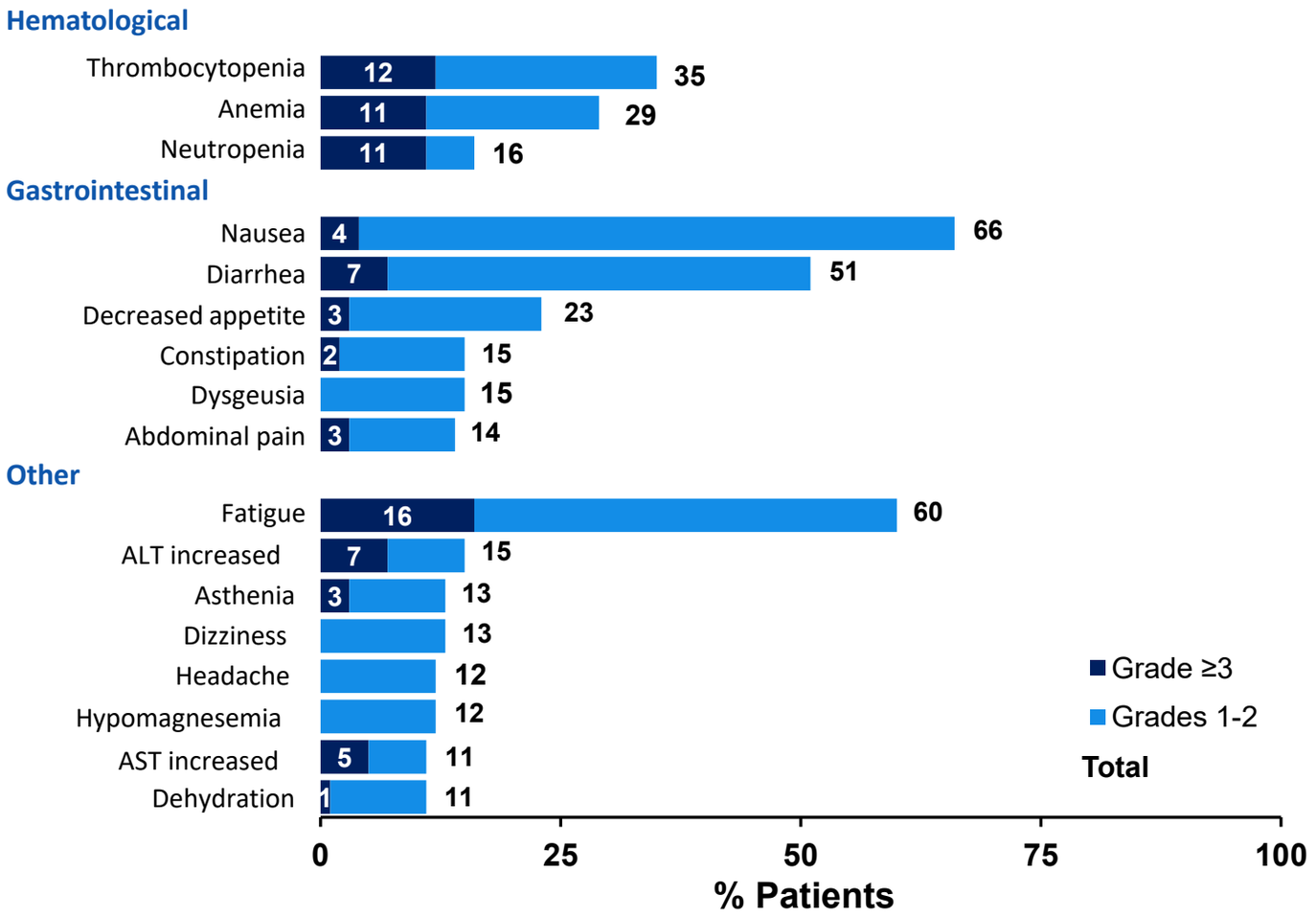


[a]mDOR is subject to change, there are 4 ongoing responders as of the January 13, 2025 data cutoff. IHC, immunohistochemistry; cPR, confirmed partial response; SD, stable disease; PD, progressive disease; mDOR, median duration of response; mPFS, median progression free survival; NE, not evaluable

DENALI Part 1b: Safety and Tolerability Summary

SGO ANNUAL MEETING ON WOMEN'S CANCER SEATTLE, WA • 2025

TRAEs occurring in ≥10% of patients[a]



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)[b]
Serious TRAEs	22 (21.6)

zentalis

Data cutoff date: January 13, 2025

[a]If a patient had multiple grades of the same adverse event, The worse grade was reported [b]One patient had sepsis, and 1 patient had pancytopenia.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; TRAE, treatment-related adverse event.

Julie Eastland

Chief Executive Officer

jeastland@zentalis.com

Haibo Wang

Chief Business Officer

hwang@zentalis.com

Aron Feingold

VP, IR and Corporate Communications

afeingold@zentalis.com

Science Center

10275 Science Center Drive

Suite 200

San Diego, CA 92121

APPENDIX

ZN-c3-001 Dose-Escalating Monotherapy Study in Solid Tumors

NCT04158336

First-in-Human Phase 1 Dose and Schedule Optimization in Solid Tumors: Therapeutic Window Established

Key Eligibility

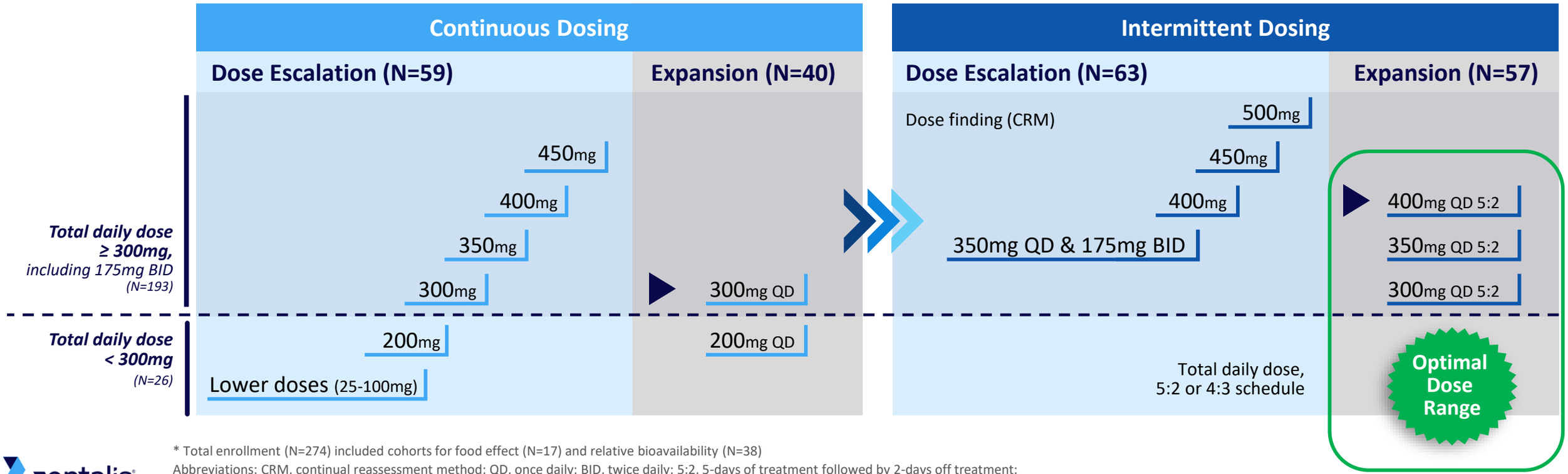
- ✓ 1+ prior lines of therapy
- ✓ Solid tumor, PROC and USC enriched
- ✓ Tissue collected for biomarker analysis

Total Enrollment

N=274 across all tumor types and dose*
N=193 at total daily dose ≥ 300mg; evaluated for safety and anti-tumor activity

Status

Fully Enrolled



* Total enrollment (N=274) included cohorts for food effect (N=17) and relative bioavailability (N=38)

Abbreviations: CRM, continual reassessment method; QD, once daily; BID, twice daily; 5:2, 5-days of treatment followed by 2-days off treatment; 4:3, 4-days of treatment followed by 3-days off treatment; DLT, dose limiting toxicity; PROC, platinum resistant ovarian cancer; USC, uterine serous carcinoma

Heavily Pre-Treated Patient Population with Multiple Tumor Types; Patients with PROC had a Median of Five Prior Lines of Therapy

Patient Demographics and Clinical Characteristics
Total Daily Dose ≥ 300 mg – Continuous and Intermittent (N=193)

	PROC N = 69	USC N = 35	Other Solid Tumors* N = 89
Age (years)			
Median	66	66	64
Range (Min-Max)	(48 – 83)	(53 – 78)	(26 – 81)
ECOG PS (n, %)			
ECOG 0	19 (28%)	8 (23%)	32 (36%)
ECOG 1	50 (72%)	26 (74%)	54 (61%)
ECOG 2	0	1 (3%)	2 (2%)
Prior Lines of Treatment			
Median (Range)	5 (1 - 19)	3 (0 - 12)	4 (0 - 11)
0	0	1 (3%)†	1 (3%)‡
1-3	22 (32%)	22 (63%)	34 (36%)
≥4	47 (68%)	12 (34%)	54 (61%)

	PROC N = 69	USC N = 35	Other Solid Tumors N = 89
Prior Therapies (n, %)			
PARPi	46 (67%)	3 (9%)	5 (6%)
VEGFi	60 (87%)	27 (77%)	39 (44%)
PD-1/PD-L1	12 (17%)	27 (77%)	35 (39%)
Cyclin E1 Status (n, %)			
Positive	26 (38%)	15 (43%)	9 (10%)
Negative	29 (42%)	11 (31%)	25 (28%)
Unknown	14 (20%)	9 (26%)	55 (62%)

*Anus, Appendix, Biliary tract, Bladder, Breast, Cecum, Cervix, Colon, Duodenum, Endometrium, Esophagus, Kidney, Lung, Other, Ovary, Pancreas, Peritoneum, Prostate, Rectum, Stomach, Uterus, Vulva/Vagina, including one patient who had unknown ECOG status; † patient had no prior therapy ; ‡ patient rolled over from the DDI study

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; SD, standard deviation; PARPi, poly-ADP ribose polymerase inhibitor; VEGFi, vascular endothelial growth factor inhibitor; PD-1/PD-L1, programmed cell death protein 1/programmed death ligand 1.

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

Tolerable at Active Dose Levels Across Tumor Types

Safety Profile
Total Daily Dose ≥ 300 mg – Continuous and Intermittent (N=193)

Treatment Related AEs*, n (%)	All Grade	Grade 3+
Gastrointestinal		
Decreased appetite	52 (26.9%)	3 (1.6%)
Diarrhea	100 (51.8%)	15 (7.8%)
Nausea	117 (60.6%)	8 (4.1%)
Vomiting	49 (25.4%)	2 (1.0%)
Dehydration	22 (11.4%)	1 (0.5%)
Fatigue	113 (58.5)	26 (13.5%)
Hematologic		
Anemia	58 (30.1%)	22 (11.4%)
Thrombocytopenia	51 (26.4%)	21 (10.9%)
Neutropenia	29 (15.0%)	25 (13.0%)
Febrile Neutropenia	2 (1.0%)	2 (1.0%)

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

Treatment Related AEs, n (%)	
Treatment-Related SAE	19 (9.8%)
TRAE leading to dose reduction	76 (39.4%)
TRAE leading to dose interruption	78 (40.4%)
TRAE leading to discontinuation	10 (5.2%)
TRAE leading to death	1 (0.5%)

- **No gastrointestinal TRAE > G3 observed**
- **Low rate of G3+ TR hematological toxicities, the majority G3**
- **Low rate of TRAE leading to treatment discontinuation**
- **One G5 TRAE previously reported**

zentalis

Neutropenia: Neutropenia, neutrophil count decreased, neutrophil percentage decreased; Thrombocytopenia: platelet count decreased and thrombocytopenia; Anemia: hematocrit decreased, hemoglobin decreased, RBC count decreased

Abbreviations: AE, adverse event; TRAE, treatment related adverse event. SAE, serious adverse event.

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

Azenosertib Demonstrated Encouraging ORR and DOR at ≥300mg Total Daily Dose, Intermittent in PROC

Clinical Activity Overview - Total Daily Doses ≥ 300 mg - Continuous and Intermittent (N=193)

Tumor Type	PROC				USC				Other Solid Tumors			
Dose Schedule	Intermittent		Continuous		Intermittent		Continuous		Intermittent		Continuous	
Cyclin E1 IHC Status	All	Cyclin E1+	All	Cyclin E1+	All	Cyclin E1+	All	Cyclin E1+	All	Cyclin E1+	All	Cyclin E1+
Number of Patients	58	23	11	3	19	11	16	4	43	4	46	5
ORR, (%), n (95% CI)	20.7%, (12/58) (11.2 - 33.4)	34.8%, (8/23) (16.4 - 57.3)	18.8% (2/11) (2.3 - 51.8)	33.3% (1/3) (0.8 - 90.6)	26.3% (5/19) (9.2 - 51.2)	36.4% (4/11) (10.9 - 69.2)	18.8% (3/16) (4.1 - 45.7)	25.0% (1/4) (0.6 - 80.6)	2.3% (1/4) (0.1 - 12.3)	0.0% (0/4) (0.0 - 60.2)	4.3% (2/46) (0.5 - 14.8)	0.0% (0/5) (0.0 - 52.2)
mDOR (mos) (95% CI)	5.1 (3.0, 5.9)	5.2 (2.8, 6.9)	7.1 (4.2, NE)	4.2 (NE, NE)	5.5 (5.4, NE)	5.5 (5.4, NE)	5.6 (4.1, NE)	6.9 (NE, NE)	4.3 (NE, NE)	NA	3.3 (3.0, NE)	NA

Greater anti-tumor activity seen with intermittent dosing schedule and Cyclin E1+ patients
Results direct focused development on doses of 300 and 400 mg at intermittent dosing schedule

[1] Not a head-to-head comparison
PROC, platinum-resistant ovarian cancer; USC, uterine serous carcinoma; ORR, objective response rate; mDOR, median duration of response; IHC, immunohistochemistry; NE, not evaluable

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

Key Takeaways from ZN-c3-001

Meaningful therapeutic window identified providing a favorable risk-benefit profile in Cyclin E1^{+} PROC patients at total daily doses of 300 and 400mg QD 5:2

- **Azenosertib studied in a large patient population across multiple tumor types**
- **Platinum-resistant ovarian cancer (PROC) identified as an indication particularly susceptible to WEE1 inhibition**
- **Cyclin E1 identified as predictive biomarker for response to azenosertib**

MAMMOTH (ZN-c3-006)

NCT05198804

MAMMOTH: Two Clinically-active Monotherapy Doses Studied in Heavily Pre-treated, PARPi-resistant PROC Patient Population

Study Design

Key Eligibility

- ✓ 1-5 prior lines of therapy
- ✓ Platinum-resistant, progressed while receiving an approved PARP inhibitor
- ✓ Mandatory sufficient tissue for biomarker analysis

Enrollment
(N=117)

Azenosertib monotherapy
300 or 400 mg QD 5:2
(N=61)

Azenosertib + niraparib
Concurrent schedule
(N=28)

Azenosertib + niraparib
Alternating schedule
(N=28)

Endpoints

- **ORR, DOR**
- **PFS**
- **Safety and Tolerability**

Status Enrollment Complete

Abbreviations: QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate DOR, duration of response; PFS, progression-free survival; PROC, platinum-resistant ovarian cancer; PARPi, poly (ADP-ribose) polymerase inhibitor

Heavily Pre-Treated PARPi-resistant PROC Population

Patient Demographics and Clinical Characteristics
Monotherapy Cohorts Only

	300 mg 5:2 (N=25)	400 mg 5:2 (N=36)
Age (years)		
Median	71.0	63.0
Range (Min-Max)	45 – 80	31 - 84
ECOG PS (n, %)		
ECOG 0	7 (28%)	16 (44%)
ECOG 1	18 (72%)	20 (56%)
Prior Lines of Treatment (n, %)		
1-3	15 (60%)	20 (56%)
≥4	10 (40%)	16 (44%)
PARP	25 (100%)	36 (100%)
Bevacizumab	24 (96%)	34 (94%)
Cyclin E1 Status (n, %)		
Positive	13 (52%)	16 (44%)
Negative	10 (40%)	15 (42%)
Unknown	2 (8%)	5 (14%)

Abbreviations: QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate DOR, duration of response; PFS, progression-free survival, PROC, platinum-resistant ovarian cancer

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

Well-characterized Safety and Tolerability in PROC Monotherapy Cohorts at 300mg QD and 400mg QD (5:2) Doses

Azenosertib Monotherapy 300 mg & 400mg QD (5:2)

Treatment-related AEs*, N (%)	300mg (N=25)		400mg (N=36)	
	All Grade	Grade 3+	All Grade	Grade 3+
Gastrointestinal				
Decreased appetite	7 (28.0%)	1 (4.0%)	11 (30.6%)	0
Diarrhea	13 (52.0%)	0	17 (47.2%)	4 (11.1%)
Nausea	15 (60.0%)	0	19 (52.8%)	1 (2.8%)
Vomiting	2 (8.0%)	0	4 (11.1%)	1 (2.8%)
Dehydration	0	0	0	0
Fatigue	6 (24.0%)	1 (4.0%)	11 (30.6%)	1 (2.8%)
Sepsis	0	0	1 (2.8%)	1 (2.8%)
Hematologic				
Anemia	10 (40.0%)	3 (12.0%)	14 (38.9%)	6 (16.7%)
Thrombocytopenia	8 (32.0%)	2 (8.0%)	13 (36.1%)	4 (11.1%)
Neutropenia	4 (12.0%)	3 (12.0%)	8 (22.2%)	5 (13.9%)
Febrile Neutropenia	0	0	1 (2.8%)	1 (2.8%)

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

Treatment-related AEs, N (%)	300mg (N=25)	400mg (N=36)
Treatment-Related SAE	4 (16.0%)	5 (13.9%)
TRAE leading to dose reduction	11 (44.0%)	15 (41.7%)
TRAE leading to dose interruption	11 (44.0%)	14 (38.9%)
TRAE leading to discontinuation	4 (16.0%)	2 (5.6%)
TRAE leading to death	0 (0.0%)	1 (2.8%)

- Similar rates of TR SAEs across doses
- Low rate of TR G3+ hematological toxicities with the majority being G3 events (only one G4 febrile neutropenia and one sepsis event)
- Low rate of TRAEs leading to treatment discontinuation
- One G5 TRAE previously reported

Neutropenia: Neutropenia, neutrophil count decreased, neutrophil percentage decreased; Thrombocytopenia: platelet count decreased and thrombocytopenia; Anemia: hematocrit decreased, hemoglobin decreased, RBC count decreased

Abbreviations: AE, adverse event; TRAE, treatment related adverse event. SAE, serious adverse event.

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

Azenosertib Demonstrated Clinically Meaningful Responses in PARPi-resistant Monotherapy Cohorts

Azenosertib Monotherapy 300 mg & 400mg QD (5:2)				
Dose and Schedule	**300mg 5:2**		**400mg 5:2**	
Cyclin E1 IHC Status	**All**	**Cyclin E1+**	**All**	**Cyclin E1+**
Number of Patients	**25**	**14**	**36**	**16**
ORR, (%), n (95% CI)	**20.0% (5/25) (6.8 - 40.7)**	**21.4% (3/14) (4.7 - 50.8)**	**22.2% (8/36) (10.1 - 39.2)**	**31.3% (5/16) (11.0 - 58.7)**
mDOR, months (95% CI)	**4.9 (2.8 - NE*)**	**4.9 (3.0 - NE*)**	**5.5 (2.7 - NE*)**	**4.2 (3.0 - NE*)**

400mg 5:2 shows numerically better ORR in Cyclin E1+ PROC patients compared to 300mg 5:2

*Not estimable due to small number of subjects and events

Abbreviations: PARPi, poly (ADP-ribose) polymerase inhibitor; IHC, immunohistochemistry; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; CI, confidence interval; mDOR, median duration of response; NE, not evaluable

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

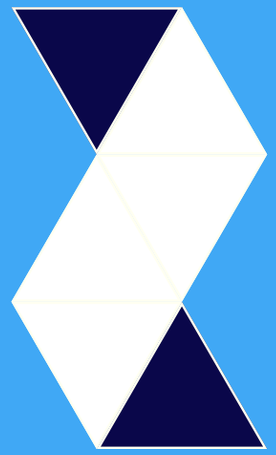
Key Takeaways from MAMMOTH Monotherapy Cohort

Learnings continue to support development of azenosertib in Cyclin E1+ PROC

- Consistent antitumor activity in PARPi-resistant patients
- Tolerability and toxicity consistent with 001 study and similar between the assessed doses
- 400mg QD 5:2 showed numerically higher response rates than 300mg QD 5:2

zentalis

Abbreviations: QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; PROC, platinum-resistant ovarian cancer; PARPi, poly (ADP-ribose) polymerase inhibitor



zentalis