# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**Washington, D.C. 20549**

# FORM 8-K

**CURRENT REPORT**

**Pursuant to Section 13 or 15(d)**
**of the Securities Exchange Act of 1934**

**Date of report (Date of earliest event reported): June 3, 2024**

# ZENTALIS PHARMACEUTICALS, INC.
**(Exact name of registrant as specified in its charter)**

| **Delaware** | **001-39263** | **82-3607803** |
|---|---|---|
| **(State or other jurisdiction of incorporation or organization)** | **(Commission File Number)** | **(I.R.S. Employer Identification No.)** |

**1359 Broadway, Suite 801**
**New York, New York 10018**
**(Address of principal executive offices) (Zip Code)**

**(212) 433-3791**
**(Registrant's telephone number, include area code)**

**N/A**
**(Former name or former address, if changed since last report)**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Securities registered pursuant to Section 12(b) of the Act:**

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common Stock, $0.001 par value per share | ZNTL | The Nasdaq Global Market |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 7.01 Regulation FD Disclosure.**

Beginning on June 3, 2024, spokespersons of Zentalis Pharmaceuticals, Inc. (the "Company") plan to present the information in the Corporate Presentation furnished as Exhibit 99.1 to this Current Report on Form 8-K (this "Current Report") and incorporated herein by reference at conferences and in meetings with investors and analysts.

The information contained in Item 7.01 of this Current Report (including Exhibit 99.1 attached hereto) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, except as expressly provided by specific reference in such a filing.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits

The following Exhibit 99.1 relating to Item 7.01 shall be deemed to be furnished, and not filed:

| ExhibitNo. | Description |
|---|---|
| 99.1 | Corporate Presentation, dated June 2024. |
| 104 | Cover Page Interactive Data File (embedded within the inline XBRL document) |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ZENTALIS PHARMACEUTICALS, INC.

Date: June 3, 2024

By: /s/ Kimberly Blackwell, M.D.
Kimberly Blackwell, M.D.
Chief Executive Officer

Exhibit 99.1

zentalis®

# Corporate Presentation

**June 2024**

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 potential for azenosertib (ZN-c3) to be first-in-class and best-in-class; the potential for azenosertib to be a blockbuster opportunity; the potential applicability of azenosertib to a broad array of tumor types, including in combination with molecularly targeted agents; the potential timing of filing our first New Drug Application for azenosertib; potential for azenosertib to have real impact for patients; our positioning to execute; our projected cash runway; our development approach for our product candidates; planned clinical trials for our product candidates, including our strategy with respect to azenosertib in platinum sensitive ovarian cancer; the potential that we are generating registrational data; the potential of azenosertib to address large unmet need across a broad array of tumor types; the potential for studies to be registrational; the potential and suitability of azenosertib to address tumors with high genomic instability; the opportunity for azenosertib in first-line maintenance in homologous repair proficient platinum sensitive ovarian cancer; the opportunity for a monotherapy approval of azenosertib in platinum resistant ovarian cancer; our strategy for azenosertib development and the potential benefits thereof, including in platinum sensitive ovarian cancer; the potential for our development approach in platinum sensitive ovarian cancer to be practice changing; pursuit of a fast-to-market strategy for azenosertib; the potential for azenosertib to provide prolonged benefit for the greatest number of ovarian cancer patients in the first-line maintenance setting; the potential for CCNE1 amplification and Cyclin E1 IHC as potential patient enrichment strategies; the opportunity to address unmet need in relapsed or refractory acute myeloid leukemia by combining azenosertib and ZN-d5; the potential for building the azenosertib franchise, including the potential that the franchise opportunity for azenosertib more than doubles as it expands beyond gynecologic malignancies; the potential unmet need in a particular indication and/or patient population; potential for generating datasets with value-creating potential; potential for combinations including our product candidates and the potential benefits thereof; our potential positioning for success with the azenosertib franchise; the potential benefits of the designs of our product candidates; the target profiles and potential benefits of our product candidates and their mechanisms of action, including as a monotherapy and/or in combination; the market opportunities for and market potential of our product candidates, including the number of potential patients per year; the timing and content of our anticipated milestones, including the timing of initiation of clinical trials and disclosure of clinical data, as well as statements that include the words such as "anticipate," "building," "continue," "could," "estimate," "expect," "milestone," "opportunity," "plan," "positioned," "potential," "predictive," "strategy," "support," "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 any diagnostic tools; the outcome of preclinical testing and early 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; our product candidates may cause serious adverse side effects; inability to maintain our collaborations, or the failure of these collaborations; 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 actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any 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 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.



Zentalis' product candidates are investigational drugs and have not yet been approved by the U.S. Food and Drug Administration or any other regulatory authority.

# Advancing Azenosertib

## First-in-class WEE1 Inhibitor with Broad Franchise Potential

### Highly Specific Agent Targeting WEE1

- Clinical-stage asset generating potentially registrational data
- Intermittent dosing allows for maximized efficacious exposures
- Differentiated from and years ahead of other agents against this target in development

### Real Impact for Patients

- Monotherapy efficacy; 37% ORR and 6.5 month mPFS in heavily pretreated ovarian and USC*
- Excellent safety and tolerability profile compared to other commercially successful anti-cancer agents
- Established dosing and efficacy in combination with multiple chemotherapeutic agents

### Blockbuster Opportunity

- At least 2 gynecologic malignancies (PROC/USC)
- Expanding to a broad array of tumor types in combination with molecularly targeted agents
- More than 10 ongoing and planned trials
- Potential first NDA in 2026

### Positioned to Execute

- Deep oncology expertise
- Industry-leading scientific and clinical advisors
- Partnerships with Pfizer and GSK
- Cash runway into mid-2026



Abbreviations: PROC, platinum resistant ovarian cancer; USC, uterine serous carcinoma; ORR, objective response rate; NDA, New Drug Application; mPFS, median progression free survival
Statements comparing azenosertib to other agents, not head-to-head comparisons

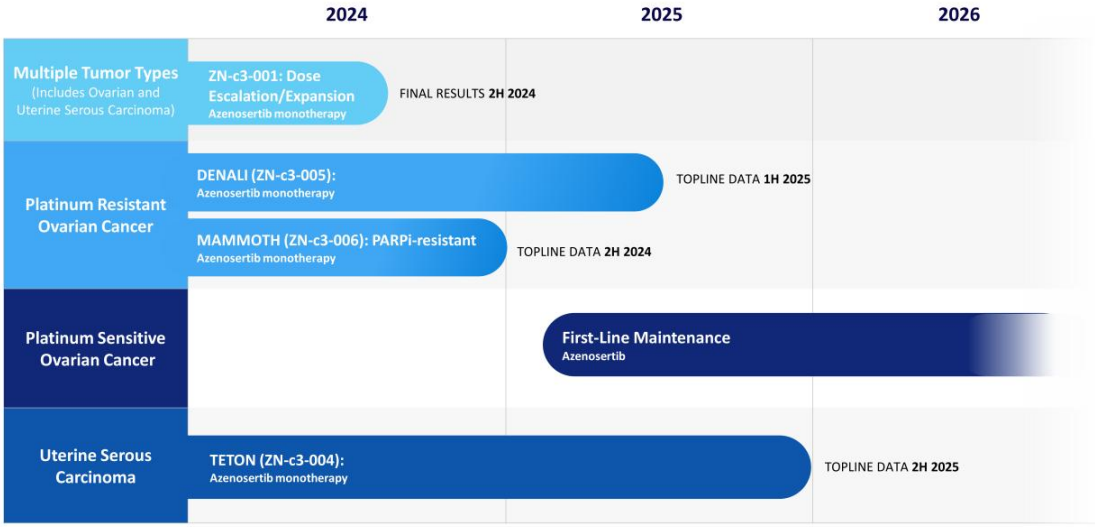
*Data cut-off: October 25, 2023

# Building Azenosertib Franchise in Gynecologic Cancers and Beyond

| | | INDICATION | TRIAL NAME + DEVELOPMENT APPROACH | Phase 1 | Phase 1b | Phase 2 | Phase 3 | EXPECTED MILESTONES |
|---|---|---|---|---|---|---|---|---|
| Azenosertib WEE1 Inhibitor | GYNECOLOGIC MALIGNANCIES | Platinum Sensitive Ovarian Cancer | Planned trial in 1L maintenance setting | | | | | Add'l details **2H 2024,** Expect initiation **2025** |
| | | Platinum Resistant Ovarian Cancer | **DENALI (ZN-c3-005)** Monotherapy | | | | | Topline data anticipated **1H 2025** |
| | | PARPi Resistant Ovarian Cancer | **MAMMOTH (ZN-c3-006)** Azenosertib monotherapy, or with niraparib | | | GSK | | Topline data anticipated **2H 2024** |
| | | Uterine Serous Carcinoma | **TETON (ZN-c3-004)** Monotherapy, FDA Fast Track Designation | | | | | Topline data anticipated **2H 2025** |
| | | Platinum Resistant Ovarian Cancer | **ZN-c3-002** Azenosertib + multiple chemo backbones | | | | | ✓ Data presented at **ASCO 2023** |
| | | Solid Tumors | **ZN-c3-001** Monotherapy | | | | | Final results anticipated **2H 2024** |
| | OTHER TUMOR TYPES | Osteosarcoma | **ZN-c3-003** Azenosertib + gemcitabine | | | | | ✓ Final results presented at **ASCO 2024** |
| | | BRAF Mutant Colorectal Cancer | **ZN-c3-016** Azenosertib + encorafenib and cetuximab | | Pfizer | | | Initial data anticipated **2H 2024** |
| | | Pancreatic Cancer | Azenosertib + gemcitabine | | | | | *Investigator initiated study* |
| | | Breast Cancer | **ZAP-IT** Azenosertib + carboplatin + pembrolizumab | | | | | *Investigator initiated study* |
| ZN-d5 BCL-2 Inhibitor | | Acute Myeloid Leukemia | **ZN-d5-004C** ZN-d5 + azenosertib | | | | | Initial data anticipated **2H 2024** |

zentalis

# Clinical Programs Position Zentalis for Multiple Datasets with Value-creating Potential



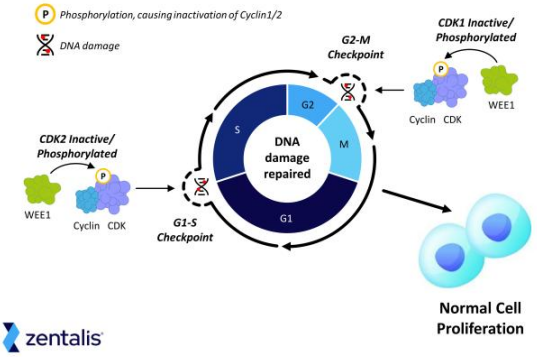

zentalis

Abbreviations: 1H, first half; 2H, second half

# Azenosertib Mechanism of Action – Inhibitor of WEE1, Master Cell Cycle Regulator

## Normal Cell Cycle Regulation

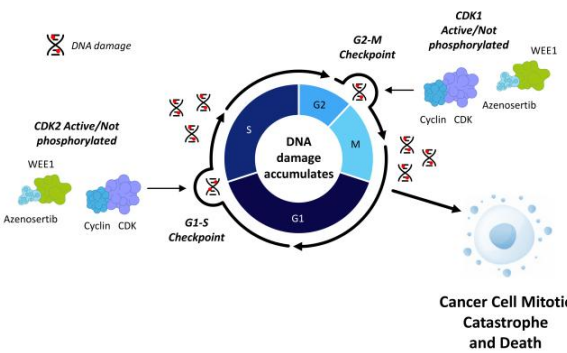
- CDKs and their cyclin binding partners promote progression through the cell cycle
- Following DNA damage, WEE1 kinase phosphorylates and inactivates Cyclin/CDK complexes at both G1-S and G2-M checkpoints to halt the cell cycle and allow for repair
- Upon DNA repair, cells progress through the cell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




Normal Cell Proliferation

## Cancer Cell and Azenosertib

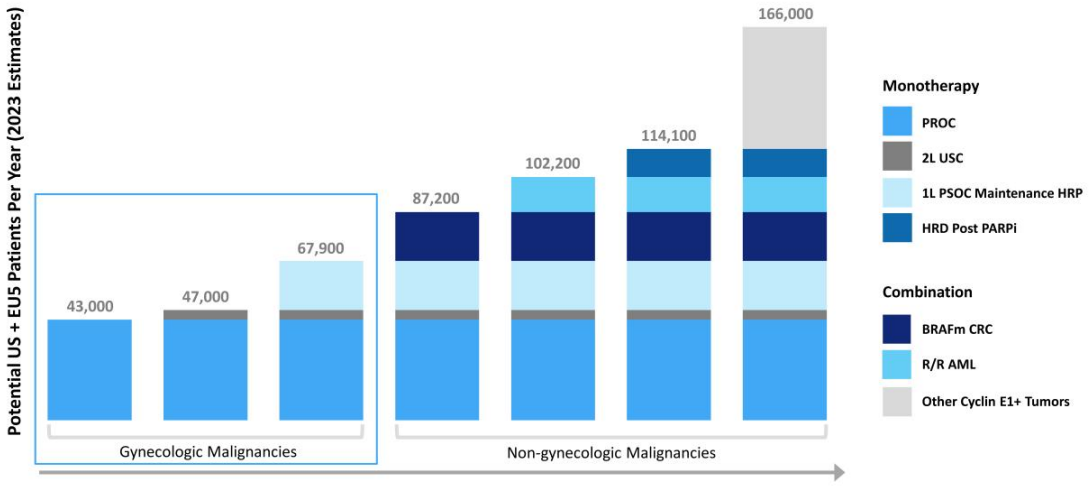
- In cancer cells, oncogene induced replication stress (e.g. Cyclin E1 activation or a driver mutation) leads to high levels of DNA damage and genomic instability
- Cancers with high levels of replication stress are sensitized to WEE1 inhibition via azenosertib
- Inhibition of WEE1 activates CDKs and increases DNA damage to intolerable levels, resulting in mitotic catastrophe and cell death




Cancer Cell Mitotic Catastrophe and Death

zentalis

# Azenosertib Treatable Patient Population More Than Doubles as Franchise Expands to Non-Gynecologic Malignancies




'Drug treatable' estimates from DRG Clarivate. For 'Other Cyclin E1+ tumors' used incidence reported by SEER and ECIS.
HRD Post PARPi tumor types: Prostate, Pancreas and Breast; Other Cyclin E1+ Tumor Types include bladder, stomach, esophageal, lung, and breast cancer
Abbreviations: PROC, platinum resistant ovarian cancer; 2L, second line; USC, uterine serous carcinoma; PSOC, platinum sensitive ovarian cancer; HRD, homologous recombination repair deficient; PARPi, poly-ADP ribose polymerase inhibitor; BRAFm CRC, BRAF V600E mutant colorectal cancer; R/R AML, relapsed or refractory acute myeloid leukemia

# Azenosertib Monotherapy Results

Monotherapy Anti-tumor Activity in Gynecologic Malignancies with Favorable Safety and Tolerability Profile

Monotherapy, ZN-c3-001

# Longer Follow Up Improves Duration of Benefit

## Strong Safety and Tolerability of Azenosertib Monotherapy

**CORPORATE CALL**
June 6, 2023

- **37% Objective Response Rate** using intermittent dosing in ovarian and USC patients
- Established monotherapy **RP2D** of 400 mg 5:2
- **Doubled steady state drug exposure** compared to continuous dosing

**UPDATED DATA**
Nov 6, 2023

- **Median follow up has increased by nearly 5 months and mPFS has increased to 6.5 months**
- **Maintained excellent safety and tolerability with intermittent dosing**

Abbreviations: USC, uterine serous carcinoma; RP2D: recommended Phase 2 dose; 5:2 refers to administration schedule of five days on therapy and two days off; mPFS, median progression free survival

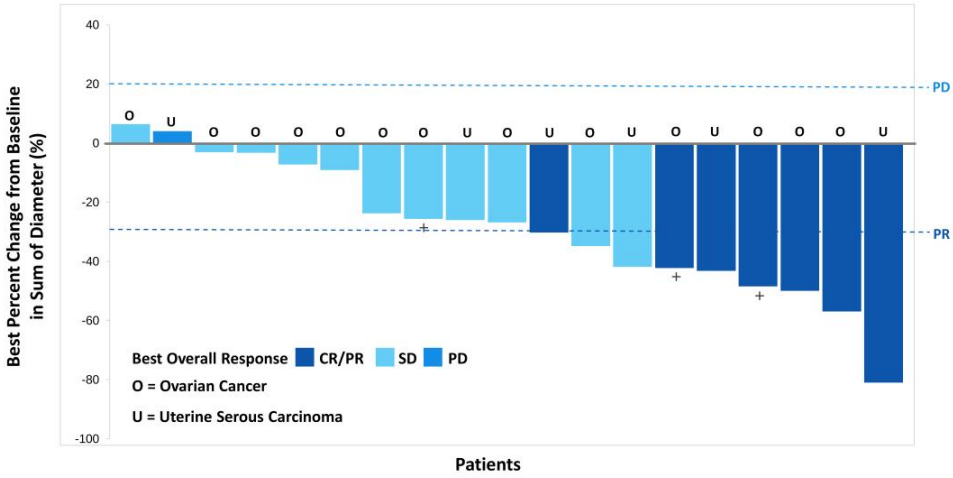
# Intermittent Monotherapy Patient Population Was Heavily Pretreated and Treatment Refractory

| | USC | HGSOC |
|---|---|---|
| | N=6 | N=13 |
| **Prior Lines of Treatment** | | |
| Median (Range) | 3.5 (1-6) | 6 (2-11) |
| Platinum Resistant* (N, %) | 5 (83.3) | 5 (38.5) |
| Platinum Refractory** (N, %) | NA | 8 (61.5) |
| **Prior Therapies** (N, %) | | |
| Prior PARP Inhibitor | 1 (16.7) | 10 (76.9) |
| Prior Experimental Agents | 0 (0.0) | 5 (38.5) |
| Prior VEGF Inhibitor | 5 (83.3) | 11 (84.6) |
| Prior Anti-PD-1/PD-L1 | 6 (100) | 1 (7.7) |

USC and HGSOC subjects who received at least one dose of azenosertib with intermittent dosing schedule, have baseline measurable disease by RECIST 1.1, and at least one post-baseline scan.
*Platinum Resistant: For USC patients, received prior platinum therapy. For HGSOC patients, progression within 90-180 days of prior dose of a platinum-based regimen in any line of therapy.
**Platinum Refractory: Progression within 90 days of prior dose of a platinum-based regimen in any line. Progression date based on progression date if available or start date of next therapy.
Abbreviations: USC, uterine serous carcinoma; HGSOC, high grade serous ovarian cancer; PARP, poly-ADP ribose polymerase; VEGF, vascular endothelial growth factor; PD-1/PD-L1, programmed cell death protein 1/programmed death ligand 1.

# Monotherapy Azenosertib Results in a 37% Confirmed Response Rate

## In Both Platinum Resistant Ovarian Cancer and Uterine Serous Carcinoma

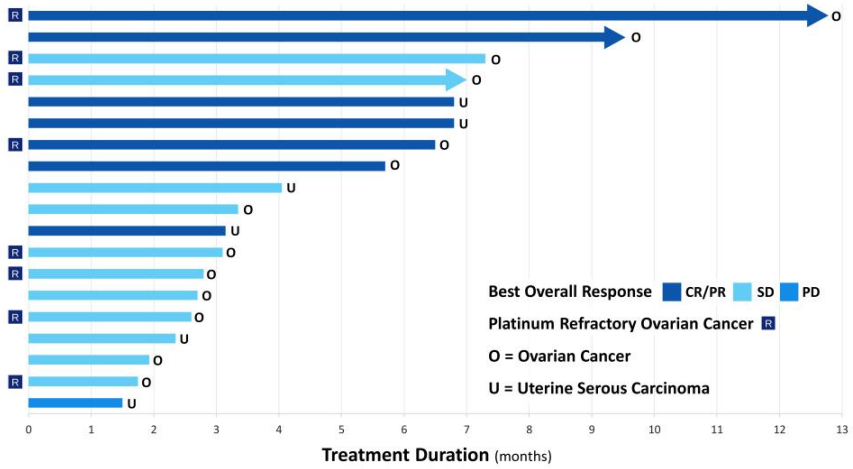



**ORR = 36.8%**

zentalis

Subjects who received at least one dose of azenosertib with intermittent dosing schedule, have baseline measurable disease by RECIST 1.1, and at least one post-baseline scan.
Abbreviations: +, patients remain on therapy at the time of data cut-off; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate

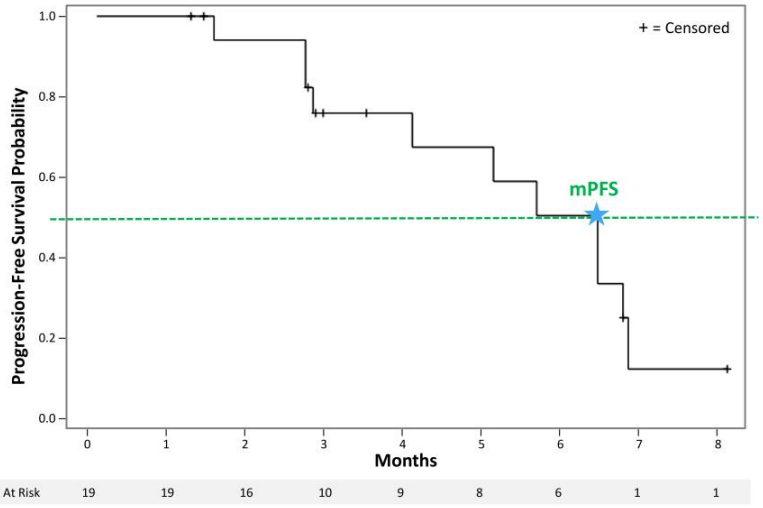
# Monotherapy Azenosertib Has Meaningful and Durable Benefit to Platinum Resistant Ovarian Cancer/USC Patients




zentalis

* Subjects who received at least one dose of azenosertib with intermittent dosing schedule, have baseline measurable disease by RECIST 1.1, and at least one post-baseline scan.
Abbreviations: PROC, platinum resistant ovarian cancer; USC, uterine serous carcinoma; CR, complete response; PR, partial response;
SD, stable disease; PD, progressive disease; Platinum Refractory: Progression within 90 days of last dose of a platinum-based regimen in any line.

# Monotherapy Azenosertib Has Meaningful and Durable Benefit to Platinum Resistant Ovarian Cancer/USC Patients




| At Risk | 19 | 19 | 16 | 10 | 9 | 8 | 6 | 1 | 1 |
|---|---|---|---|---|---|---|---|---|---|

**mPFS (95% CI): 6.5 months (2.79, 6.87)**

zentalis

* Subjects who received at least one dose of azenosertib with intermittent dosing schedule, have baseline measurable disease by RECIST 1.1, and at least one post-baseline scan.
Abbreviations: USC, uterine serous carcinoma; mPFS, median progression-free survival

# Azenosertib Monotherapy Continues to Demonstrate Excellent Safety Profile with Additional Patients Across Tumor Types*

## Treatment Related AEs, n (%)

| | ALL GRADES | GRADE 3/4 |
|---|---|---|
| **Gastrointestinal** | | |
| Nausea | 20 (43.5) | 2 (4.3) |
| Diarrhea | 22 (47.8) | 4 (8.7) |
| Vomiting | 8 (17.4) | 1 (2.2) |
| Decreased appetite | 4 (8.7) | 1 (2.2) |
| Dehydration | 5 (10.9) | 0 |

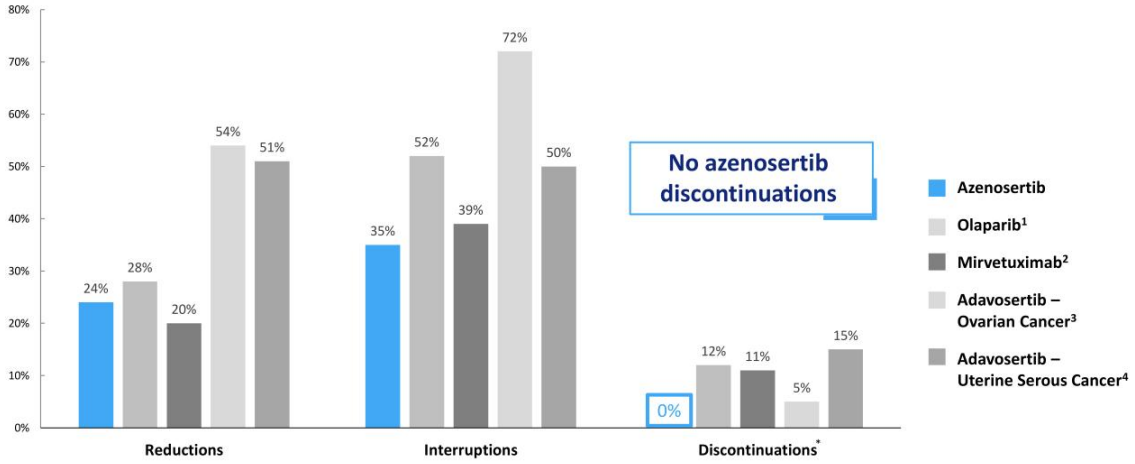
| | ALL GRADES | GRADE 3/4 |
|---|---|---|
| **Fatigue** | | |
| | 18 (39.1) | 5 (10.9) |
| **Hematologic** | | |
| Anemia | 11 (23.9) | 5 (10.9) |
| Thrombocytopenia | 9 (19.6) | 4 (8.7) |
| Neutropenia | 9 (19.6) | 7 (15.2) |

**No cases of febrile neutropenia or sepsis**

zentalis

*Safety Evaluable Population (All tumor types; n=46) as of Sept 27, 2023 versus n=27 reported on June 6, 2023 corporate call: Received at least one dose of drug; Intermittent 350 5:2 and 400 5:2; Treatment Related AEs > 10% for entire trial and treatment related AEs of interest. Abbreviations: AE, adverse event; 5:2, 5-days of treatment followed by 2-days off treatment

# Azenosertib is Well Tolerated with Similar or Better Tolerability Compared to Other Gynecologic Malignancy Therapies




Safety Evaluable Population (All tumor types; n=46): Received at least one dose of drug; Intermittent 350 5:2 and 400 5:2; Not head-to-head comparisons; *Discontinuations due to treatment related adverse events

1 Poveda A, et al. Lancet Oncol 2021;22:620-631; 2 Moore K, et al. J Clin Oncol 2023;41:abstr LBA5507; 3 Westin S, et al. J Clin Oncol 2021 39:15_suppl, 5505;
4 Liu JF, et al. Society of Gynecologic Oncology Annual Meeting on Women's Cancer; March 25-28; Tampa, Florida. Abstract 219

# Monotherapy Conclusions

## Data Supports Ongoing Azenosertib Monotherapy Potentially Registrational Studies in Ovarian Cancer and Uterine Serous Carcinoma

**MONOTHERAPY EFFICACY**
37% confirmed ORR

**mPFS of 6.5 MONTHS**

**EXCELLENT TOLERABILITY & SAFETY**
Consistent or better than other available agents

**DEFINITIVE DATA**
Supports differentiation from other clinical WEE1 inhibitors

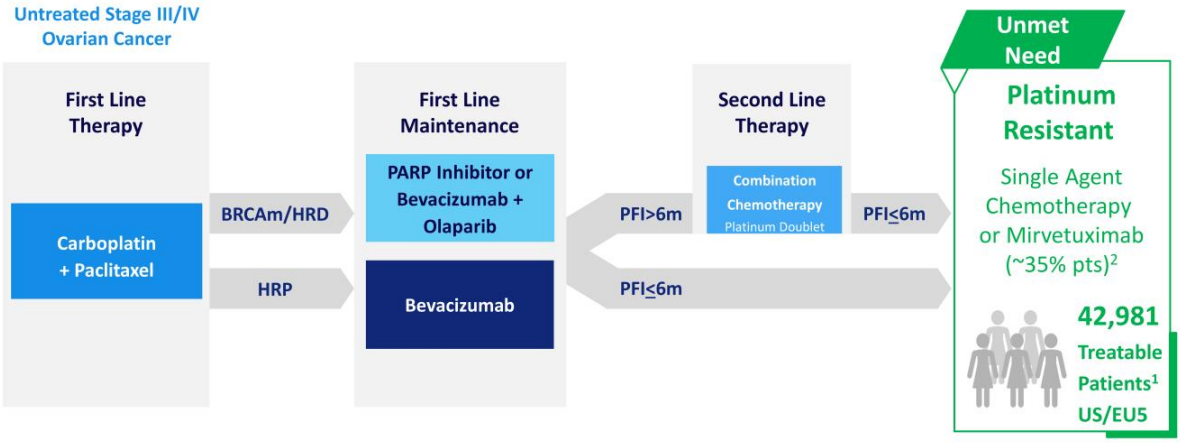
zentalis

Abbreviations: ORR, objective response rate; mPFS, median progression free survival; Comparisons to other agents are not head-to-head.

# Phase 2 Trials of Azenosertib

Potential Paths to Registration in Platinum Resistant Ovarian Cancer and Uterine Serous Carcinoma

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



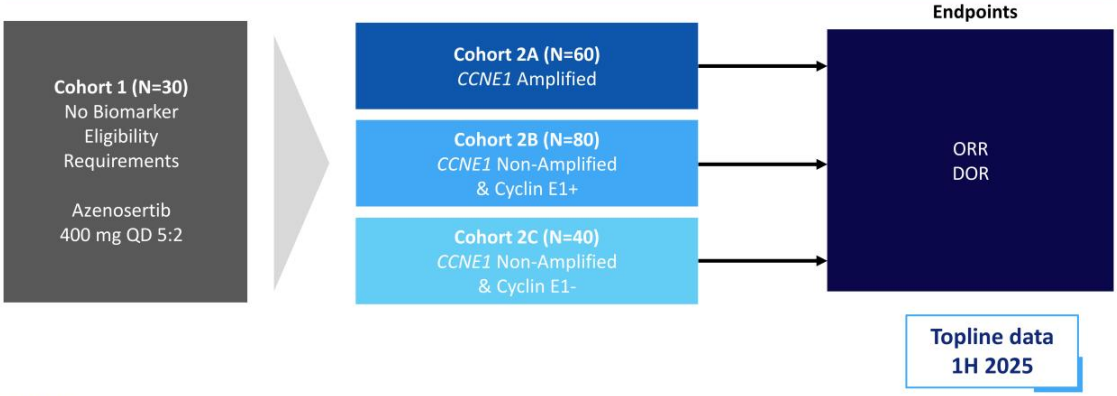

zentalis

1 Figures represent Company estimates of U.S. and EU5 patients with conditions covered by the Company's targeted indications; Source: IQVIA, DRG Clarivate;
2 Matulonis U. JCO 2023 41:13:2436-2445; Abbreviations: BRCAm, BRCA mutant; HRD, homologous-recombination repair deficient; HRP, homologous-recombination repair proficient; PFI, platinum-free interval

# DENALI (ZN-c3-005): Prospective Evaluation of *CCNE1* Amplification and Cyclin E1+ in Platinum Resistant High-Grade Serous Ovarian Cancer

## CURRENTLY ACCRUING

**Key Eligibility: 1-5 prior lines of therapy in Cohort 1 (1-4 prior lines in Cohort 2); Mandatory Sufficient Tissue; Cannot be Platinum Refractory (DFI < 3month from last platinum based therapy)**




**Topline data 1H 2025**

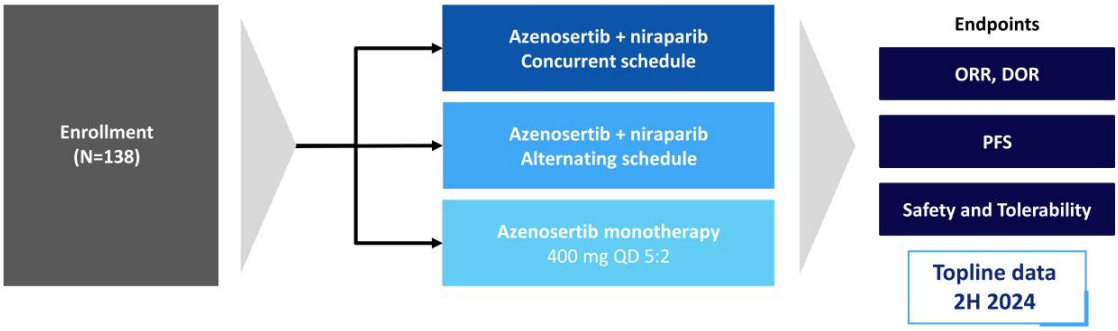
Note: Cyclin E1+ refers to protein overexpression determined by immunohistochemistry
Abbreviations: QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; DOR, Duration of Response; 1H, first half

NCT05128825

# MAMMOTH (ZN-c3-006): Phase 1/2 Study of Azenosertib in Combination with Niraparib or Alternating with Niraparib or as a Monotherapy in Patients with PARP-Resistant High-Grade Epithelial Ovarian Cancer

**CURRENTLY ACCRUING**

**Key Eligibility: 1-5 prior lines of therapy; platinum-resistant, progressed while receiving an approved PARP inhibitor; Mandatory Sufficient Tissue; Cannot be Platinum Refractory (DFI < 3 months from last platinum based therapy)**




NCT05198804

zentalis

Abbreviations: PARP, poly-ADP ribose polymerase; 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; 2H, second half

# New Treatment Options Needed in 2L+ Uterine Serous Carcinoma

Stage IV
or Recurrent USC

1L Carboplatin + Paclitaxel +
Pembrolizumab/Dostarlimab

Unmet Need

2L+ Single-Agent
Chemotherapy

4,103
Treatable
Patients[1]
US/EU5

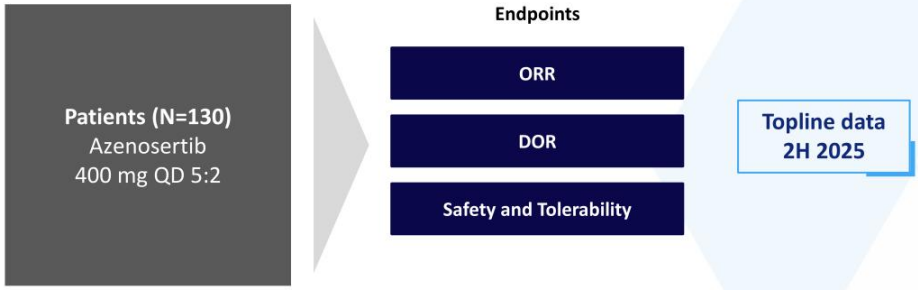
zentalis

1 Figures represent Company estimates of U.S. patients with conditions covered by the Company's targeted indications and are dependent upon regulatory approvals; Source: IQVIA, DRG Clarivate, Kantar Health;
Abbreviations: 2L+, second line maintenance plus; USC, uterine serous carcinoma; 1L, first line

# TETON (ZN-c3-004): Azenosertib Monotherapy in Women with ≥2L Advanced Uterine Serous Carcinoma

**CURRENTLY ACCRUING - FDA Fast Track Designation**

**Key Eligibility: ≥1 prior platinum-based chemotherapy regimen; prior anti-PD(L)1**



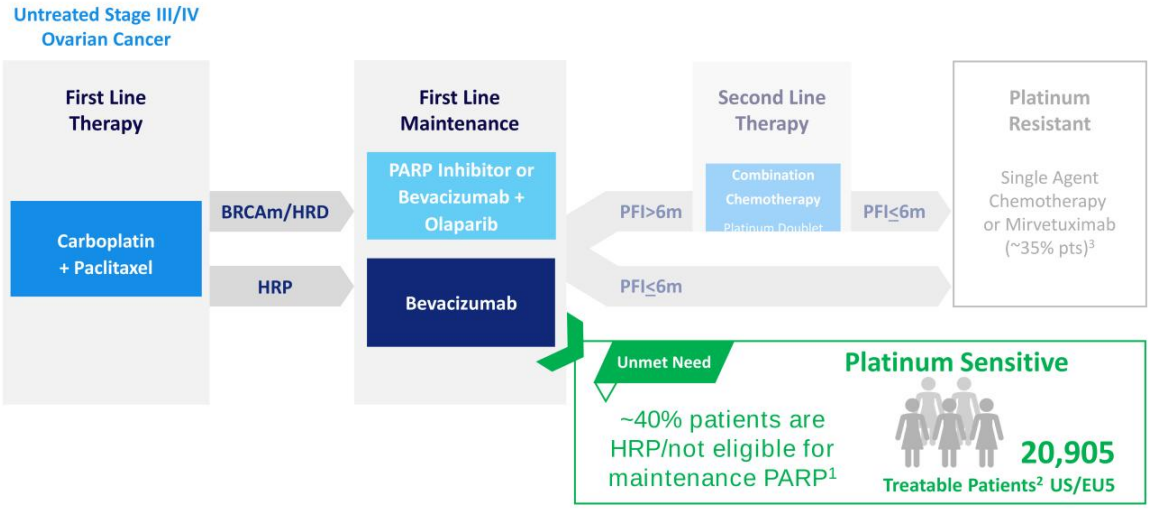

Abbreviations: 2L, two lines; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; DOR, duration of response; 2H, second half; The FDA granted Fast Track designation in November 2021 to azenosertib in patients with advanced or metastatic USC who have received at least one prior platinum-based chemotherapy regimen for management of advanced or metastatic disease.

NCT04814108

# Azenosertib in Platinum Sensitive Ovarian Cancer

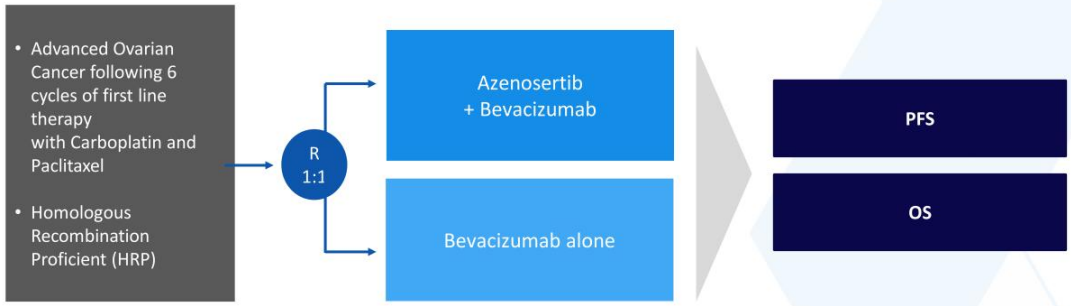
1L Maintenance Opportunity to Provide Prolonged Benefit for a Larger Number of Patients

# Opportunity for Azenosertib in First Line Maintenance in Homologous Repair Proficient (HRP) Platinum Sensitive Ovarian Cancer




1 Ray-Coquard I. N Engl J Med 2019; December 2019 381:2416-2428; 2 Figures represent Company estimates of U.S. and EU5 patients with conditions covered by the Company's targeted indications; Source: IQVIA, DRG Clarivate;
3 Matulonis U. JCO 2023 41:13:2436-2445; Abbreviations: BRCAm, BRCA mutant; HRD, homologous-recombination repair deficient; HRP, homologous-recombination repair proficient; PFI, platinum-free interval

# Azenosertib in 1L Maintenance Setting for Platinum Sensitive Ovarian Cancer




zentalis

Abbreviations: 1L, one line; PFS, progression free survival; OS, overall survival; 2H, second half

# Potential for Azenosertib to Impact the Greatest Number of Ovarian Cancer Patients in the 1L Maintenance Setting

**2x** as **many patients**

receive 1L maintenance treatment compared to 2L treatment[1]

Evolving labels and prescribing practice for PARPi **presents an opportunity**

for a new 1L maintenance oral therapy for patients with HRP/unknown tumors

**>40%** of **1L maintenance patients**

are HRP[2] and not eligible to receive a PARPi

**Azenosertib uniquely positioned for success in maintenance setting**

Oral non-chemotherapy agent
Clear global regulatory pathways

zentalis

1 Figures represent Company estimates of U.S. and EU5 patients with conditions covered by the Company's targeted indications; Source: IQVIA, DRG Clarivate Kantar and DRG;
2 Ray-Coquard I., N Engl J Med 2019; December 2019 381:2416-2428; Abbreviations: 1L, first line treatment; 2L, second line treatment; HRP, homologous-recombination repair proficient; PARPi, poly-ADP ribose polymerase inhibitor

# Azenosertib as 1L Maintenance Therapy in Platinum Sensitive Ovarian Cancer Patients

## Additional trial details in 2H 2024

"Zentalis' frontline maintenance study of WEE1 inhibition could be practice changing for our patients with poor prognosis ovarian cancer"

**Professor Alexandra Leary, MD, PhD**
Deputy Chair of Medical Oncology,
Institut de Cancérologie Gustave Roussy, France
GINECO and ENGOT Investigator

"Advancing azenosertib into the first-line HRP maintenance setting has the potential to reach the largest number of patients with ovarian cancer"

**Professor Premal Thaker, MD, MS**
Distinguished Chair of Obstetrics and Gynecology
Washington University School of Medicine in St. Louis
GOG Investigator

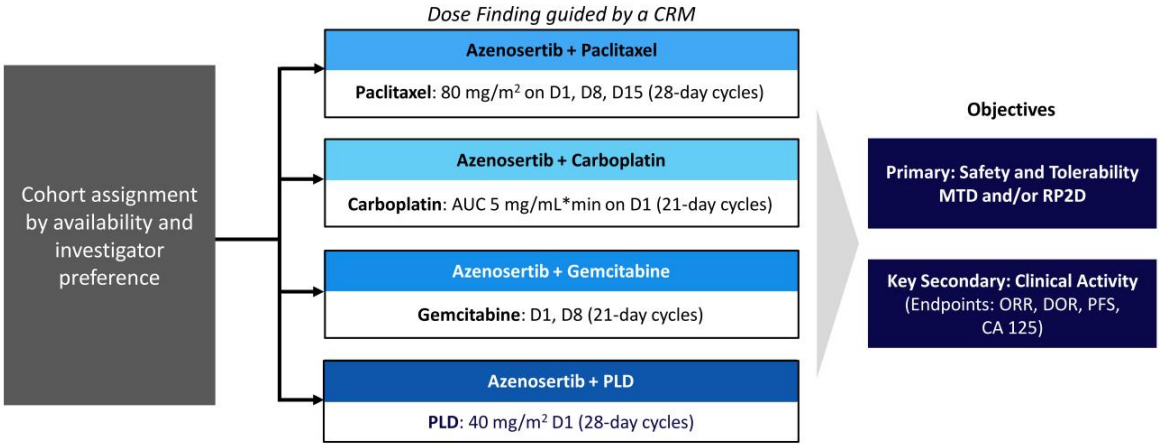
zentalis

# Azenosertib Combination with Chemotherapy

Clinical Data Shows Strong Efficacy and Favorable Safety Profile in Platinum Resistant Ovarian Cancer

# ZN-c3-002: Phase 1b Combination Study in Platinum Resistant Ovarian Cancer

**Key Eligibility: Platinum-resistant/refractory; Up to 3 prior lines of chemotherapy**




NCT04516447

zentalis

Liu JF, et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 5513-5513; Abbreviations: CRM, continuous reassessment model; QD, once daily; D, day; AUC, area under the curve; PLD, pegylated liposomal doxorubicin; MTD, maximum tolerated dose; RP2D, recommended Phase 2 dose; ORR, objective response rate; DOR, duration of response; PFS, progression-free survival

# Encouraging Efficacy and Durability with Azenosertib* in Combination with Chemotherapy in Platinum Resistant Ovarian Cancer

| Endpoint | Azenosertib + Paclitaxel (N=26) | Azenosertib + Carboplatin (N=36) | Azenosertib + Gemcitabine (N=18) | Azenosertib + PLD (N=35) | Total (N=115) |
|---|---|---|---|---|---|
| Response-Evaluable* (N) | 22 | 28 | 13 | 31 | 94 |
| ORR (confirmed), N (%) | 11 (50.0) | 10 (35.7) | 5 (38.5) | 6 (19.4) | 32 (34.0) |
| Median DOR (95% CI) in months | 5.6 (3.8-NE) | 11.4 (8.3-NE) | 6.2 (NE) | 7.3 (1.5-NE) | 8.3 (5.6-12.4) |
| Clinical Benefit Rate (CR + PR + SD for ≥ 16 weeks), N (%) | 18 (81.8) | 16 (57.1) | 6 (46.2) | 24 (77.4) | 64 (68.1) |
| Median PFS (95% CI) in months | 7.4 (5.5-NE) | 10.4 (3.3-14.5) | 8.3 (3.3-NE) | 6.3 (3.7-11.0) | 9.0 (5.8-13.7) |

zentalis

*Response-evaluable subjects are treated subjects with baseline measurable disease per RECIST version 1.1 and at least one post-baseline assessment. All objective responses were confirmed per RECIST v 1.1. Data include patients on all schedules of azenosertib plus chemotherapy. Liu JF, et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 5513-5513; Abbreviations: PLD, pegylated liposomal doxorubicin; ORR, objective response rate; DOR, duration of response; CI, confidence interval; NE, not estimable; CR, complete response; PR, partial response; SD, stable disease; PFS, progression-free survival; RECIST, response evaluation criteria in solid tumors

Data cut-off: April 10, 2023

# Azenosertib* in Combination with Chemotherapy Demonstrates Favorable Safety Profile

| Treatment-Related Adverse Event ≥20% N (%) | | Azenosertib + Paclitaxel (N=19) | | Azenosertib + Carboplatin (N=14) | | Azenosertib + Carboplatin (N=8) | | Azenosertib + Gemcitabine (N=10) | | Azenosertib + PLD (N=8) | | Total (N=59) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | All Doses* | | All Doses | | Doses ≤ MTD | | All Doses** | | All Doses* | | | |
| Grade | | All Gr | Gr ≥3 | All Gr | Gr ≥3 | All Gr | Gr ≥3 | All Gr | Gr ≥3 | All Gr | Gr ≥3 | All Gr | Gr ≥3 |
| Hematologic | Neutropenia | 11 (57.9) | 5 (26.3) | 7 (50.0) | 1 (7.1) | 4 (50.0) | 0 | 7 (70.0) | 4 (40.0) | 3 (37.5) | 3 (37.5) | 28 (54.9) | 13 (25.5) |
| | Thrombo-cytopenia | 4 (21.1) | 0 | 9 (64.3) | 5 (35.7) | 4 (50.0) | 2 (25.0) | 8 (80.0) | 6 (60.0)* | 3 (37.5) | 3 (37.5) | 24 (47.1) | 14 (27.5) |
| | Anemia | 8 (42.1) | 1 (5.3) | 10 (71.4) | 4 (28.6) | 4 (50.0) | 1 (12.5) | 5 (50.0) | 2 (20.0) | 2 (25.0) | 1 (12.5) | 25 (49.0) | 8 (15.7) |
| Gastro-intestinal | Nausea | 7 (36.8) | 1 (5.3) | 6 (42.9) | 0 | 3 (37.5) | 0 | 5 (50.0) | 0 | 4 (50.0) | 1 (12.5) | 22 (43.1) | 2 (3.9) |
| | Vomiting | 2 (10.5) | 1 (5.3) | 2 (14.3) | 0 | 2 (25.0) | 0 | 1 (10.0) | 0 | 4 (50.0) | 1 (12.5) | 9 (17.6) | 2 (3.9) |
| | Diarrhea | 6 (31.6) | 1 (5.3) | 5 (35.7) | 0 | 3 (37.5) | 0 | 6 (60.0) | 0 | 2 (25.0) | 0 | 19 (37.3) | 1 (2.0) |
| Other | Fatigue | 8 (42.1) | 2 (10.5) | 5 (35.7) | 1 (7.1) | 4 (50.0) | 0 | 6 (60.0) | 2 (20.0) | 2 (25.0) | 0 | 21 (41.2) | 5 (9.8) |

zentalis

*All doses were at or below MTD and were intermittent; **A MTD for gemcitabine + azenosertib has not been determined, further dose cohorts are ongoing.
Liu JF, et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 5513-5513; Abbreviations: MTD, maximum tolerated dose; PLD, pegylated liposomal doxorubicin

# Addition of Azenosertib to Single Agent Chemotherapy Increases Response Rates and Durability of Response in Ovarian Cancer Compared to Chemotherapy Alone

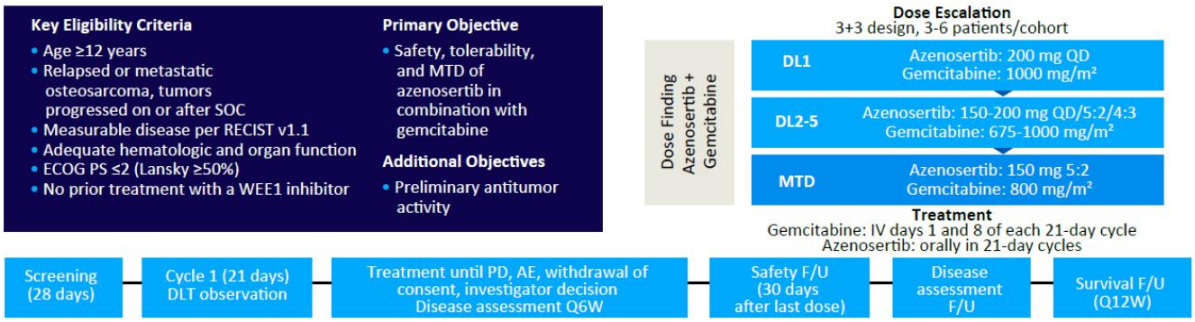
- 50% **50% Objective Response Rate** with 7.4-month Progression Free Survival in paclitaxel combination
- Superior durability in carboplatin combination with **10.4-month Progression Free Survival** and 36% Objective Response Rate
- Overall tolerability of paclitaxel and carboplatin combinations **compares favorably to SOC** chemotherapy doublets paclitaxel-carboplatin or PLD-carboplatin
- **Cyclin E1+ status** associated with **superior Objective Response Rate and longer Progression Free Survival** across response-evaluable patient population

zentalis

Liu JF, et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 5513-5513; Abbreviations: SOC, standard of care; PLD, pegylated liposomal doxorubicin

# Azenosertib in Osteosarcoma

# ZN-c3-003: Phase 1 Study Design and Subject Flow




- 31 patients were enrolled and treated. 31 patients were evaluable for safety; 29 patients were evaluable for DLTs (2 received <75% of study drug during the DLT period for an unrelated AE) and 28 were efficacy evaluable (had ≥1 post baseline-tumor assessment)

4:3, 4 days on, 3 days off; 5:2, 5 days on, 2 days off; A, azenosertib; AE, adverse event; DL, dose level; ECOG, Eastern cooperative Oncology Group; F/U, follow-up; G, gemcitabine; IV, intravenous; MTD, maximum tolerated dose; PS, performance status; OD, once daily; RECIST 1.1, Response Evaluation Criteria in Solid Tumors 1.1; SOC, standard of care.

Avutu et al, Phase 1 Results of the WEE1 Inhibitor, Azenosertib, in Combination With Gemcitabine in Adult and Pediatric Patients With Relapsed or Refractory Osteosarcoma. Abstract ##11525, ASCO 2024.

# Doses Evaluated and Dose-Limiting Toxicities

| Dose level | Azenosertib | 200 mg QD | 150 mg QD | 200 mg 5:2 | 200 mg 5:2 | 200 mg 4:3 | MTD 150 mg 5:2 |
|---|---|---|---|---|---|---|---|
| | Gemcitabine | 1000 mg/m² | 800 mg/m² | 800 mg/m² | 675 mg/m² | 800 mg/m² | 800 mg/m² |
| Patients treated, n | | 9 | 5 | 3 | 6 | 2 | 6 |
| Patients DLT-evaluable, n | | 8 | 5 | 3 | 5 | 2 | 6 |
| Patients with DLTs, n | | 3 | 2 | 2 | 1 | 1 | 0 |
| **DLT, n** | | | | | | | |
| Grade 4 thrombocytopenia | | 3 | 0 | 1 | 1 | 0 | 0 |
| Grade 3 nausea/vomiting/diarrhea | | 0 | 1 | 0 | 0 | 0 | |
| Grade 2 thrombocytopenia with bleeding | | 0 | 1 | 0 | 0 | 0 | |
| AE leading to <75% dose intensity | | | | | | | |
| Grade 4 neutropenia | | 0 | 0 | 1 | 0 | 0 | |
| Grade 2 thrombocytopenia | | 0 | 0 | 0 | 0 | 1 | |

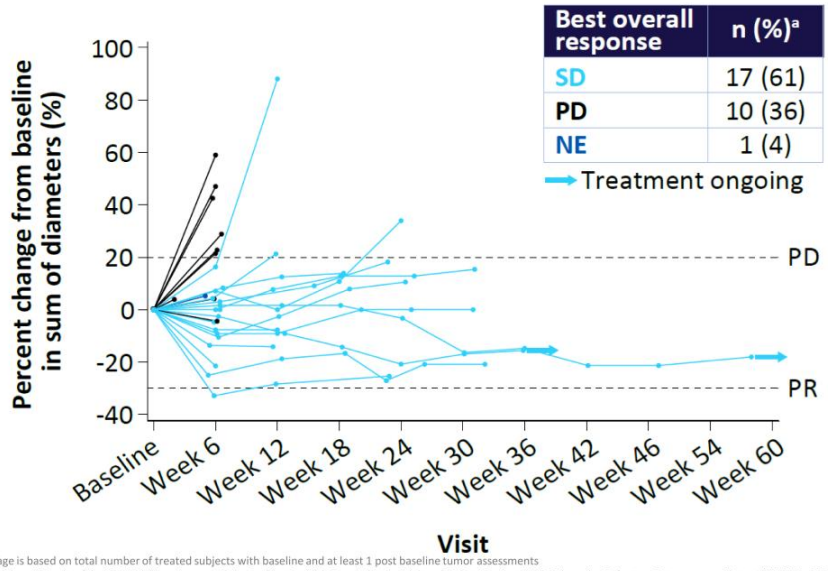
No evidence of a drug-drug interaction between azenosertib and gemcitabine was observed

Pharmacokinetic results were consistent with those seen in azenosertib monotherapy and other chemotherapy combination studies with azenosertib

zentalis

Avutu et al, Phase 1 Results of the WEE1 Inhibitor, Azenosertib, in Combination With Gemcitabine in Adult and Pediatric Patients With Relapsed or Refractory Osteosarcoma. Abstract ##11525, ASCO 2024.
Data cut-off: January 9, 2024

# Percent Change From Baseline in the Sum of Longest Diameters for Target Lesions




| Best overall response | n (%)[a] |
|---|---|
| SD | 17 (61) |
| PD | 10 (36) |
| NE | 1 (4) |

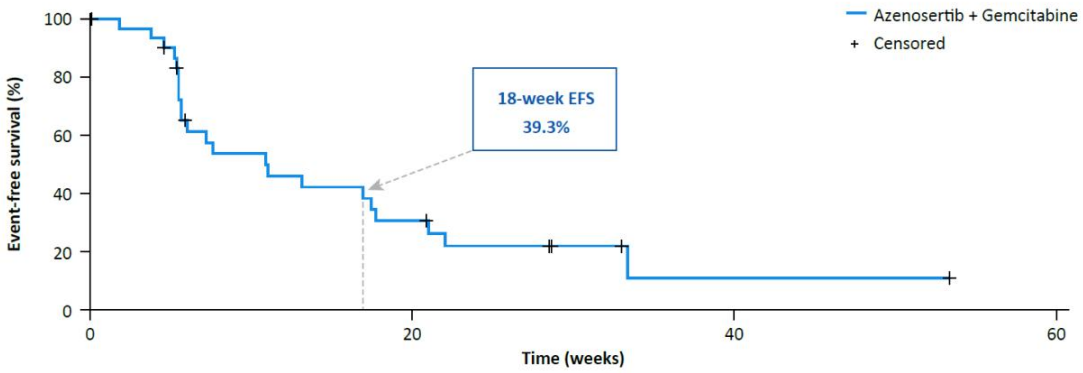
Treatment ongoing

zentalis

• Percentage is based on total number of treated subjects with baseline and at least 1 post baseline tumor assessments

Avutu et al, Phase 1 Results of the WEE1 Inhibitor, Azenosertib, in Combination With Gemcitabine in Adult and Pediatric Patients With Relapsed or Refractory Osteosarcoma. Abstract ##11525, ASCO 2024.

# Event-Free Survival Among Patients Receiving Azenosertib + Gemcitabine




| Patients at risk | 31 | 14 | 8 | 3 | 1 | 1 |
|---|---|---|---|---|---|---|

Clinical data as of 9 Jan 2024.

zentalis

Avutu et al, Phase 1 Results of the WEE1 Inhibitor, Azenosertib, in Combination With Gemcitabine in Adult and Pediatric Patients With Relapsed or Refractory Osteosarcoma. Abstract ##11525, ASCO 2024.

# Treatment-Emergent Adverse Events Occurring in >20% of Patients

- The MTD was identified as Azenosertib 150 mg (5:2) + gemcitabine 800 mg/m$^2$
- Azenosertib + gemcitabine was associated with a manageable safety profile and no new safety signals were identified
- There were no grade 4 thrombocytopenia events or instances of febrile neutropenia at the MTD

| Adverse Event | All Cohorts All Grades [n(%)] N=31 | All Cohorts Grade ≥ 3 [n(%)] N=31 | MTD All Grades [n(%)] n=6 | MTD Grade ≥ 3 [n (%)] n=6 |
|---|---|---|---|---|
| Thrombocytopenia (combined) | 25 (80.6%) | 13 (41.9%) | 3 (50%) | 2 (33.3%) |
| Anemia (combined) | 15 (48.4%) | 6 (19.4%) | 2 (33.3%) | 1 (16.7%) |
| Fatigue | 15 (48.4%) | 4 (12.9%) | 4 (66.7%) | 1 (16.7%) |
| Nausea | 12 (38.7%) | 0 | 1 (16.7%) | 0 |
| Leukopenia (combined) | 11 (35.5%) | 6 (19.4%) | 1 (16.7%) | 0 |
| Neutropenia (combined) | 11 (35.5%) | 11 (35.5%) | 0 | 0 |
| Pyrexia | 10 (32.3%) | 1 (3.2%) | 3 (50%) | 0 |
| Headache | 9 (29%) | 0 | 2 (33%) | 0 |
| Lymphopenia (combined) | 8 (25.8%) | 6 (19.4%) | 2 (33%) | 2 (33%) |
| ALT Increase | 7 (22.6%) | 0 | 1 (16.7%) | 0 |
| Constipation | 7 (22.6%) | 0 | 1 (16.7%) | 0 |
| Diarrhea | 7 (22.6%) | 1 (3.2%) | 1 (16.7%) | 0 |
| Hypoalbuminemia | 7 (22.6%) | 1 (3.2%) | 3 (50%) | 1 (16.7%) |
| Hypokalemia | 7 (22.6%) | 2 (6.5%) | 2 (33%) | 1 (16.7%) |

zentalis

Avutu et al, Phase 1 Results of the WEE1 Inhibitor, Azenosertib, in Combination With Gemcitabine in Adult and Pediatric Patients With Relapsed or Refractory Osteosarcoma. Abstract ##11525, ASCO 2024.

Data cut-off: January 9, 2024

# Targeting Tumors with High Genomic Instability Using Azenosertib

# Multiple Mechanisms Leading to Genomic Instability Enhance Sensitivity to Azenosertib

## High Genomic Instability[1] Can be Caused By:

### Cyclin E1+ Activation

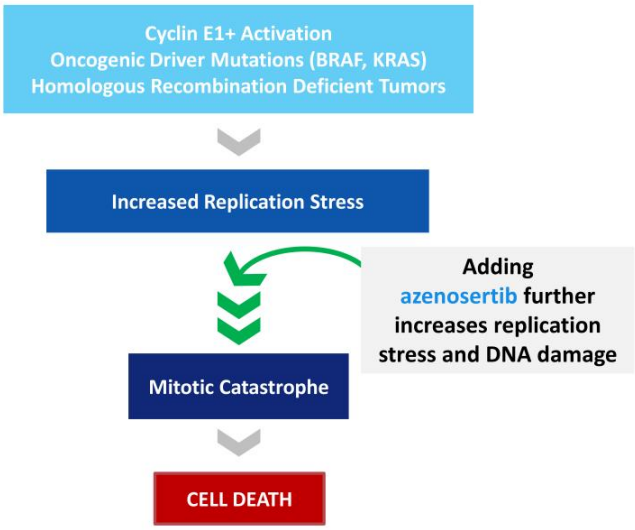
- Activation of Cyclin E1/CDK2 increases cell proliferation, resulting in higher replication stress and contributing to genomic instability

### Tumors with Oncogenic Driver Mutations[2]

- Driver mutations, such as BRAF or KRAS, accelerate G1/S cell cycle transition, inducing DNA replication stress, leading to DNA damage and genomic instability

### Homologous Recombination Deficient Tumors[3]

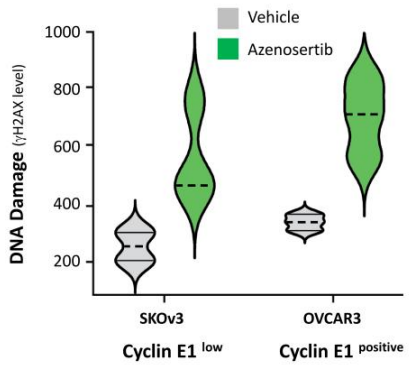
- Genomic instability results from inability to repair double stranded DNA breaks



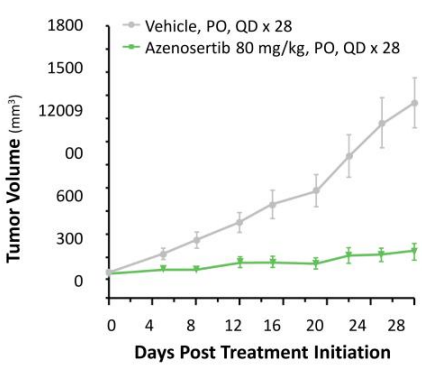

zentalis

1 Fagundes R, et al. Front Cell Dev Biol. 2021; 2 Stewart MD, Oncologist. 2022; 3 Zhang, J, et al. Genes 2016; Abbreviations: BRAF, V-Raf Murine Sarcoma Viral Oncogene Homolog B; KRAS, Kirsten rat sarcoma viral oncogene homolog

# Azenosertib Results in Higher Levels of DNA Damage and Tumor Growth Inhibition in Cyclin E1 Positive Tumors




- OVCAR3 tumors (Cyclin E1 $^{positive}$) have higher baseline levels of DNA damage than SKOV3 tumors (Cyclin E1 $^{low}$)
- **Azenosertib treatment further increases DNA damage**



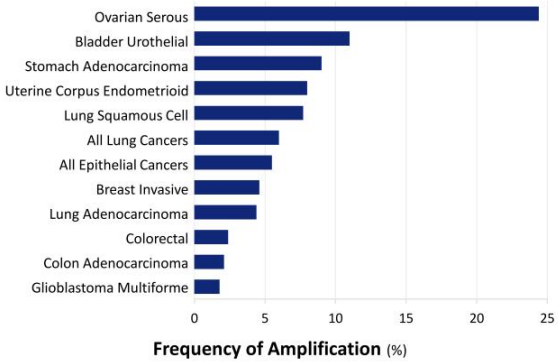

- Azenosertib treatment results in 88% Tumor Growth Inhibition (TGI) in xenografted Cyclin E1 $^{positive}$ OVCAR3 tumors

zentalis

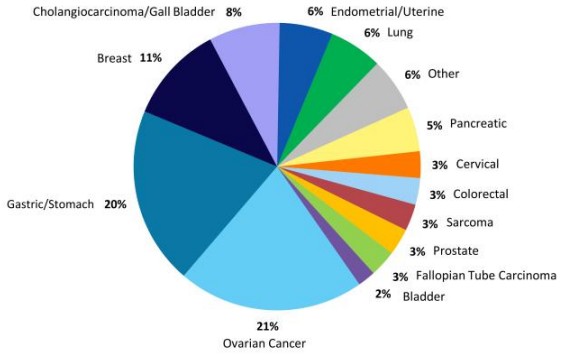
Ma, et al. Cancer Res (2023) 83 (7_Supplement): 2153; Abbreviations: PO, orally; QD, daily

# Cyclin E1 Amplification Particularly Prevalent in Gynecologic Malignancies But Occurs in Many Other Tumor Types

## TCGA Pan Cancer Analysis (6547 samples)[1]



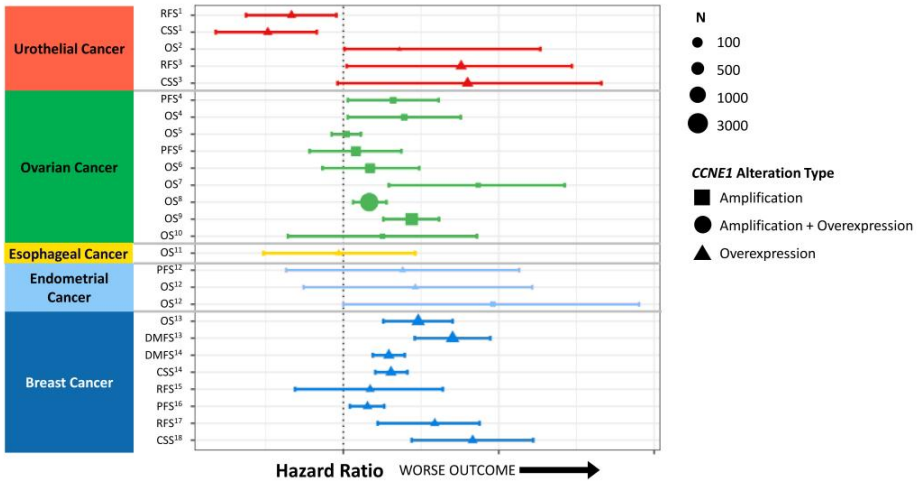

## Frequency of *CCNE1* Amplification Across Tumor Types[2]




zentalis

1 Etemadmoghadam D., et al. Proc Natl Acad Sci USA 2013; 2 Yao, S., et al. Sci Rep 12, 8701 2022. 3. TCGA GENIE: 2161/119807 (1.8%). 4. Foundation Insights database: 18802/541919 (3.5%)

# *CCNE1* Amplified and/or Cyclin E1+ Cancers Have a Worse Outcome Across Multiple Tumor Types

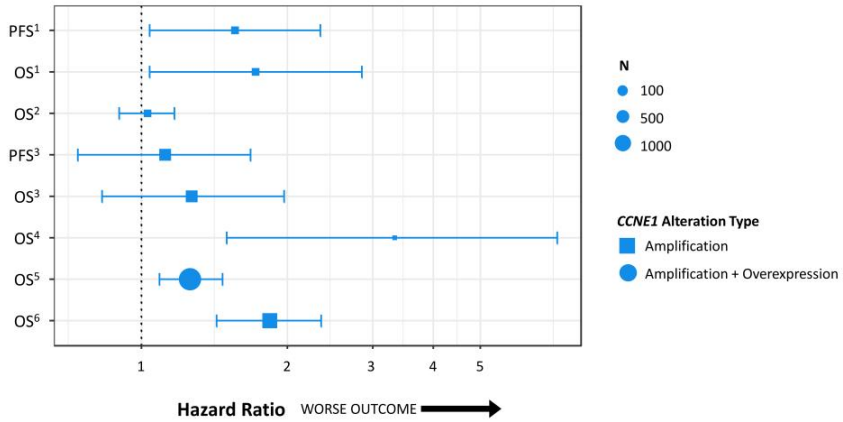



1 Shariat SF, et al. Human Path. 2006; 2 Matsushita R, et al. British J Cancer 2015; 3 Lotan Y, et al. Euro Assoc Urology 2013; 4 Stronach E, et al. Mol Cancer Res 2018; 5 Pils D, et al. Euro J Cancer 2014;
6 Petersen S, et al. Gynecol Oncol 2020; 7 Nakayama N, et al. Cancer 2010; 8 Kang E, et al. Cancer 2023; 9 Chan A, et al. J Path: Clin Res 2020; 10 Ayhan A, et al. Mod Path 2017; 11 Zhou Z, et al. BMC Gastroenterology 2014;
12 Nakayama K J Oncol. 2016; 13 Sieuwerts AM, et al. Clin Cancer Res 2006; 14 Lundgren C, et al. Acta Oncologica 2015; 15 Luhtala S, et al. Tumor Biol 2016; 16 Jansen MP, et al. Breast Cancer Res Treat 2012;
17 Desmedt C, et al. Int J Cancer 2006; 18. Chappuis PO, et al. Annals of Oncology 2005
Abbreviations: RFS, recurrence free survival, CSS; cancer specific survival, OS; overall survival; PFS, progression free survival; DMFS; distant metastasis free survival

# Ovarian Cancer Patients with *CCNE1* Amplified and/or Cyclin E1+ Cancers Have a Worse Outcome Following Platinum-Based Chemotherapy Treatment Independent of Platinum-Sensitivity Status

## 6 Studies; n=5,404

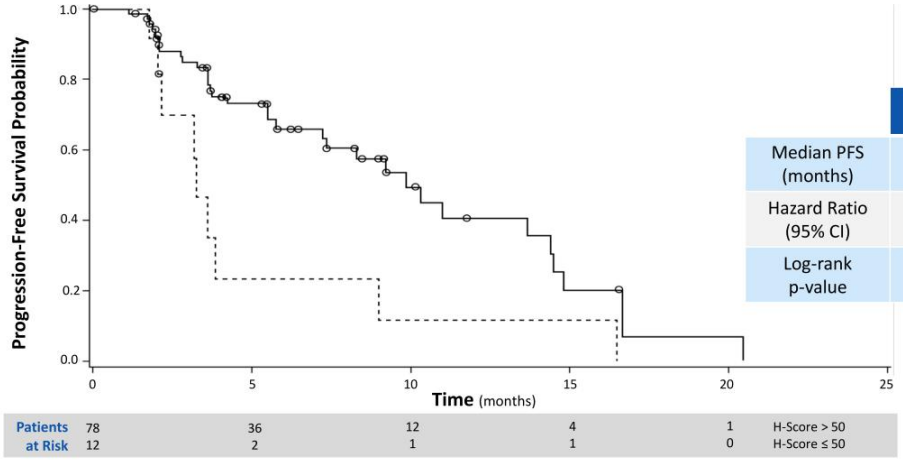
- 4 studies where timing of tissue collection was available- all were platinum sensitive tissue collected after ≤ 1 course of chemotherapy; 3,533/5,404 (65%)
- Other 2 studies did not disclose timing of tissue collection




zentalis

1 Stronach, et al. Mol Cancer Res 2018;16:1103-11; 2 Pils, et al. Eur J Cancer 2014;50:99-110; 3 Peterson, et al. Gynecol Oncol 2020;157:405-10; 3 Nakayama, et al. Cancer 2010;116:2621-34; 5 Kang, et al. Cancer 2023;129:697-713; 6 Chan, et al. J Pathol Clin Res 2020;6:252-62; *Timing of tissue collection was not disclosed. Abbreviations: PFS: progression free survival, OS; overall survival

# Progression Free Survival Triples in Patients with Cyclin E1+ Tumors Compared to Cyclin E1- Tumors in Azenosertib Chemotherapy Combinations (ZN-c3-002)

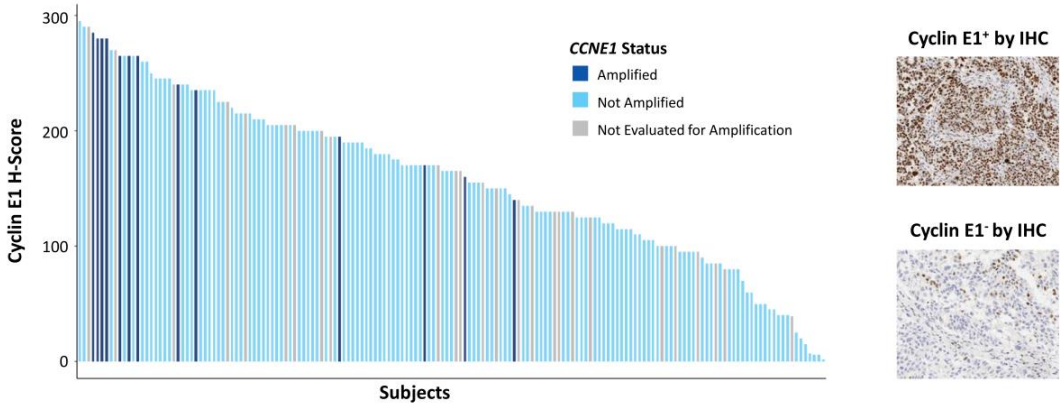



| | H-Score ≤ 50 (N=12) | H-Score > 50 (N=78) |
|---|---|---|
| Median PFS (months) | 3.25 | 9.86 |
| Hazard Ratio (95% CI) | 0.37 (0.18 – 0.79) | |
| Log-rank p-value | 0.0078 | |

zentalis

H-scores calculated by multiplying the percentage of cells (0 to 100%) with intensity of Cyclin E1 expression (0 to 3); Liu JF., et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 5513-5513;
Abbreviations: CI, confidence interval; PFS, progression free survival

# Analysis of Zentalis Clinical Trial Samples Confirms Cyclin E1 Protein Expression is High in the Majority of Ovarian Cancers



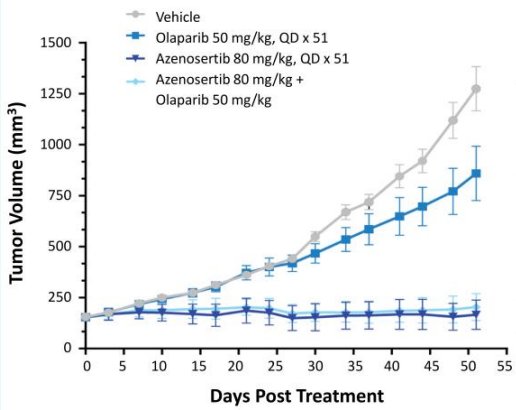

- HGSOC samples from an ongoing azenosertib clinical trial (ZN-c3-002, N=111) as well as 56 procured samples
- Cyclin E1 H-scores* were determined using a validated IHC assay and *CCNE1* amplification status was determined by tissue-based NGS
- Cyclin E1 IHC positivity is prevalent and occurs in tumors both with and without *CCNE1* amplification

zentalis

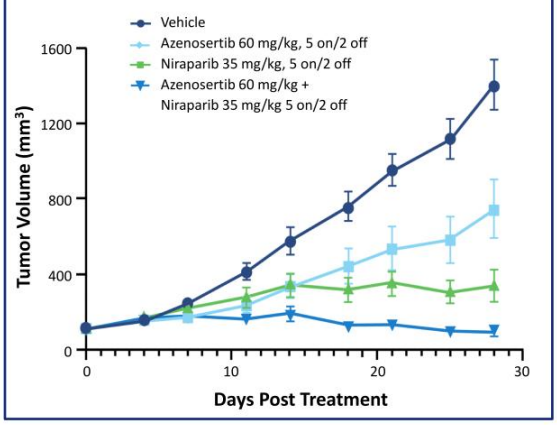
*H-scores calculated by multiplying the percentage of cells (0 to 100%) with intensity of Cyclin E1 expression (0 to 3).
Harismendy, et al. Presented at the AACR Special Conference in Cancer Research: Ovarian Cancer. October 5 - 7, 2023 - Boston, MA; Abbreviations: HGSOC, high-grade serous ovarian cancer; IHC, immunohistochemistry; NGS, next generation sequencing

# Monotherapy Azenosertib +/- PARP Inhibitor Combinations are Active in HRD Tumors, Including Models with Acquired PARP Resistance

**CDX Model PARPi Resistant Model** (MDA-MB-436; *BRCA1*mt)



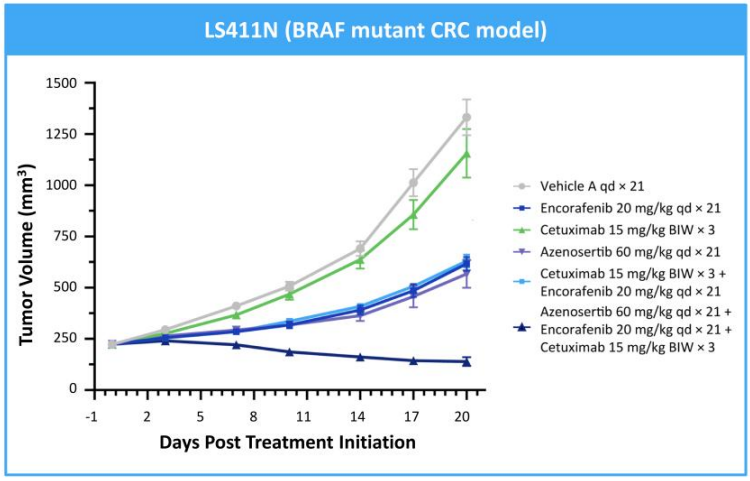

**PDX TNBC Model** (HBCx-10; *BRCA2*mt)




zentalis

Zentalis data on file; Abbreviations: PARP, poly-ADP ribose polymperase; HRD, homologous recombination repair deficient; PARPi, PARP inhibitor; CDX, cell line derived xenograft; PDX, patient derived xenograft; TNBC, triple-negative breast cancer

# Preclinical Data Supports the Combination of Azenosertib with Encorafenib and Cetuximab (BEACON Regimen)



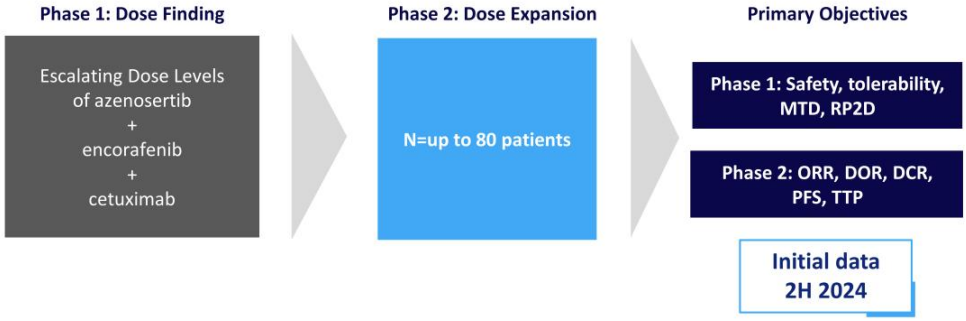

- Oncogene-induced replication stress in mutationally driven cancers leads to DNA damage and genomic instability[1]
- Azenosertib further increases replication stress and DNA damage, providing mechanistic basis for synergy with EGFR/BRAF inhibition
- Addition of azenosertib to the BEACON regimen is well tolerated and provides superior efficacy in an *in vivo* model of BRAF mutant CRC

zentalis

Zentalis Data on File; 1. Kotsantis P, et al. Cancer Discov. 2018. Abbreviations: BRAF, V-Raf Murine Sarcoma Viral Oncogene Homolog B; CRC, colorectal cancer; EGFR, epidermal growth factor receptor

# ZN-c3-016: Phase 1/2 Trial in BRAF mCRC in Collaboration with Pfizer

**Key Eligibility: BRAF V600E mutated mCRC; Disease progression after 1 or 2 previous regimens for metastatic disease; Prior therapy may include BRAF and/or EGFR directed therapy (e.g., may have progressed after BEACON regimen)**



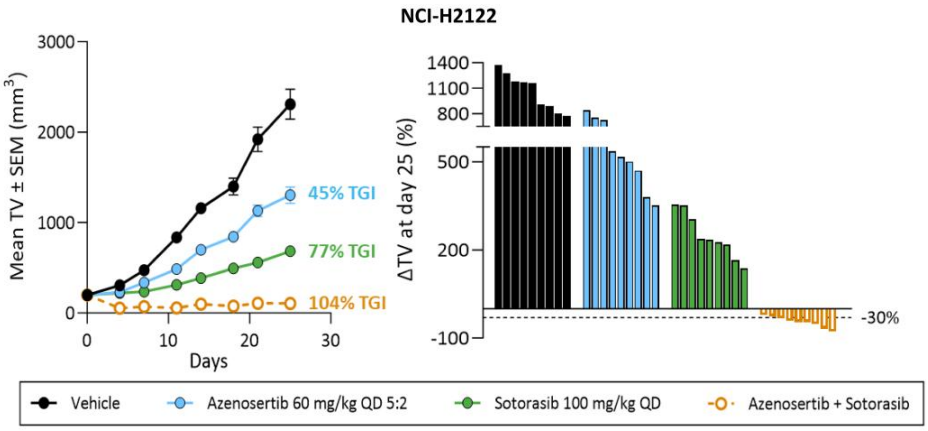

**Encorafenib in combination with cetuximab (BEACON) is the standard of care for 2L treatment of BRAF V600E mCRC**

NCT05743036

zentalis

Abbreviations: BRAF, V-Raf Murine Sarcoma Viral Oncogene Homolog B; mCRC, metastatic colorectal cancer; EGFR, epidermal growth factor receptor; MTD, maximum tolerated dose; RP2D, recommended phase 2 dose; ORR, objective response rate; DOR, duration of response; DCR, disease control rate; PFS, progression free survival; TTP, time to progression; 2H, second half; 2L, second line

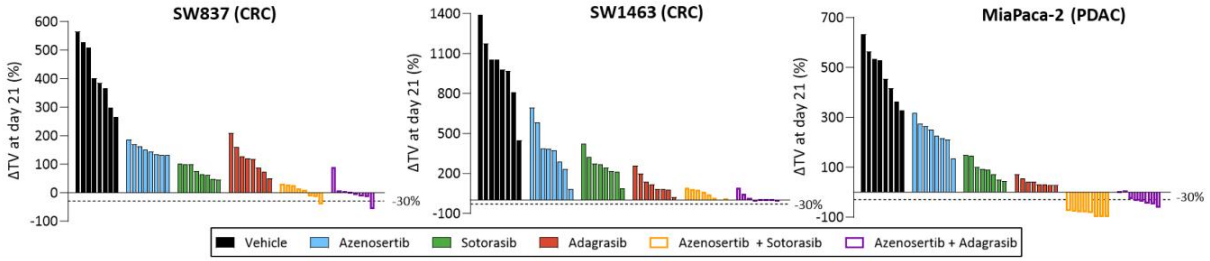
# The Combination of Azenosertib with the KRAS$^{G12C}$ Inhibitor Sotorasib Demonstrates Tumor Regressions in a NSCLC Model




Source: Zentalis AACR poster 2024, Jameson, et al

Abbreviations: TV, tumor volume; SEM, standard error of the mean; TGI, tumor growth inhibition; ΔTV, change in tumor volume; NSCLC, non small cell lung cancer

# Combination of Azenosertib with KRAS$^{G12C}$ Inhibitors Improves Efficacy and Drives Tumor Regression in Colorectal (CRC) and Pancreatic (PDAC) Models




Source: Zentalis AACR poster 2024, Jameson, et al

Abbreviations: ΔTV, change in tumor volume

# Strong Rationale Supports Ongoing Clinical Development of Azenosertib in Cancers with High Genomic Instability

**1 Cyclin E1 status is predictive of azenosertib sensitivity in preclinical models**

- DENALI (ZN-c3-005) is prospectively evaluating *CCNE1* amplification and Cyclin E1 IHC as potential patient enrichment strategies

**2 Azenosertib has monotherapy activity in multiple HRD models**

- MAMMOTH (ZN-c3-006) is evaluating monotherapy and combination with niraparib in PARP resistant, platinum resistant ovarian cancer

**3 Azenosertib enhances the efficacy of BRAF + EGFR inhibition in preclinical models of colorectal cancer**

- ZN-c3-016 is evaluating azenosertib in combination with encorafenib and cetuximab in BRAFV600E metastatic colorectal cancer

zentalis

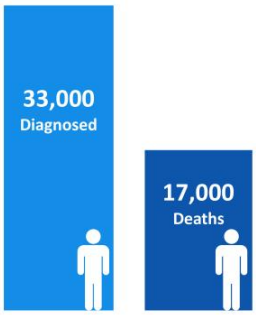
Abbreviations: IHC, immunohistochemistry; PARP, poly-ADP ribose polymerase; BRAF, V-Raf Murine Sarcoma Viral Oncogene Homolog B; EGFR, epidermal growth factor receptor; HRD, homologous recombination repair deficient

# BCL-2 Inhibitor (ZN-d5) in Combination with Azenosertib

Represents Opportunity to Address Acute Myeloid Leukemia Patients with Known Poor Prognosis and High Unmet Need

# Relapsed/Refractory Acute Myeloid Leukemia Remains a Devastating Disease and Represents a Major Unmet Medical Need

**2023 US/EU5 Estimated New Cases and Patient Deaths[1]**



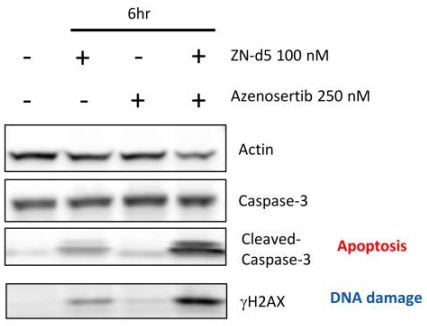

**2023 US/EU5 Drug Treatable[2]**


- Most common form of acute leukemia in adults; estimated 5-yr survival ~10% for patients ≥ 60 years old[3]
- 57% of patients either relapse after CR, are primary refractory, or die within 12 months[3]
- R/R patients have particularly dismal prognosis with median OS 3-6 months[3]
- BCL-2 inhibitors (e.g., venetoclax) are foundational treatments for AML[4]

1. American Cancer Society. Cancer Facts & Figures 2023, SEER and ECIS. 2 Figures represent company best estimates based on US patients with conditions covered by the companies target indication. Sources DRG Clarivate, Kantar Health 3 Shimony, S, et al. Am J Hematol. 2023; 98(3): 502-526; 4 Maiti A, et al. The Cancer Journal 28(1) 2022
Abbreviations: CR, complete response; R/R, relapsed/refractory; OS, overall survival; AML, acute myeloid leukemia

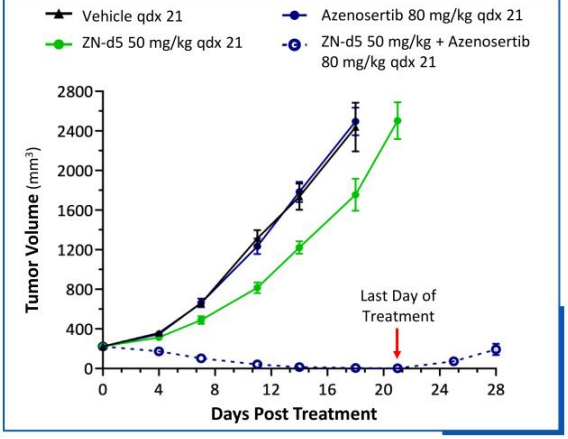
# Combination of ZN-d5 and Azenosertib Results in Enhanced Apoptosis, DNA Damage and Synergistic Anti-Tumor Activity in an AML Model

## HL-60 (in vitro)




**Synergistic effects seen at sub-efficacious doses of both agents**

## HL-60 (in vitro)




zentalis

Izadi H, et al. AACR 2022 Cancer Res (2022) 82 (12_supplement):2591; Data / Report On File, Zentalis Pharmaceuticals

# Despite Recent Progress and Evolving Treatment Paradigm in AML, Many Patients Still Lack Treatment Options After Relapse

AML Incidence (2021)
US + EU5 = ~33,212

Newly Diagnosed: Front Line → Maintenance → Relapsed/Refractory

**Unmet Need**

**1st Relapse Chemo/SCT Ineligible: Without Actionable Mutation**

~10,500
treatment eligible

**2nd Relapse: After Mutation Directed Therapy**

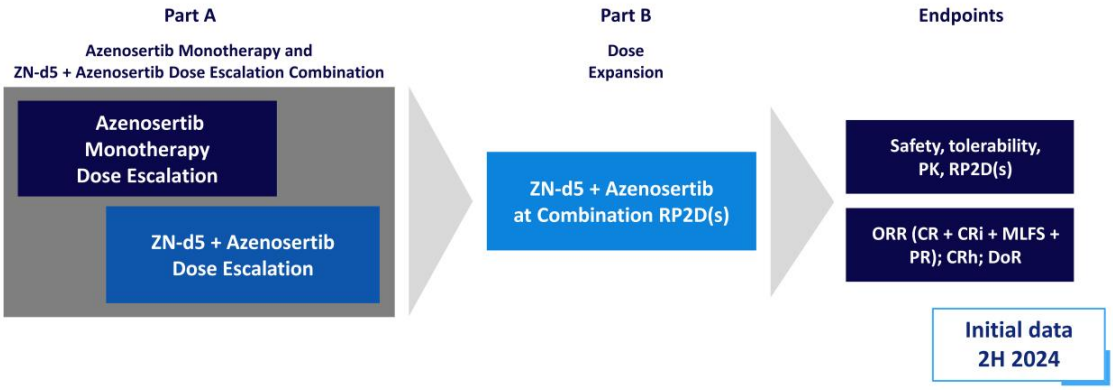
~4,500
treatment eligible

zentalis

Adapted from Heuser, Y. et. Al. Annals of Oncology 31 (6) 697-712 2020; Abbreviations: AML, acute myeloid leukemia; SCT, stem cell transplant

# ZN-d5-004C: Enrolling Phase 1/2 Study of ZN-d5 and Azenosertib in R/R AML

**Key Eligibility: R/R AML; Must have received at least 1 prior line of therapy for AML**



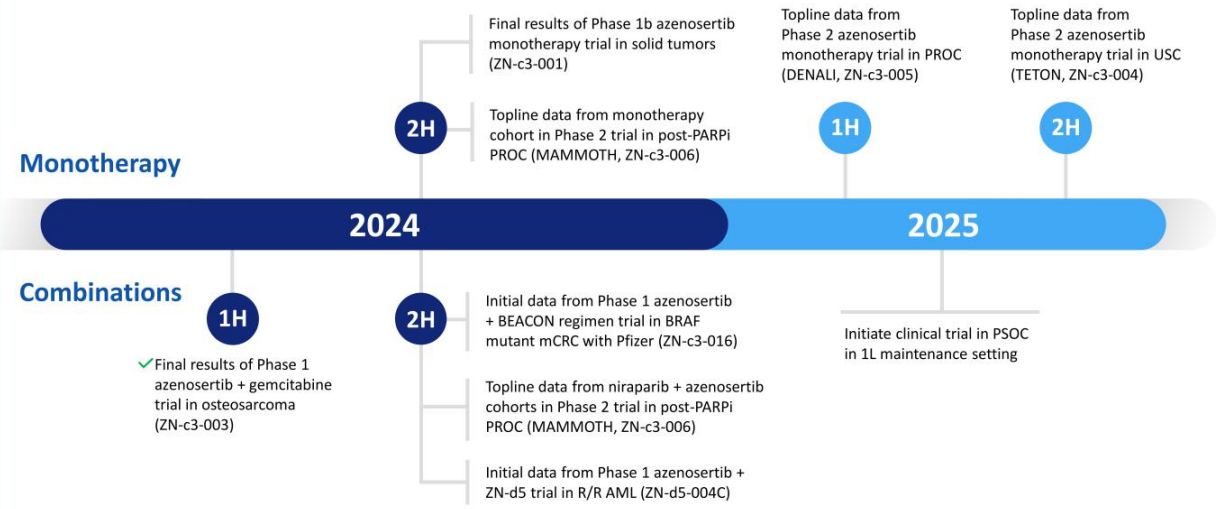

NCT05682170

zentalis

Abbreviations: R/R, relapsed/refractory; AML, acute myeloid leukemia; RP2D, recommended Phase 2 dose; PK, pharmacokinetics; ORR, objective response rate; CR, complete response; CRi: complete response with incomplete count recovery; MLFS: morphologic leukemia free state; PR, partial response; CRh: complete response with partial hematologic recovery; DoR; duration of response; 2H, second half

# Executing on the Franchise Potential of Azenosertib

# Upcoming Clinical Milestones




zentalis

Abbreviations: 1H, first half; 2H second half; BRAF, V-Raf murine sarcoma viral oncogene homolog B; mCRC, metastatic colorectal cancer; PARPi, poly-ADP ribose polymerase inhibitor; R/R AML, relapsed or refractory acute myeloid leukemia; PROC, platinum resistant ovarian cancer; USC, uterine serous carcinoma; PSOC, platinum sensitive ovarian cancer; 1L, first line

# Zentalis is Positioned for Success with Azenosertib Franchise

## Potentially First- and Best-in-Class WEE1 Inhibitor

- Monotherapy efficacy; 37% ORR and 6.5 months mPFS in heavily pretreated ovarian and USC*
- Efficacy and safety clearly differentiate azenosertib from other WEE1 inhibitors
- Years ahead of other WEE1 inhibitors in development

## Clinical Strategy Supports Blockbuster Opportunity

- Pursuing fast-to-market strategy with azenosertib monotherapy in platinum resistant ovarian cancer (PROC), ~43,000 treatable patients[1]
- Planned trial as 1L maintenance in ovarian cancer offers potential to benefit greatest number of patients, ~21,000 treatable patients[1]
- Expanding to a broad array of tumor types in combination with targeted agents

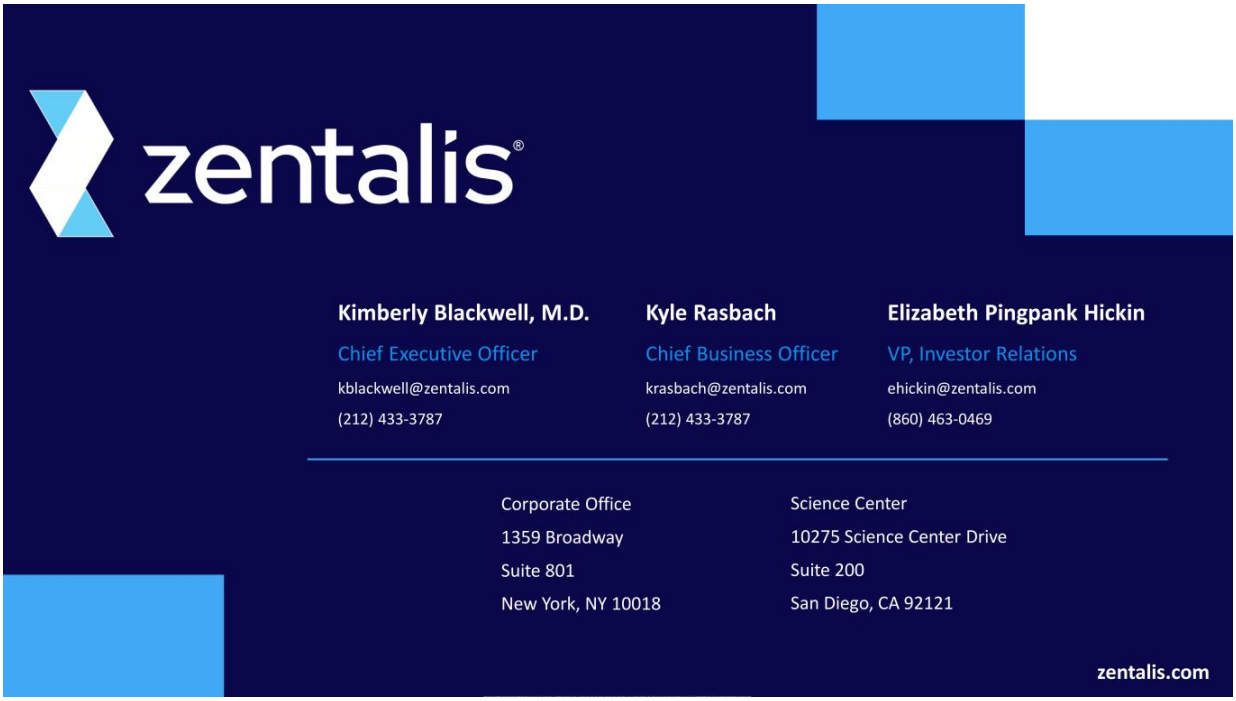
## Multiple Near-Term Value Inflection Points

- Readouts from 3 Phase 2 trials in 2024 and 2025 in addition to other data updates
- Potential first NDA in 2026
- Supported by strong cash balance and runway into mid-2026

zentalis

1 Figures represent Company estimates of U.S. and EU5 patients with conditions covered by the Company's targeted indications; Source: IQVIA, DRG Clarivate
Abbreviations: mPFS: median progression free survival; ORR, objective response rate; USC, uterine serous carcinoma; 1L, first line NDA, New Drug Application; Statements comparing azenosertib to other agents, not head-to-head comparisons

*Data cut-off: October 25, 2023


zentalis®
Kimberly Blackwell, M.D.
Chief Executive Officer
kblackwell@zentalis.com
(212) 433-3787
Kyle Rasbach
Chief Business Officer
krasbach@zentalis.com
(212) 433-3787
Elizabeth Pingpank Hickin
VP, Investor Relations
ehickin@zentalis.com
(860) 463-0469
Corporate Office
1359 Broadway
Suite 801
New York, NY 10018
Science Center
10275 Science Center Drive
Suite 200
San Diego, CA 92121
zentalis.com