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 6, 2023

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.

On June 6, 2023, Zentalis Pharmaceuticals, Inc. (the "Company") issued the press release furnished as Exhibit 99.1 to this Current Report on Form 8-K (this "Current Report") and incorporated herein by reference. In addition, beginning on June 6, 2023, spokespersons for the Company plan to present the information in the Corporate Presentation and Investor Presentation furnished as Exhibits 99.2 and 99.3, respectively, to this Current Report and each 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 Exhibits 99.1, 99.2 and 99.3 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 8.01 Other Events.

On June 6, 2023, the Company announced the monotherapy recommended Phase 2 dose ("RP2D") for azenosertib, the Company's potentially first-in-class WEE1 inhibitor. Based on encouraging Phase 1 dose optimization clinical data, the RP2D for azenosertib as a monotherapy is 400 mg daily ("QD") on a five days on, two days off ("5:2") weekly administration schedule.

As of April 24, 2023, a total of 127 heavily pretreated patients with advanced solid tumors were treated with monotherapy azenosertib at doses ≥ 300 mg at either continuous daily dosing or intermittent weekly administration schedules. Across all tumor types, 74 patients were treated with continuous dosing schedules and 53 patients were treated with intermittent dosing schedules.

- As of June 2, 2023, the confirmed objective response rate ("ORR") was 36.8% (7/19) in the combined ovarian cancer and uterine serous carcinoma ("USC") subgroups who received an intermittent dosing schedule, versus 19.2% (5/26) in those who received a continuous dosing schedule.
- Steady state exposure, as measured by $AUC_{0\text{-}24}$, more than doubled at the new intermittent RP2D, compared to AUC observed at 300 mg QD with continuous administration.
- Intermittent dosing maintained azenosertib safety and improved tolerability as compared to continuous dosing. Gastrointestinal, fatigue, and hematologic Grade 3 and 4 treatment-related adverse events ("TRAEs") were comparable or favorable versus continuous dosing. No discontinuations due to TRAEs were observed in the intermittent cohorts.

The Company is currently enrolling patients at the new RP2D in three ongoing Phase 2 trials evaluating monotherapy azenosertib in the following patient populations:
- Cyclin E1+, platinum-resistant high-grade serous ovarian cancer;
- USC; and
- PARP inhibitor-resistant and platinum-resistant ovarian cancer (new cohort of ongoing study).

The Company plans to update efficacy data from its Phase 1 monotherapy dose optimization study and provide program timeline updates for these three azenosertib Phase 2 monotherapy trials currently enrolling patients at the RP2D in the second half of 2023. In addition, the Company believes azenosertib has potential applicability in a broad array of tumor types, including non-gynecological malignancies.

Cautionary Note Regarding Forward-Looking Statements

Statements in this Current Report regarding the Company's strategy, plans, prospects, expectations, beliefs, intentions and goals are forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements regarding the Company's plan to provide clinical data and program timeline updates, and the timing thereof; the potential for azenosertib to be first-in-class; the Company's plans to enroll patients in ongoing Phase 2 trials; and the potential applicability of azenosertib in a broad array of tumor types, including non-gynecological malignancies. The terms "believe," "intend," "plan," "potential," "will" and similar references are intended to identify forward-looking statements, although not all

forward-looking statements contain these identifying words. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause the Company's 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: the Company's limited operating history, which may make it difficult to evaluate the Company's current business and predict the Company's future success and viability; the Company has and expects to continue to incur significant losses; the Company's need for additional funding, which may not be available; the Company's plans, including the costs thereof, of development of any companion diagnostics; the Company's substantial dependence on the success of its lead product candidates; 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; the Company's product candidates may cause serious adverse side effects; inability to maintain collaborations, or the failure of these collaborations; the Company's reliance on third parties; effects of significant competition; the possibility of system failures or security breaches; risks relating to intellectual property; the Company's ability to attract, retain and motivate qualified personnel, and risks relating to management transitions; significant costs as a result of operating as a public company; and the other important factors discussed under the caption "Risk Factors" in the Company's most recently filed periodic report on Form 10-K or 10-Q and subsequent filings with the U.S. Securities and Exchange Commission ("SEC") and the Company's other filings with the SEC. These forward-looking statements (except as otherwise noted) speak only as of the date of this Current Report, and the Company does not undertake, and specifically disclaims, any obligation to update any forward-looking statements contained in this Current Report.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

The following Exhibits 99.1, 99.2 and 99.3 relating to Item 7.01 shall be deemed to be furnished, and not filed:

ExhibitNo.	Description
99.1	Press Release issued on June 6, 2023
99.2	Corporate Presentation, dated June 6, 2023
99.3	Investor Presentation, dated June 6, 2023
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 6, 2023

By: /s/ Melissa Epperly
Melissa Epperly
Chief Financial Officer

Exhibit 99.1

Zentalis Announces Intermittent Azenosertib Monotherapy Dosing Nearly Doubles Efficacy Over Continuous Dosing

ORR of 36.8% in heavily pretreated platinum-resistant ovarian cancer and USC patients treated with intermittent dosing

Establishes monotherapy RP2D of 400 mg QD with 5:2 dosing schedule; New RP2D more than doubles exposure levels, maintains safety and improves tolerability with no treatment-related discontinuations

Company plans to update efficacy data from Phase 1 monotherapy dose optimization study and provide program timeline updates for three azenosertib Phase 2 monotherapy trials currently enrolling patients at the RP2D in the second half of 2023

Investor call at 8:00 a.m. ET today to review azenosertib monotherapy data supporting dose selection and chemotherapy combination data presented at ASCO

NEW YORK & SAN DIEGO, June 6, 2023 – Zentalis® Pharmaceuticals, Inc. (Nasdaq: ZNTL), a clinical-stage biopharmaceutical company discovering and developing clinically differentiated small molecule therapeutics targeting fundamental biological pathways of cancers, today announced the monotherapy recommended Phase 2 dose (RP2D) for azenosertib, the Company's potentially first-in-class WEE1 inhibitor. Based on encouraging Phase 1 dose optimization clinical data, the RP2D for azenosertib as a monotherapy is 400 mg daily (QD) on a 5 days on, 2 days off (5:2) weekly administration schedule. This intermittent dosing schedule more than doubled steady state drug exposure in comparison to continuous dosing, and achieved promising efficacy signals, while maintaining safety and improving tolerability.

"With this new optimized monotherapy dosing schedule for azenosertib, we believe we have unlocked the therapeutic potential of WEE1 inhibition, achieving monotherapy activity levels few oncology agents have been able to attain," said Kimberly Blackwell, M.D., Chief Executive Officer of Zentalis. "Having demonstrated favorable anti-tumor activity as both a monotherapy and in combination with chemotherapy, we are confident azenosertib has tremendous promise to help patients with difficult-to-treat cancers. With our focus on platinum-resistant ovarian cancer for azenosertib as a monotherapy and platinum-sensitive ovarian cancer for azenosertib in chemotherapy combinations, we have the potential to address the majority of ovarian cancer patients. We are committed to rapidly advancing our azenosertib clinical strategy, concentrating on the fastest paths to market to reach patients in need."

Summary of Phase 1 Monotherapy Dose Optimization Data:

As of April 24, 2023, a total of 127 heavily pretreated patients with advanced solid tumors were treated with monotherapy azenosertib at doses ≥ 300 mg at either continuous daily dosing or intermittent weekly administration schedules. Across all tumor types, 74 patients were treated with continuous dosing schedules and 53 patients were treated with intermittent dosing schedules.

- The confirmed objective response rate (ORR) was 36.8% (7/19) in the combined ovarian cancer and uterine serous carcinoma (USC) subgroups who received an intermittent dosing schedule, versus 19.2% (5/26) in those who received a continuous dosing schedule.

- Steady state exposure, as measured by $AUC_{0\text{-}24}$, more than doubled at the new intermittent RP2D, compared to AUC observed at 300 mg QD with continuous administration.
- Intermittent dosing maintained azenosertib safety and improved tolerability as compared to continuous dosing. Gastrointestinal, fatigue, and hematologic Grade 3 and 4 treatment-related adverse events (TRAEs) were comparable or favorable versus continuous dosing. No discontinuations due to TRAEs were observed in the intermittent cohorts.
- The Company is currently enrolling patients at the new RP2D in three ongoing Phase 2 trials evaluating monotherapy azenosertib in the following patient populations:
    - Cyclin E1+, platinum-resistant high-grade serous ovarian cancer
    - USC
    - PARP inhibitor-resistant and platinum-resistant ovarian cancer (new cohort of ongoing study)

“WEE1 inhibition by monotherapy azenosertib has the potential to address the significant unmet need in ovarian cancer and uterine serous carcinoma, where patients often have limited treatment options,” said Funda Meric-Bernstam, M.D., Chair of the Department of Investigational Cancer Therapeutics -- the Phase 1 Program at The University of Texas MD Anderson Cancer Center, and a member of the Zentalis Scientific Advisory Board. “Today’s data supporting the newly established monotherapy dose – which demonstrates promising efficacy and improved tolerability – coupled with data supporting the combination of azenosertib with chemotherapy, suggest that this promising molecule has potential to be a highly effective therapeutic tool to fight difficult-to-treat cancers.”

Dr. Blackwell added, “These data sets underpin our broader strategy to expand options for patients in a broad array of tumor types.”

Conference Call

The Company will host a webcast today at 8:00 a.m. ET to review the azenosertib Phase 1 monotherapy data supporting dose selection, as well as the positive azenosertib plus chemotherapy Phase 1b combination data presented at the 2023 ASCO Annual Meeting. The webcast will be accessible via the Investors page of Zentalis’ website, www.zentalis.com. The archived webcast and presentation will be available on the Company’s website after the event.

About Azenosertib

Azenosertib is a potentially first-in-class and best-in-class small molecule WEE1 inhibitor in development for the treatment of cancer. Inhibition of WEE1, a DNA damage response kinase, drives cancer cells into mitosis without being able to repair damaged DNA, resulting in cell death. Currently, there are no FDA-approved WEE1 inhibitors, and azenosertib has been designed for superior selectivity and pharmacokinetic properties. Azenosertib is being developed in therapeutic areas of high unmet need and is being evaluated as a monotherapy, in combination with chemotherapy, and in combination with molecularly targeted agents.

About Zentalis Pharmaceuticals

Zentalis® Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company discovering and developing small molecule therapeutics targeting fundamental biological pathways of cancers. Utilizing its Integrated Discovery Engine, the Company is developing a focused pipeline of potentially best-in-class oncology candidates, which include azenosertib (ZN-c3), a WEE1 inhibitor for advanced solid tumors, ZN-d5, a BCL-2 inhibitor for hematologic malignancies and related disorders, and a heterobifunctional degrader of BCL-xL for solid and hematological malignancies. The Company is also leveraging its

extensive experience and capabilities across cancer biology and medicinal chemistry to advance its research on protein degraders. Zentalis has operations in both New York and San Diego.

For more information, please visit www.zentalis.com. Follow Zentalis on Twitter at @ZentalisP and on LinkedIn at www.linkedin.com/company/zentalis-pharmaceuticals.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including statements regarding our plans to provide clinical data and program timeline updates, and the timing thereof; the potential for azenosertib to be first-in-class and best-in-class; the potential benefits of azenosertib; our belief that we have unlocked the therapeutic potential of WEE1 inhibition; our belief and confidence that azenosertib has tremendous promise to help patients with difficult-to-treat cancer; the potential addressable patient population of azenosertib, including the ovarian cancer patient population; our plans to rapidly advance our azenosertib clinical and regulatory strategy; the potential for azenosertib to address significant unmet need in ovarian cancer and USC; the potential for azenosertib to be a highly effective therapeutic tool to fight difficult-to-treat cancers; our broader strategy to expand options for patients in a broad array of tumor types; the potential benefits of the design of azenosertib; and the potential for our product candidates to be best-in-class. The terms "believe," "committed," "confident," "design," "encouraging," "plan," "potential," "promising," "strategy," "suggest," "to be," "will," and similar references are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. 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; significant costs as a result of operating as a public company; and the other important factors discussed under the caption "Risk Factors" in our most recently filed periodic report on Form 10-K or 10-Q and subsequent filings with the U.S. Securities and Exchange Commission (SEC) and our other filings with the SEC. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

Investor Contacts:
Adam D. Levy, PhD, MBA
alevy@zentalis.com

Emily White

Solebury Strategic Communications
ewhite@soleburystrat.com

Media Contact:
Danielle Cantey
Evoke Canale
danielle.cantey@evokegroup.com
(619) 826 4657

zentalis®

Corporate Presentation

June 2023

Nasdaq: ZNTL

Forward Looking Statement 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 potential for our product candidates to be first-in-class and/or best-in-class; potential for accelerated approval paths; potential for our product candidates to be developed as monotherapies and in combination; potential for azenosertib (ZN-c3) to address large unmet need across an array of cancers; potential benefits of intermittent dosing for our product candidates; our development approach for our product candidates, including azenosertib and ZN-d5; plans for and potential benefits of dose optimization, and the anticipated timing of updates on dosing optimization, including timing of declaring a monotherapy RP2D for ZN-d5; timing of providing updates on azenosertib program timelines and potential paths to registration; timing of preclinical and clinical program updates; the potential unmet need in a particular indication and/or patient population; potential for combinations including our product candidates and the potential benefits thereof; the target profiles and potential benefits of our product candidates and their mechanisms of action, including as a monotherapy and/or in combination; our belief that we have strengthened our clinical development plans, including for azenosertib; clinical and regulatory progress of our product candidates, including the estimated timing of IND-enabling studies, enrollment, initiation of clinical trials and data announcements; the market opportunities for and market potential of our product candidates; timing of initiating Phase 3 trial of azenosertib in combination with chemotherapy in Cyclin E1+ platinum sensitive ovarian cancer; timing of advancement of our preclinical programs, including BCL-xL and protein degrader programs; our anticipated milestones, as well as statements that include the words "continue," "design," "estimate," "expect," "may," "milestone," "opportunity," "plan," "potential," "predicts," "strategy," "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.

We Are a Clinical-Stage Oncology Company Focused on Difficult-to-Treat Cancers

Azenosertib: First-in-Class WEE1i Candidate with Broad Franchise Potential

Accelerating Development

- High levels of monotherapy anti-tumor activity
- Best-in-class safety and tolerability to date supports use in earlier lines and maintenance settings
- Demonstrated synergistic activity with chemotherapy and molecularly targeted agents
- Enriched activity in tumors with high genomic instability including Cyclin E1+ and HRD+ cancers
- 8 trials; large indications; 400+ patients dosed

Blockbuster Commercial Opportunity

- Direct registrational path with multiple shots on goal across monotherapy and chemotherapy combination
- Potential to cover 88% of ovarian cancer across multiple lines of therapy
  - Represents treatable population of ~56K patients / year
- Potential to expand to broad set of tumors as monotherapy or in combination, addressing ~140K per year
- Global commercial rights (ex-China)
- IP – U.S. composition of matter 2039

Highly Selective BCL-2 Inhibitor

- Multiple indications; Best-in-class potential in heme malignancies
- 100+ patients dosed across 3 ongoing studies
- Positioned to potentially demonstrate monotherapy activity in AL amyloidosis
- Attractive commercial opportunity as potential first registered drug in AL amyloidosis

Promising Preclinical Programs

- Discovering assets leveraging distinctive chemistry expertise

Positioned to Execute and Deliver

- Deep oncology experience
- Veteran scientific, clinical advisors
- Partnerships with Pfizer, GSK

zentalis®

Pipeline Addresses Difficult to Treat Cancers with Large Commercial Opportunities

COMPOUND	INDICATION + DEVELOPMENT APPROACH	PRECLINICAL	Phase 1	Phase 1b	Phase 2	Phase 3	STATUS / EXPECTED MILESTONES
Azenosertib WEE1 Inhibitor	**Platinum Sensitive Ovarian Cancer** + Paclitaxel or Carboplatin						Initiate Q1 2024
	Cyclin E1 Positive Ovarian Cancer Monotherapy						Enrolling
	Uterine Serous Carcinoma Monotherapy						Enrolling; FDA Fast Track Designation
	PARP Resistant Ovarian Cancer Azenosertib monotherapy, alternating with niraparib or concurrent with niraparib				GSK		Enrolling
	Dose Optimization in Solid Tumors **Monotherapy**						Enrolling
	Osteosarcoma + gemcitabine						Enrolling
	BRAF Mutant Colorectal Cancer + encorafenib and cetuximab		Pfizer				Enrolling
	Pancreatic Cancer + gemcitabine						Dana Farber Cancer Institute, funded by SU2C/Lustgarten
ZN-d5 BCL-2 Inhibitor	**Light Chain (AL) Amyloidosis** Monotherapy						Enrolling; Provide interim clinical data and declare RP2D for monotherapy 2H23
	Non-Hodgkins Lymphoma (NHL) Monotherapy						Enrolling
	Acute Myeloid Leukemia (AML) + azenosertib						Enrolling; Provide preliminary data from clinical trial 2H23
BCL-xL Degrader	**Solid Tumors and Heme Malignancies**						Declared development candidate; IND enabling activities initiated

zentalis®

Azenosertib

WEE1 Inhibitor with Potential to Address Large Unmet Need Across Array of Cancers

Azenosertib Monotherapy Dose Optimization Supports Advancement into Multiple Difficult-to-Treat Tumor Types

- **37% Objective Response Rate** with durable responses using intermittent dosing in ovarian and USC patients
- Monotherapy **RP2D** established: 400 mg 5:2
- **Doubled steady state drug exposure** compared to continuous dosing
- **Maintained safety and improves tolerability** compared to continuous dosing
- **No treatment-related discontinuations** in patients who were administered intermittent dosing

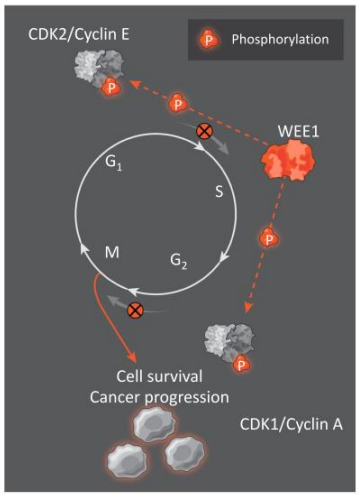
Three ongoing Phase 2 monotherapy trials have the potential to support rapid paths to registration in ovarian cancer and USC

zentalis®

Abbreviations: RP2D: recommended phase 2 dose; 5:2 refers to administration schedule of five days on therapy and two days off; USC, uterine serous carcinoma

Azenosertib Targets WEE1, a Critical Protein for Cancer Cell Survival

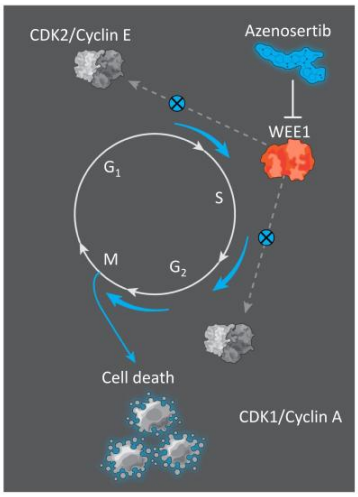
WEE1 activity in untreated cancer cell



- **WEE1 phosphorylates CDK/Cyclin complexes to engage cell cycle checkpoints, allowing DNA repair to occur**
- **Azenosertib inhibits WEE1:**
  - **Leads to inactivation of CDK 1 and 2**
  - **Removes 2 cell cycle checkpoints: G1/S and G2/M**
  - **Cell cycle progresses without sufficient DNA repair**
  - **Cancer cells accumulate DNA damage, resulting in apoptosis and mitotic catastrophe**

Azenosertib's MOA and early monotherapy clinical activity made dose optimization critical

Azenosertib blocks WEE1 resulting in cancer cell death



Establishing RP2D is significant milestone in path to drugging this high-potential oncology target

zentalis®

Luserna di Rora, et al. 2020. J Hem Onc. 13:126. Elbaek et al. 2022. Cell Reports. 38:110261. Abbreviation: MOA, mechanism of action

Monotherapy Dose and Biomarker Enrichment Is Foundational To Our Clinical Strategy

Tumors with High Genomic Instability are Sensitive to Azenosertib

High genomic instability can be caused by:

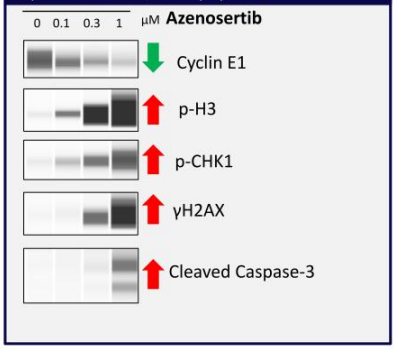
Cyclin E1+ Tumors

- Cyclin E1+ drives accelerated entry into S-phase through its partnership with CDK2
- Replication machinery is overloaded, resulting in genomic instability

Homologous Recombination Repair Defective (HRD+) Tumors

- Results in genomic instability through tumors inability to repair double stranded DNA breaks.

Azenosertib induces markers of DNA damage, replicative stress, and apoptosis*



*OVCAR3 Cyclin E1 positive cells, 16-hour treatment

zentalis®

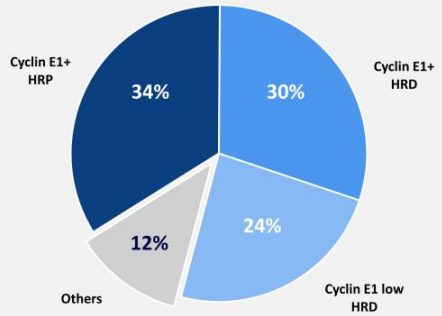
Potential to Transform Treatment Paradigm for Patients and Capture Significant Market Share in Ovarian Cancer

Azenosertib Monotherapy Potentially Addresses 88% Of High Grade Serous Ovarian Cancer

- Ongoing clinical programs address Cyclin E1+ and HRD+ patient populations
  - Opportunity is much larger than recently approved therapies
- Data support potential role for azenosertib at every stage of metastatic therapy:
  - **Platinum sensitive**: combination with chemotherapy
  - **Platinum resistant**: monotherapy and combination with chemotherapy

Potential to transform standard of care

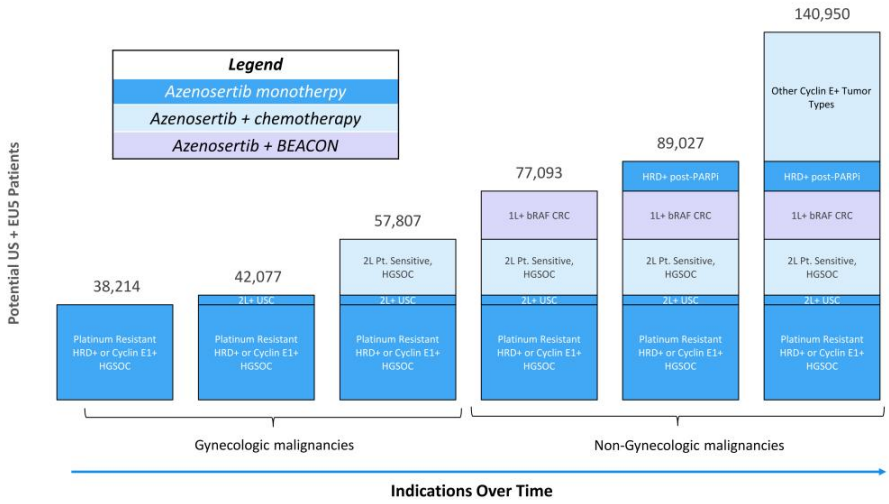
High Grade Serous Ovarian Cancer Patient Segments



HRD: Homologous recombination deficient
HRP: Homologous recombination proficient

Sources:
1. HRD prevalence derived from Konstantinopoulos, et al *Cancer Discov* (2015)
2. CCNE1 amplification prevalence of ~20% reported in Aziz et al *Gynecol Oncol* (2018) and TGCA Network *Nature* volume 474 (2011)
3. Cyclin E1 expression and copy number extracted from the digital analysis of Aziz et al Figure 3B to infer full distribution of Cyclin E1 H-scores and overlap with CCNE1 amplification based on Cyclin E1 high definition of H-score >50
4. HRD prevalence and proportion of overlap with CCNE1 amplification from Konstantinopoulos et al, Figure 2
5. Total HGSOC incidence estimates (US, EU5) sourced from SEER and ECIS are 35, 388 individuals/year

Addressable Patient Population More than Doubles as Franchise Expands to Non-Gynecological Malignancies

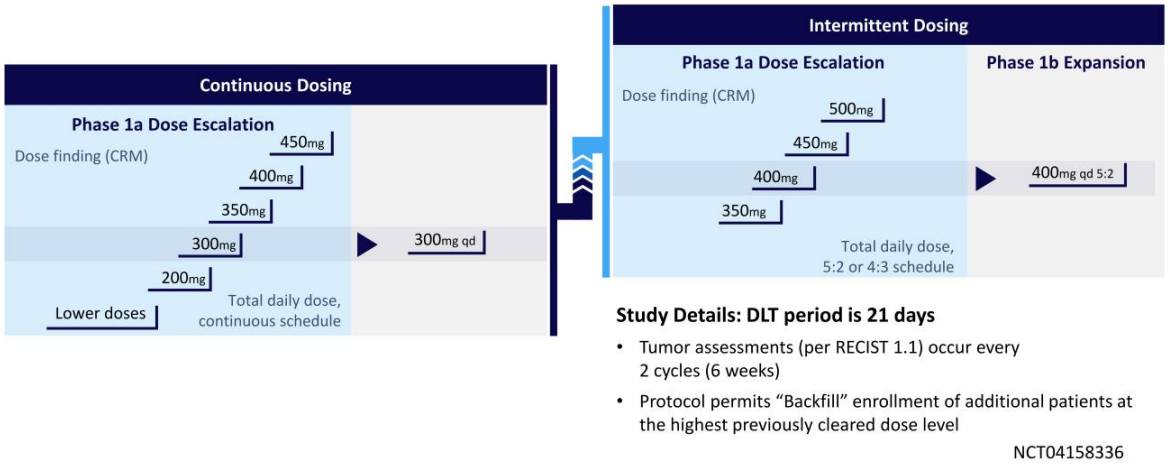


Source: Used 'drug-treatable' estimates from DRG Clarivate for all Ovarian, USC, CRC, Breast, Prostate and Pancreatic. For 'Other Cyclin-E1 driven solid tumors' used incidence reported by SEER and ECIS.
Cyclin E1 prevalence in platinum sensitive ovarian cancer derived from Petersen, et al CCNE1 and BRD4 co-amplification in high-grade serous ovarian cancer is associated with poor clinical outcomes, Gynecologic Oncology,Volume 157, Issue 2, 2020
Abbreviations: bRAF+ CRC: bRAF mutant Colorectal Cancer; HRD+ : Homologous Recombinant Repair Deficiency; HGSOC: High Grade Serous Ovarian Cancer; 2L: Second Line
HRD+ Post PARPi tumor types: Prostate, Pancreas and Breast; Other Cyclin E+ Tumor Types include bladder, stomach, esophageal, lung squamous, lung adenocarcinoma, and breast cancer

Azenosertib

Azenosertib Intermittent Monotherapy Dose Substantially Improves Antitumor Activity and Tolerability

Zentalis 001 Study Enabled Rapid and Efficient Approach to Dose Optimization



Study Details: DLT period is 21 days

- Tumor assessments (per RECIST 1.1) occur every 2 cycles (6 weeks)
- Protocol permits "Backfill" enrollment of additional patients at the highest previously cleared dose level

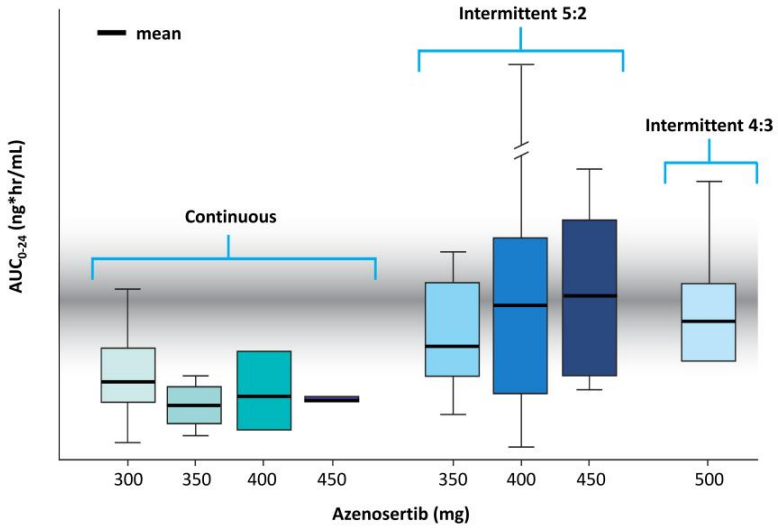
NCT04158336

Primary objectives: Safety, PK (Steady State Exposure (AUC_{0-24}) & Concentration Maximum (C_{max}))

zentalis®

Abbreviations: CRM, continual reassessment method; qd, once 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; RECIST, response evaluation criteria in solid tumors; PK, pharmacokinetics; AUC, area under the curve

Intermittent Dosing Resulted In A Significant Increase In Steady State Exposure



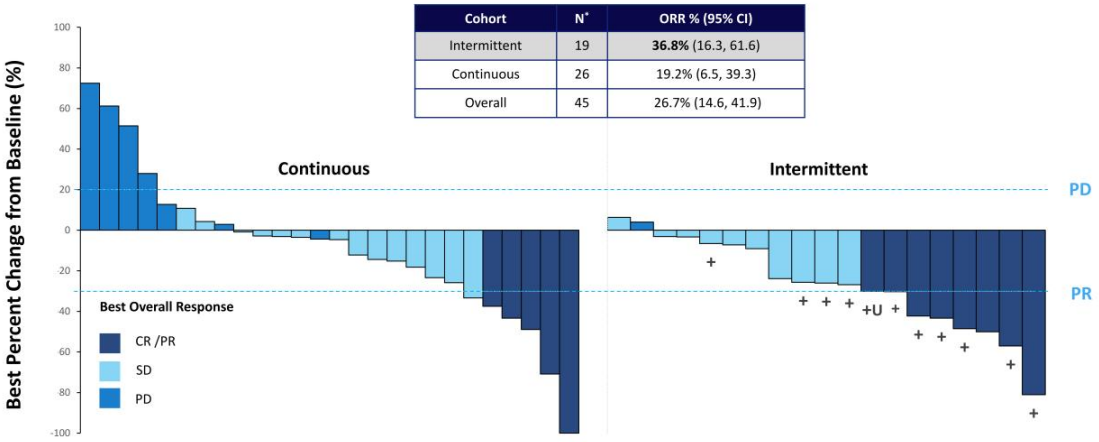
With intermittent dosing, more patients reach the projected target efficacious steady-state exposure (AUC_{0-24})

zentalis®

Patients who received ≥300 mg; Abbreviations: 5:2, 5-days of treatment followed by 2-days off treatment; AUC, area under the curve

Azenosertib Intermittent Dosing Schedule Doubles Objective Response Rate In Ovarian/USC Populations

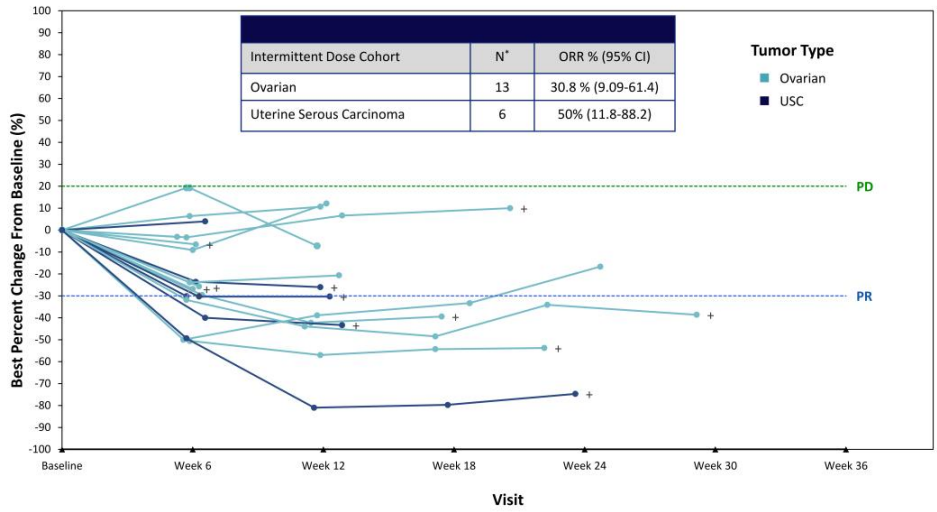
Cohort	N*	ORR % (95% CI)
Intermittent	19	**36.8%** (16.3, 61.6)
Continuous	26	19.2% (6.5, 39.3)
Overall	45	26.7% (14.6, 41.9)



*Response evaluable: have baseline measurable disease by RECIST 1.1, at least one post baseline scan, and received at least one dose of drug
Patients who received ≥300 mg. Abbreviations: USC, uterine serous carcinoma; CR, complete response; PR, partial response;
SD, stable disease; PD, progressive disease; ORR, objective response rate; CI, confidence interval; +: Patients remain on therapy at the time of data cut-off

Data cut-off: June 2, 2023

Azenosertib Monotherapy Intermittent Dosing: 89% of Ovarian and USC Patients Had Target Lesion Reductions from their Baseline Scans



Intermittent Dose Cohort	N*	ORR % (95% CI)
Ovarian	13	30.8 % (9.09-61.4)
Uterine Serous Carcinoma	6	50% (11.8-88.2)

- 12/19 (63%) patients remain on therapy
- Median follow up of 4.4 months
- mPFS of 5.68 months (2.79, NR)
- 10/13 (77%) of ovarian cancer patients had received a prior PARP inhibitor

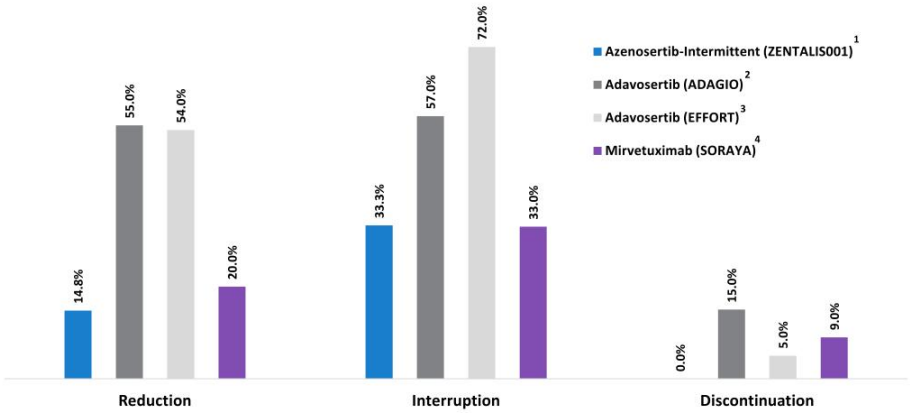
*Response evaluable: have baseline measurable disease by RECIST 1.1, at least one post baseline scan, and received at least one dose of drug; Patients who received ≥300 mg.
Abbreviations: USC, uterine serous carcinoma; HGSOC, high-grade serous ovarian cancer SD, stable disease; PR, partial response; ORR, confirmed objective response rate; mPFS, median progression free survival; complete response; NR, Not reached, +: Patients remain on therapy at the time of data cut-off

Intermittent Dosing Maintains Safety And Tolerability

Treatment Related AEs, N (%)	Continuous (n=67)		Intermittent (n=27)		Total* (n=94)	
	All Grade	Grade 3/4	All Grade	Grade 3/4	All Grade	Grade 3/4
Gastrointestinal						
Nausea	46 (68.7)	2 (3.0)	9 (33.3)	-	55 (58.5)	2 (2.1)
Diarrhea	31 (46.3)	4 (6.0)	11 (40.7)	3 (11.1)	42 (44.7)	7 (7.4)
Vomiting	28 (41.8)	-	3 (11.1)	-	31 (33.0)	-
Decreased appetite	20 (29.9)	1 (1.5)	4 (14.8)	1 (3.7)	24 (25.5)	2 (2.1)
Dehydration	6 (9.0)	-	3 (11.1)	-	9 (9.6)	-
Fatigue	30 (44.8)	8 (11.9)	11 (40.7)	2 (7.4)	41 (43.6)	10 (10.6)
Hematologic						
Anemia	6 (9.0)	2 (3.0)	6 (22.2)	3 (11.1)	12 (12.8)	5 (5.3)
Thrombocytopenia	4 (6.0)	3 (4.5)	2 (7.4)	-	6 (6.4)	3 (3.2)
Neutropenia**	1 (1.5)	1 (1.5)	4 (14.8)	3 (11.1)	5 (5.3)	4 (4.3)

*Safety Evaluable Population: Received at least one dose of drug;
**No incidence of febrile neutropenia in either dosing group
Continuous 300, 350, 400; Intermittent 350 5:2 and 400 5:2
Treatment Related AEs > 10% and treatment related AEs of interest: All Tumor Types
Abbreviations: AE, adverse event

Azenosertib: Improved Tolerability Compared To Other Agents



1. ZENTALIS 001: data on file
2. (ADAGIO Phase 2b Study) Liu et. al. Presented at the Society of Gynecologic Oncology Annual Meeting, March 23–28, 2023
3. (EFFORT Phase 2 Study) Westin et. al. DOI: 10.1200/JCO.2021.39.15_suppl.5505 Journal of Clinical Oncology 39, no. 15_suppl (May 20, 2021) 5505-5505.
4. (SORAYA Phase 2 Study) Matulonis et al. DOI: 10.1200/JCO.22.01900 Journal of Clinical Oncology 41, no. 13 (May 01, 2023) 2436-2445.
Comparisons to adavosertib and Mirvetuximab are not head-to-head comparisons

zentalis®

Azenosertib Monotherapy

Paving Path to Registration with Three Ongoing Trials Accruing at New Intermittent Dose

Zentalis 004 (TETON): Azenosertib Monotherapy In Women With ≥2L Advanced Uterine Serous Carcinoma

CURRENTLY ACCRUING- FDA Fast track designation

Key Eligibility: Recurrent or persistent USC; ≥1 prior platinum-based chemotherapy regimen; Prior HER-2 directed therapy for known HER-2+; Prior anti-PDL-1; Measurable disease; ECOG PS 0-1; No prior WEE1 inhibitor; No prior cell cycle checkpoint inhibitor.

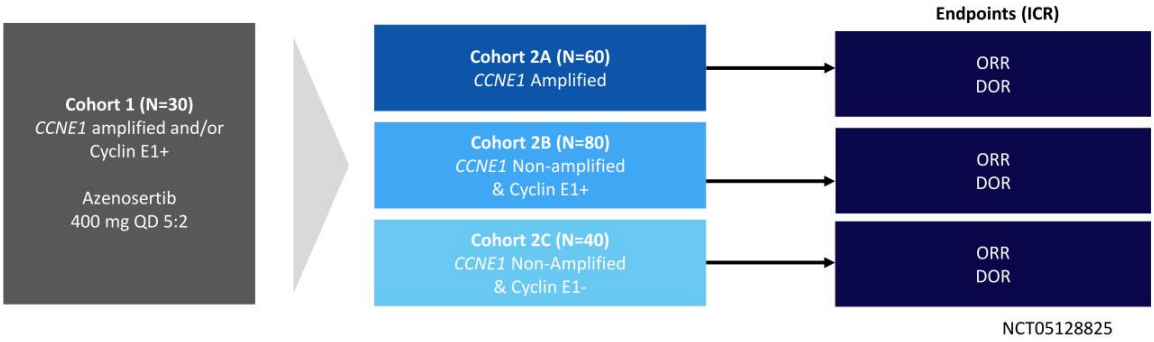
NCT04814108

Abbreviations: 2L, two lines; USC, uterine serous carcinoma; ECOG PS, Eastern Cooperative Oncology Group performance score; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; DOR, duration of response
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.

Zentalis 005 (DENALI): Evaluating Impact of *CCNE1* Amplification and Cyclin E1+ in Platinum-Resistant High-Grade Serous Ovarian Cancer

CURRENTLY ACCRUING

Key Eligibility: High-Grade Serous Ovarian Cancer; ECOG PS 0-1; Platinum-resistant (excluding Platinum-refractory); 1-3 prior lines of chemotherapy; Measurable disease per RECIST v 1.1; Cyclin E1 IHC+ and/or CCNE1 amplified.



NCT05128825

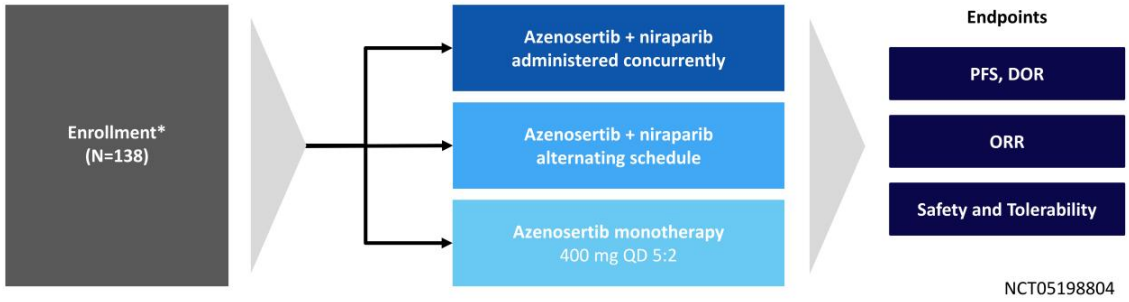
zentalis®

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance score; RECIST, response evaluation criteria in solid tumors; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; DOR, Duration of Response; ICR, Independent Central Review

Zentalis 006 (MAMMOTH): Revised Phase 1/2 Study Of Azenosertib In Combination With Niraparib Or Alternating With Niraparib Or As A Monotherapy in Patients With PARP-resistant Ovarian Cancer

CURRENTLY ACCRUING

Key Eligibility: Recurrent high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancer (serous, clear cell or endometrioid); 1 – 5 prior lines for advanced/metastatic disease; Relapsed within 6 months of platinum therapy (platinum resistant), progressed after taking at least 3 months of PARPi as maintenance treatment.



NCT05198804

* Enrollment Based on Slot Availability

zentalis®

Abbreviations: PARPi, poly-ADP ribose polymerase inhibitor; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; PFS, progression free survival; ORR, objective response rate

Azenosertib Combination with Chemotherapy

Strong and Durable Efficacy Signals and Favorable Safety Profile Across Chemotherapy Backbones Enable Advancement into Phase 3 in Ovarian Cancer

Addition of Azenosertib to Chemotherapies Increases Response Rates and Durability of Response in Ovarian Cancer Compared to Chemotherapy Alone

- **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

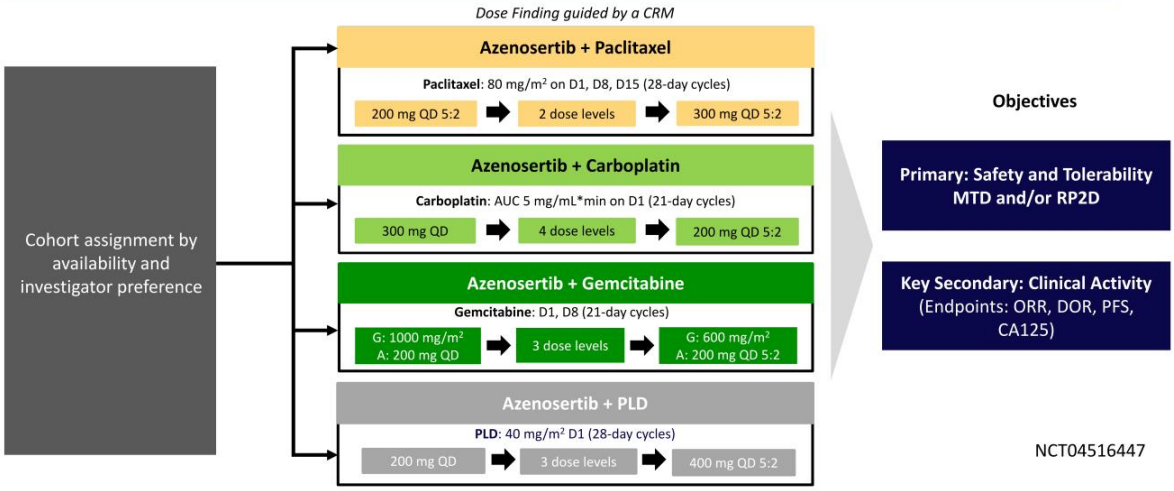
Registrational Phase 3 Trial Announced in Platinum Sensitive Ovarian Cancer

zentalis®

SOC, standard of care; PLD, pegylated liposomal doxorubicin

Zentalis 002: Phase 1b Combination Study To Define RP2D Dosing

Key Eligibility: High-Grade Serous Ovarian Cancer; ECOG Performance Status 0-2; Platinum-resistant/refractory; Up to 3 prior lines of chemotherapy; Measurable disease per RECIST v 1.1



NCT04516447

Abbreviations: ; ECOG, Eastern Cooperative Oncology Group; RECIST, response evaluation criteria in solid tumors; 5:2, 5-days of treatment followed by 2-days off treatment; CRM, continuous reassessment model; QD, once daily; D, day; AUC, area under the curve; G, gemcitabine; A, azenosertib; 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;

Liu, J., et al. "Correlation of Cyclin E1 expression and clinical outcomes in a Phase 1b dose-escalation study of Azenosertib (ZN-c3), a WEE1 inhibitor, in combination with chemotherapy (CT) in patients (pts) with platinum-resistant or refractory (R/R) epithelial ovarian, peritoneal, or fallopian tube cancer (EOC)." Poster presented ASCO 2023

Encouraging Efficacy and Durability in Azenosertib Chemotherapy Doublets

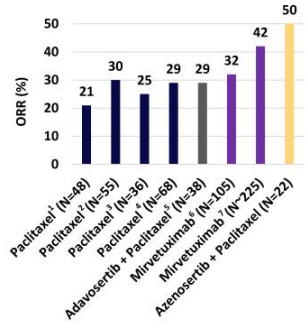
Endpoint	Azenosertib + Paclitaxel (N=26)	Azenosertib + Carboplatin (N=36)	Azenosertib + Gemcitabine (N=18)	Azenosertib + PLD (N=35)	Total (N=115)
Response-Evaluable* (N)	22	28	13	31	94
ORR (confirmed), N (%)	11 (50.0)	10 (35.7)	5 (38.5)	6 (19.4)	32 (34.0)
Median DOR (95% CI) in months	5.6 (3.8-NE)	11.4 (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)

*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.
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

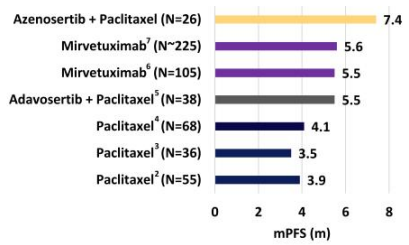
Liu, J., et al. "Correlation of Cyclin E1 expression and clinical outcomes in a Phase 1b dose-escalation study of Azenosertib (ZN-c3), a WEE1 inhibitor, in combination with chemotherapy (CT) in patients (pts) with platinum-resistant or refractory (R/R) epithelial ovarian, peritoneal, or fallopian tube cancer (EOC)." Poster presented ASCO 2023

Activity of Azenosertib + Paclitaxel is Robust and Competitively Favorable

Objective Response Rate (ORR)



Median Progression Free Survival (mPFS)



References: 1. Markman et al. Gynecol Oncol 2006;101:436-40. 2. AURELIA: Avastin USPI 3. MITO11: Pignata et al. Lancet Oncol 2015;16:561-68. 4. OCTOPUS: Banerjee et al. ESMO 2019. 5. GYN49: Moore et al. Clin Cancer Res 2022;28:36-44. 6. SORAYA: Matulonis et al. J Clin Oncol 2023;41:2436-45. 7. MIRASOL: Immunogen Press Release May 3, 2023.

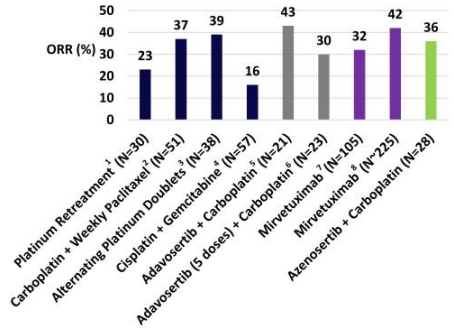
Abbreviations: ORR, objective response rate; mPFS, median progression free survival; m, months

Comparisons to historic benchmarks on this slide are not head-to-head comparisons

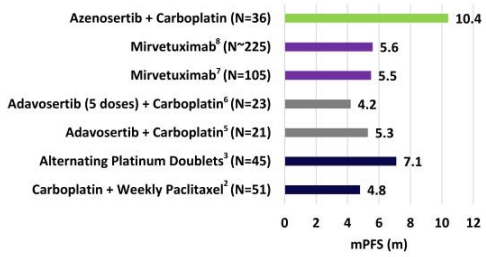
Liu, J., et al. "Correlation of Cyclin E1 expression and clinical outcomes in a Phase 1b dose-escalation study of Azenosertib (ZN-c3), a WEE1 inhibitor, in combination with chemotherapy (CT) in patients (pts) with platinum-resistant or refractory (R/R) epithelial ovarian, peritoneal, or fallopian tube cancer (EOC)." Poster presented ASCO 2023

Activity of Azenosertib + Carboplatin is Robust and Highly Differentiated on Durability

Objective Response Rate (ORR)

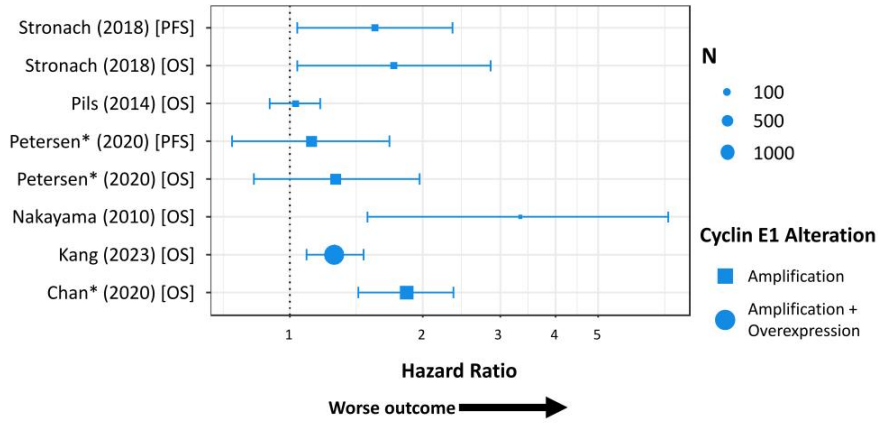


Median Progression Free Survival (mPFS)



References: 1. Leitao et al. Gynecol Oncol 2003;91:123-9. 2. CARTAXHY: Lortholary et al. Ann Oncol 2012;23:346-52. 3. Pectasides et al. Gynecol Oncol 2010;118:52-7. 4. Brewer et al. Gynecol Oncol 2006;103:446-50. 5. MK-1775-009: Leijen et al. J Clin Oncol 2016;34:4354-61. 6. GYN-49: Moore et al. Clin Cancer Res 2022;28:36-44. 7. SORAYA: Matulonis et al. J Clin Oncol 2023;41:2436-2445. 8. MIRASOL: Immunogen Press Release May 3, 2023.
Abbreviations: ORR, objective response rate; mPFS, median progression free survival; m, months
Comparisons to historic benchmarks on this slide are not head-to-head comparisons
Liu, J., et al. "Correlation of Cyclin E1 expression and clinical outcomes in a Phase 1b dose-escalation study of Azenosertib (ZN-c3), a WEE1 inhibitor, in combination with chemotherapy (CT) in patients (pts) with platinum-resistant or refractory (R/R) epithelial ovarian, peritoneal, or fallopian tube cancer (EOC)." Poster presented ASCO 2023

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

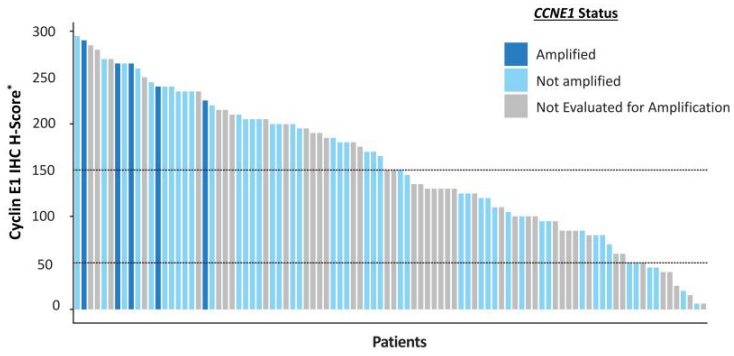


- 6 Studies; n=5404
- 4 Studies where timing of tissue collection was available-all were platinum sensitive tissue collected after ≤ 1 course of chemotherapy); 3533/5404 (65%)
- Other 2 Studies did not disclose timing of tissue collection

zentalis®

*Timing of tissue collection was not disclosed. Abbreviations: PFS: progression free survival, **OS; overall survival**

Zentalis 002: Majority of Ovarian Cancers are Cyclin E1+

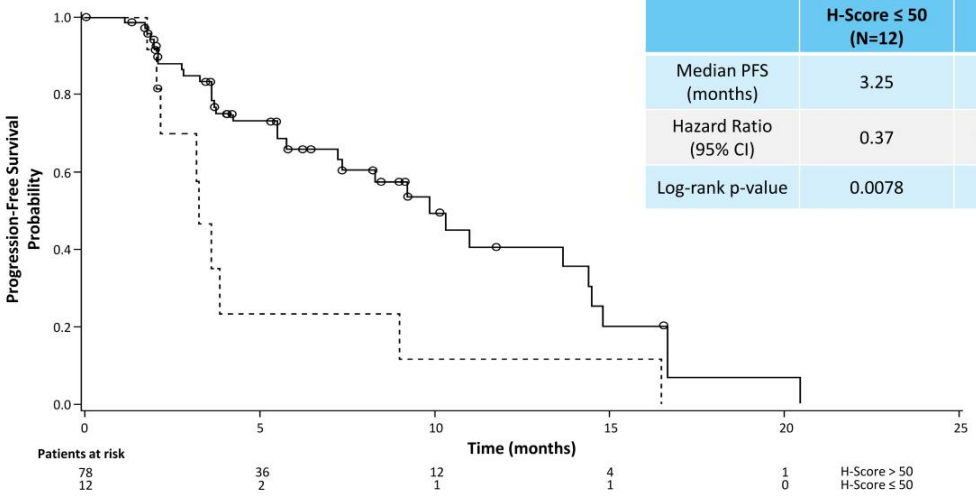


IHC H-Score*	>150	≤ 150 to > 50	≤ 50
CCNE1 Amplified	5	0	0
CCNE1 Not Amplified	25	15	6
Tissue Not Evaluated for Amplification	16	21	6

- H-score > 50 includes all *CCNE1* amplified tumors
- Prevalence of Cyclin E1-IHC+, H-score > 50 of all safety evaluable patients with tissue is 82/94 (**87**%);
- Prevalence of Cyclin E1+ in the response evaluable patients with tissue is 70/82 **(85%).**

*H-scores calculated by multiplying the percentage of cells (0 to 100%) with intensity of Cyclin E1 expression (0 to 3); IHC: Immunohistochemistry
Safety evaluable: received at least one dose of drug; Response evaluable: have baseline measurable disease by RECIST 1.1, at least one post baseline scan, and received at least one dose of drug
Liu, J., et al. "Correlation of Cyclin E1 expression and clinical outcomes in a Phase 1b dose-escalation study of Azenosertib (ZN-c3), a WEE1 inhibitor, in combination with chemotherapy (CT) in patients (pts) with platinum-resistant or refractory (R/R) epithelial ovarian, peritoneal, or fallopian tube cancer (EOC)." Poster presented ASCO 2023

Durability Triples in Patients with Cyclin E1+ Tumors Independent of Chemotherapy Backbone



	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	

*Response evaluable patients (having received at least one scan)
Abbreviations: IHC, immunohistochemistry ; CI, confidence interval
Liu, J., et al. "Correlation of Cyclin E1 expression and clinical outcomes in a Phase 1b dose-escalation study of Azenosertib (ZN-c3), a WEE1 inhibitor, in combination with chemotherapy (CT) in patients (pts) with platinum-resistant or refractory (R/R) epithelial ovarian, peritoneal, or fallopian tube cancer (EOC)." Poster presented ASCO 2023

Intermittent Dosing Across Chemotherapy Backbones Has Favorable Safety Profile

Treatment-Related Adverse Event ≥20% N (%)			Azenosertib + Paclitaxel (Continuous, N=7; Intermittent, N=19) All Doses*		Azenosertib + Carboplatin (Continuous, N=22; Intermittent, N=14) All Doses		Azenosertib + Carboplatin (Continuous, N=14; Intermittent, N=8) Doses ≤ MTD		Azenosertib + Gemcitabine (Continuous N=8; Intermittent, N=10) All Doses**		Azenosertib + PLD (Continuous N=27; Intermittent, N=8) All Doses*		Total (Continuous, N=64; Intermittent, N=51)	
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	C	5 (71.4)	5 (71.4)	9 (40.9)	7 (31.8)	4 (28.6)	3 (21.4)	7 (87.5)	6 (75.0)	19 (70.4)	17 (63.0)	40 (62.5)	35 (54.7)
		I	11 (57.9)	5 (26.3)	7 (50.0)	1 (7.1)	4 (50.0)	-	7 (70.0)	4 (40.0)	3 (37.5)	3 (37.5)	28 (54.9)	13 (25.5)
	Thrombo-cytopenia	C	4 (57.1)	2 (28.6)	16 (72.7)	11 (50.0)	11 (78.6)	6 (42.9)	8 (100.0)	5 (62.5)	9 (33.3)	2 (7.4)	37 (57.8)	20 (31.3)
		I	4 (21.1)	-	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	C	5 (71.4)	-	10 (45.5)	3 (13.6)	5 (35.7)	1 (7.1)	6 (75.0)	2 (25.0)	11 (40.7)	4 (14.8)	32 (50.0)	9 (14.1)
		I	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	C	4 (57.1)	-	15 (68.2)	1 (4.5)	10 (71.4)	1 (7.1)	5 (62.5)	-	16 (59.3)	2 (7.4)	40 (62.5)	3 (4.7)
		I	7 (36.8)	1 (5.3)	6 (42.9)	-	3 (37.5)	-	5 (50.0)	-	4 (50.0)	1 (12.5)	22 (43.1)	2 (3.9)
	Vomiting	C	3 (42.9)	1 (14.3)	8 (36.4)	-	6 (42.9)	-	1 (12.5)	-	11 (40.7)	2 (7.4)	23 (35.9)	3 (4.7)
		I	2 (10.5)	1 (5.3)	2 (14.3)	-	2 (25.0)	-	1 (10.0)	-	4 (50.0)	1 (12.5)	9 (17.6)	2 (3.9)
	Diarrhea	C	4 (57.1)	1 (14.3)	4 (18.2)	-	1 (7.1)	-	1 (12.5)	-	8 (29.6)	-	17 (26.6)	1 (1.6)
		I	6 (31.6)	1 (5.3)	5 (35.7)	-	3 (37.5)	-	6 (60.0)	-	2 (25.0)	-	19 (37.3)	1 (2.0)
Other	Fatigue	C	6 (85.7)	1 (14.3)	8 (36.4)	-	3 (21.4)	-	3 (37.5)	1 (12.5)	8 (29.6)	3 (11.1)	25 (39.1)	5 (7.8)
		I	8 (42.1)	2 (10.5)	5 (35.7)	1 (7.1)	4 (50.0)	-	6 (60.0)	2 (20.0)	2 (25.0)	-	21 (41.2)	5 (9.8)

zentalis®

Abbreviations: C, Continuous azenosertib dosing; I, Intermittent azenosertib dosing; MTD, maximum tolerated dose; PLD, pegylated liposomal doxorubicin
*All doses were at or below the MTD
**A MTD for Gemcitabine + Azenosertib has not been determined, further dose cohorts are ongoing.

Liu, J., et al. "Correlation of Cyclin E1 expression and clinical outcomes in a Phase 1b dose-escalation study of Azenosertib (ZN-c3), a WEE1 inhibitor, in combination with chemotherapy (CT) in patients (pts) with platinum-resistant or refractory (R/R) epithelial ovarian, peritoneal, or fallopian tube cancer (EOC)." Poster presented ASCO 2023

Data cut-off: April 10, 2023

Data Supports Advancement of Azenosertib-Chemotherapy Combination into Platinum-Sensitive Ovarian Cancer & Earlier Line Therapy

RP2D established for paclitaxel, carboplatin and PLD combinations

RP2D		
	Azenosertib	Chemotherapy
Paclitaxel	300 mg QD 5:2	80 mg/m^2 on D1, D8, D15 (28-day cycles)
Carboplatin	200 mg QD 5:2	AUC=5 on D1 (21-day cycles)
Gemcitabine	TBD*	TBD*
PLD	400 mg QD 5:2	40 mg/m^2 D1 (28-day cycles)

Main Takeaways

- Strong and durable efficacy signal across chemotherapy backbones
- Cyclin E1 status predicts benefit of azenosertib addition to chemotherapy
  - Suggests azenosertib restores chemotherapy sensitivity in heavily pre-treated platinum-resistant ovarian cancer
- **Plans to initiate Phase 3 study of azenosertib in combination with paclitaxel or with carboplatin in Cyclin E1+ platinum sensitive ovarian cancer**

zentalis®

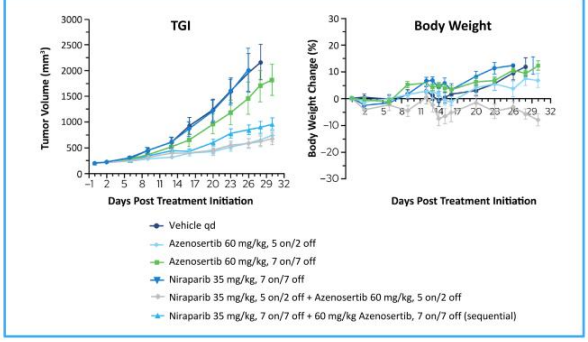
*Gemcitabine + Azenosertib has exciting and durable activity-a MTD has not been determined, further dose cohorts are ongoing.
Abbreviations: RP2D, recommended phase 2 dose; PLD pegylated liposomal doxorubicin; QD, once daily;
5:2, 5-days of treatment followed by 2-days off treatment; D, day; AUC, area under the curve; mg/mL*min

Azenosertib

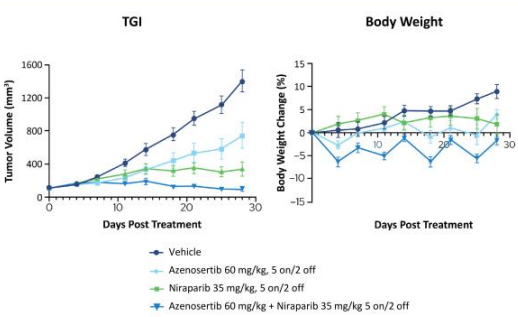
Advancing Programs Investigating Post-PARPi Treatment and Post-BEACON BRAF mCRC, Supported by Strong Body of Preclinical Data

Monotherapy Azenosertib +/- PARP Inhibitor Combinations are Active in both Ovarian CDX and TNBC PDX Models

CDX Ovarian Cancer Model (OVCAR3; *CCNE1* Amp)



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



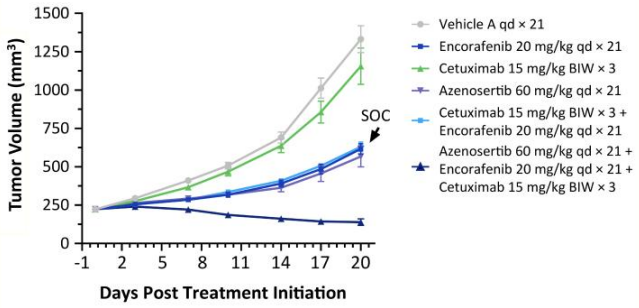
- Combination of PARP and WEE1 inhibitors in TNBC results in synergistic cell killing in preclinical models with either BRCA mutations or high levels of Cyclin E1 [1]

zentalis®

1. Chen X Cancers (Basel). 2021 Apr 1;13(7). Abbreviations: PARP, poly (ADP-ribose) polymerase; CDX, cell line derived xenograft; TNBC, triple-negative breast cancer; PDX, patient derived xenograft; TGI, tumor growth inhibition

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

LS411N (BRAF mutant CRC model)



- Oncogene-induced replication stress in mutationally driven cancers such as BRAF mutant colorectal cancer leads to DNA damage and genomic instability
- Oncogene activation disrupts replication regulation leading to slow and stalled replication forks and other defects and leads to DNA damage
- Dependency of cancers with replication stress on WEE1 signaling provides a 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

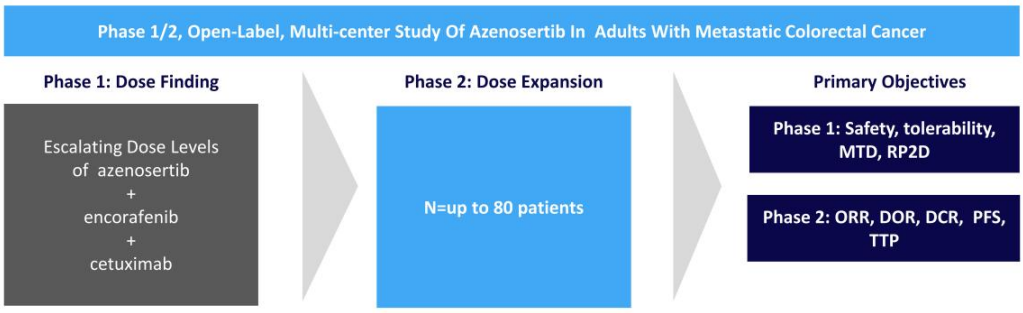
zentalis®

Source: Zentalis Data on File

Kotsantis, et al. Cancer Discov. 2018 May; 8(5): 537–555.

BRAF mCRC Study in Collaboration with Pfizer

Key Eligibility: Patients with mCRC and documented BRAFV600E mutation; 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)



Triplet Combination to be Investigated in Patients With Significant Unmet Need

- Median OS in BRAF mutant CRC patients <1 year, vs. BRAF WT >2 years2
- While targeted BRAF inhibition (e.g., vemurafenib) has been successful in melanoma with response rates >80%, this strategy has failed in CRC (OR ~5%) due to innate resistance3
- Encorafenib in combination with cetuximab (BEACON) was approved for BRAF V600E mCRC in April 2020 and is now the standard of care

zentalis®

1 Sorbye H, Dragomir A, Sundström M, et al. High BRAF Mutation Frequency and Marked Survival Differences in Subgroups According to KRAS/BRAF Mutation Status and Tumor Tissue Availability in a Prospective Population-Based Metastatic Colorectal Cancer Cohort. PLoS One. 2015;10(6):e0131046. 2 Corcoran et al. Combined BRAF and MEK Inhibition With Dabrafenib and Trametinib in BRAF V600–Mutant Colorectal Cancer. J Clin Oncol (2015) Dec 1; 33(34): 4023-4031 3 Kopetz et al. Encorafenib, Binimetinib, and Cetuximab in BRAF V600E–Mutated Colorectal Cancer. NEJM (2019) 381: 1632-1643 Zentalis maintains full economic ownership and control of azenosertib, apart from Greater China rights (Zentara).

Abbreviations: mCRC, metastatic colorectal cancer; 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; OS, overall survival

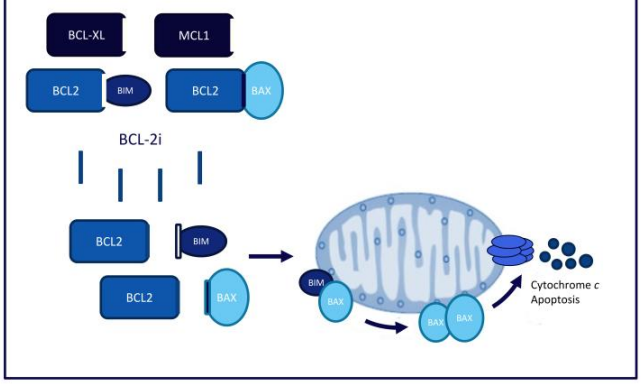
ZN-d5

BCL-2 Inhibitor with Potential Best-in-Class Profile

BCL-2: A Clinically Validated Oncology Target

- BCL-2 is an anti-apoptotic protein involved in tumor survival and resistance to chemotherapy [1]
- The intrinsic apoptotic pathway is controlled by the BCL-2 protein family on outer mitochondrial membrane [2, 3]
- BCL-2 inhibitors may restore the normal apoptosis process, making it an important cancer therapeutic target

Mechanism of Action of BCL-2 Inhibitors [1]



1. Konopleva M et al. Cancer Discov. 2016 Oct;6(10):1106-1117 2. Konopleva M and Letai A. Blood. 2018 Sep 6;132(10):1007-1012 3. Bhola PD and Letai A. Mol Cell. 2016;61(5):695-704

ZN-d5: A Potent BCL-2 Inhibitor Designed with Improved Selectivity for BCL-2

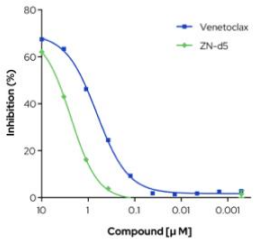
ZN-d5 has 10x Improved Selectivity for BCL-2 vs BCL-xL and Binds With Higher Affinity to BCL-2 Mutants than Venetoclax

Compound ID	Affinity (Kd, nM)			IC_{50} (nM) BCL-2 Type			
	BCL-2	BCL-xL	MCL-1	WT	G101V	F104L	D103Y
Venetoclax	0.41	28	>30000	1.3	7.3	8.4	18.3
ZN-d5	0.29	190	>30000	1.4	3.7	1.4	5.0

ZN-d5 Exhibits Potent In Vitro Activity Across Multiple Tumor Cell Lines

Compound ID	CTG IC_{50} (nM)							
	ALL	MCL		DLBCL		AML		
	RS4;11	Mino-1	Granta-519	DOHH-2	Toledo	HL-60	Molm-13	MV4-11
Venetoclax	2.9	1.1	161	43	191	26	18	3.8
ZN-d5	5.1	0.1	89	50	92	21	39	5.1

ZN-d5: Less Human Platelet Toxicity Compared to Venetoclax in an *in vitro* Assay



Compound ID	CTG (24 h) IC_{50} (mM)
Venetoclax	0.6
ZN-d5	2.4

ZN-d5 shows activity in preclinical models of ALL, NHL and AML

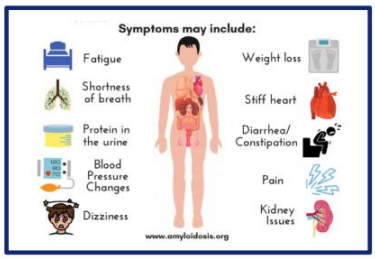
zentalis®

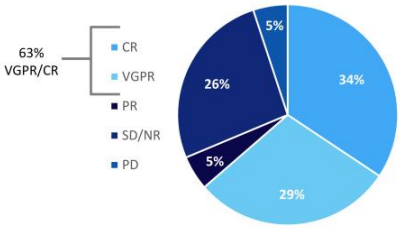
*Venetoclax data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than obtained from the pharmaceutical company developing the compound

ZN-d5 in AL (Primary) Amyloidosis

AL Amyloidosis study is currently enrolling patients

- AL Amyloidosis: Deposition of immunoglobulin light chains
  - Clonal plasma cell population secretes misfolding light chain
  - Progressive systemic amyloid accumulation causes widespread organ damage
  - High morbidity and mortality
- Orphan disease
- Estimated worldwide prevalence is 75,000 [1]
- About 4k new cases/year in the US [2]
- Not a cancer, but treated like one
  - Agents active in multiple myeloma used in first-line and relapsed/refractory settings
  - Daratumumab only approved therapy, for first-line use with CyBorD
- Relapsed/refractory setting is a high unmet medical need

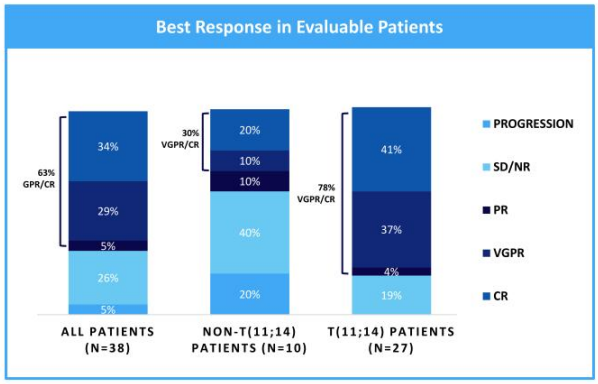


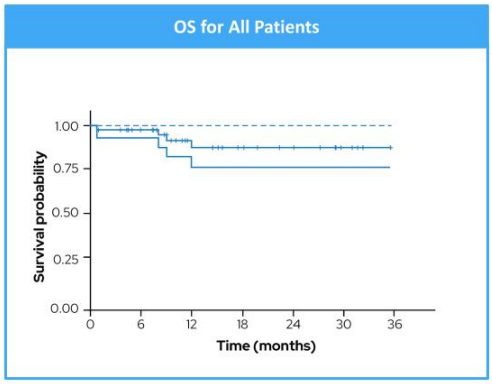


zentalis®

1. Zhang et al. Clin Lymphoma Myeloma Leuk. 2019;19(suppl 10):e339 2. Kyle et al, Mayo Clin Proc. 2019;94:465-471 3. Premkumar et al, Blood Cancer J 2021;11:10; hematologic response rate in 38 evaluable patients.

BCL-2 Inhibition has Shown Robust Clinical Activity in AL Amyloidosis





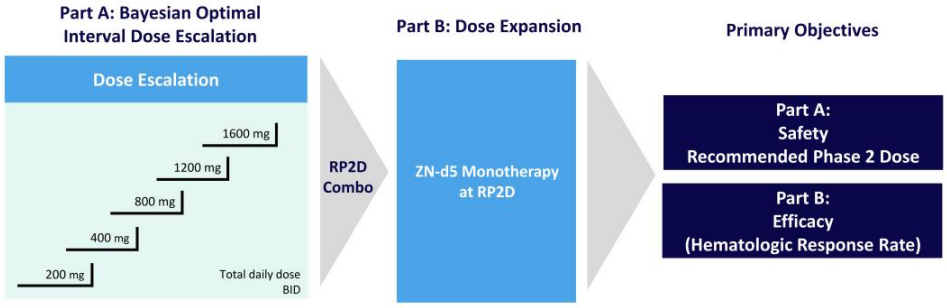
- Patients with the t(11;14) translocation have a worse prognosis than the general AL amyloidosis population[1]
- BCL-2 inhibition showed an improved response rate in the t(11;14) cohort with a trend towards better survival

zentalis®

1. Premkumar et al, Blood Cancer J 2021;11:10; hematologic response rate in 38 evaluable patients.

ZN-d5-003: Phase 1 Multicenter International Clinical Trial in R/R AL Amyloidosis

Key Eligibility: AL amyloidosis ; R/R to 1-3 prior lines of therapy; dFLC ≥20 mg/L; ECOG PS ≤2; Adequate hematologic and organ function



Study Details: DLT Period is 28 days

- Hematologic disease response assessments done every cycle for the first 6 months
- Protocol permits Backfill enrollment of additional patients at or below the highest previously cleared dose level

NCT05199337

zentalis

Abbreviations: R/R, refractory/resistant; AL, amyloid light chain; dFLC, difference between involved minus uninvolved serum free light chains; ECOG PS, Eastern Cooperative Oncology Group performance score; BID, twice daily; RP2D, recommended Phase 2 dose

BCL-xL Protein Degrader

Compelling Discovery Program

BCL-xL Degrader Background and Rationale

Declared development candidate and initial IND enabling activities

Therapeutic Hypothesis

- BCL-xL is a member of the anti-apoptotic BCL-2 proteins and is clinically validated. [1, 2]
- Expression of BCL-xL contributes to therapeutic resistance mechanisms. [3, 4, 5]
- Degrading BCL-xL will induce cell death and overcome resistance mechanisms in multiple cancer types, while reducing the possibility of on-target thrombocytopenia.

Therapeutic Window

- BCL-xL is required for platelet viability and BCL-xL inhibitors (e.g. navitoclax) are dose limited in the clinic due to on-target thrombocytopenia.[6]
- A degradation approach with a non-functional or dysfunctional E3 ubiquitin ligase complex in platelets could help mitigate thrombocytopenia.[7, 8]
- Efficacy may be achieved at lower doses and frequencies due to the catalytic MOA of degraders, further reducing the chance of thrombocytopenia and increasing the therapeutic index.

Patient Selection

- Heme malignancies
- Solid tumors

Chemical Modality

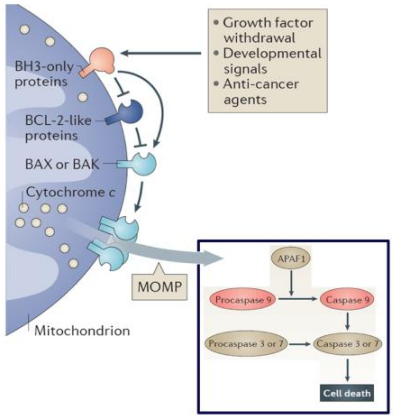
Heterobifunctional degrader linking a BH3 binding moiety to an E3 binding moiety

Internal Combination Opportunities

Azenosertib (WEE1 inhibitor) and ZN-d5 (BCL-2 inhibitor)

Competitive Landscape

Multiple inhibitors and one degrader in the clinic (Ph1/2)

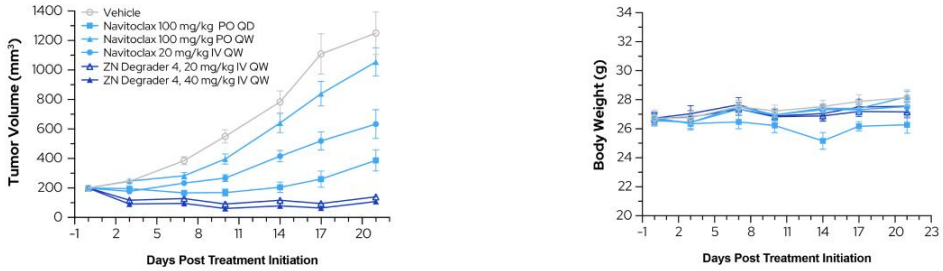


zentalis®

1. Bhola PD and Letai A. Mol Cell. 2016;61(5):695-704 2. Konopleva M and Letai A. Blood. 2018 Sep 6;132(10):1007-1012 3. Rahman SFA et al., Future Oncology, 2020, 16(28) 4. Yue et al., Cnacer Cell Int., 2020, 20(254)
5. cbioportal.org 6. Wilson WY et al., Lancet Oncol., 2010; 11(12):1149-1159 7. Khan et al. Nature Med 12, 1938-1947 (2019) 8. He et al. Nature Comm 11, (2020) Figure from: Delbridge, A. R. D., et. al. Nat Rev Cancer 16, 99-109 (2016)

BCL-xL Degrader is More Efficacious than BCL-xL Inhibitor (Navitoclax) in MOLT4 (T-ALL) Model

MOLT4 tumor model (T-ALL)



- BCL-xL degrader demonstrates excellent efficacy in the MOLT4 tumor model (T-ALL) and is well-tolerated at efficacious doses
- BCL-xL degrader is more efficacious than Navitoclax

zentalis®

Navitoclax data based on evaluation of comparable proxy chemical compound purchased from commercial sources rather than obtained from the pharmaceutical company developing the compound

2023 is a Catalyst Rich Year – Key Milestones

Azenosertib WEE1 Inhibitor

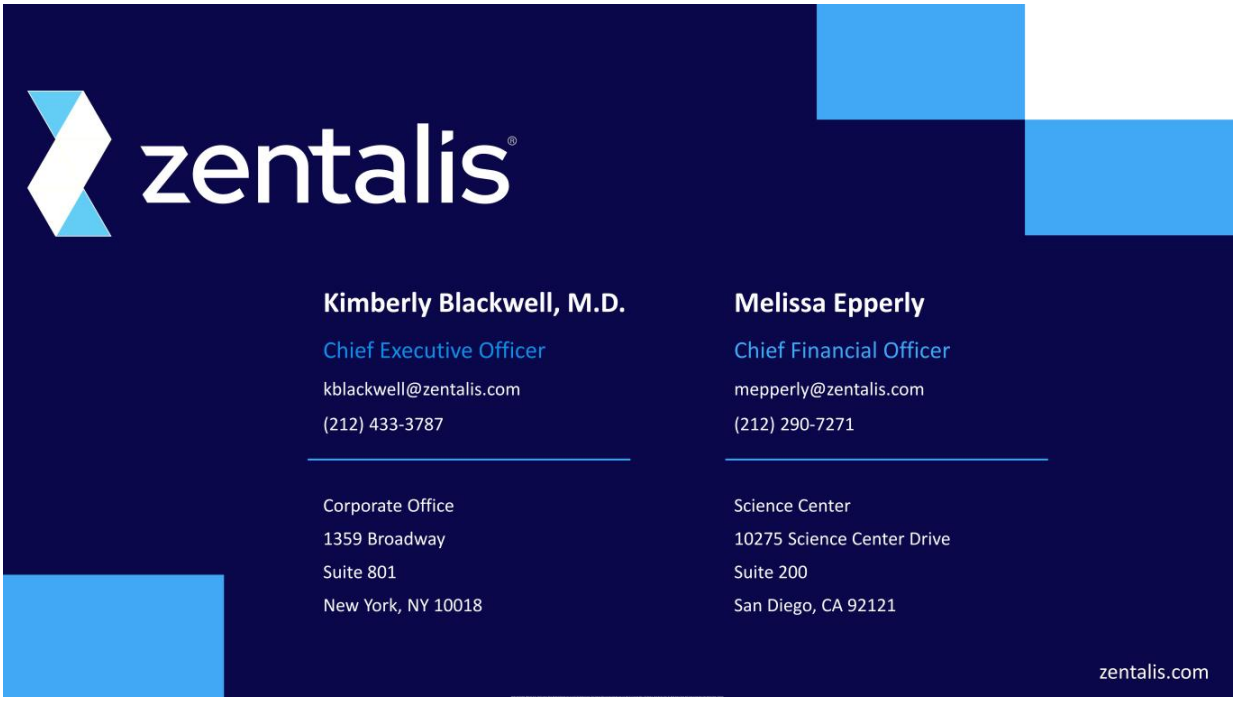
✓ 1Q 2023	Initiate enrollment in the BRAF mutant colorectal cancer BEACON regimen combination clinical trial in collaboration with Pfizer
✓ 1H 2023	Provide preclinical rationale for Cyclin E1 enrichment strategy at a scientific conference
✓ 1H 2023	Declare monotherapy RP2D and provide update on dose optimization activities, program timelines and potential paths to registration
✓ 1H 2023	Results from Phase 1b ovarian chemotherapy combination trial, including clinical translational data on Cyclin E1 amplification / overexpression
2H 2023	Update interim efficacy clinical data from monotherapy dose optimization in solid tumors
2H 2023	Update monotherapy program timelines and potential paths to registration
1Q 2024	Initiate randomized Phase 3 Trial of azenosertib + Chemotherapy in Cyclin E1+ platinum sensitive ovarian cancer

ZN-d5 BCL-2 Inhibitor

2H 2023	Provide interim clinical data and declare RP2D for Phase 1/2 monotherapy trial in amyloidosis
2H 2023	Provide preliminary data from clinical trial of azenosertib + ZN-d5 in relapsed / refractory acute myeloid leukemia

Discovery

2023	Continue to advance the BCL-xL protein degrader program through IND enabling studies
2023	Advance ongoing research on protein degrader programs of undisclosed targets


zentalis
Kimberly Blackwell, M.D.
Chief Executive Officer
kblackwell@zentalis.com
(212) 433-3787
Corporate Office
1359 Broadway
Suite 801
New York, NY 10018
Melissa Epperly
Chief Financial Officer
mepperly@zentalis.com
(212) 290-7271
Science Center
10275 Science Center Drive
Suite 200
San Diego, CA 92121
zentalis.com

zentalis®

Azenosertib Clinical Update

Dose Selection, Monotherapy and Chemotherapy Combinations Efficacy and Safety and Ongoing Development

June 2023

Nasdaq: ZNTL

Forward Looking Statement 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 potential for our product candidates to be first-in-class and/or best-in-class; potential for accelerated approval paths; potential for our product candidates to be developed as monotherapies and in combination; potential for azenosertib (ZN-c3) to address large unmet need across an array of cancers; potential benefits of intermittent dosing for our product candidates; our development approach for azenosertib; timing of providing updates on azenosertib program timelines and potential paths to registration; timing of preclinical and clinical program updates; the potential unmet need in a particular indication and/or patient population; potential for combinations including our product candidates and the potential benefits thereof; the target profiles and potential benefits of our product candidates and their mechanisms of action, including as a monotherapy and/or in combination; our belief that we have strengthened our clinical development plans, including for azenosertib; timing of NDAs or final data read outs; the size of the potentially addressable patient populations; clinical and regulatory progress of our product candidates, including enrollment, initiation of clinical trials and data announcements; the market opportunities for and market potential of our product candidates; timing of initiating Phase 3 trial of azenosertib in combination with chemotherapy in Cyclin E1+ platinum sensitive ovarian cancer;, as well as statements that include the words "design," "estimate," "may," "opportunity," "plan," "potential," "predicts," "promising," "strategy," "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.

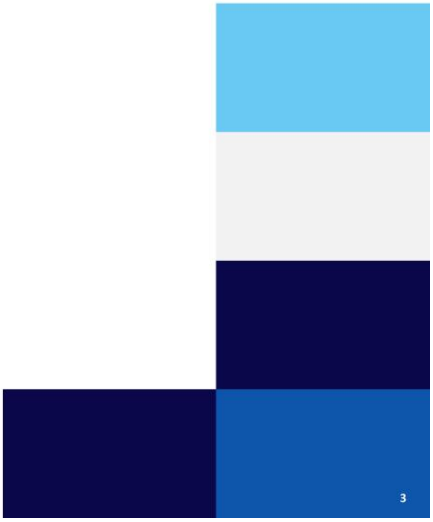
This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. These data involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. 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.

Today's Agenda

1. Review of Azenosertib Monotherapy Trial Results: Declaration of New Azenosertib Monotherapy Dose
2. Currently Accruing Trials in Ovarian Cancer and USC
3. Review of Azenosertib + Chemotherapy in Platinum-Resistant Ovarian Cancer (Presented Yesterday: ASCO Abstract 5513)
4. Proposed Phase 3 Chemotherapy Combination Trial
5. Q&A

zentalis



Joining the Call Today

Kimberly Blackwell, MD
Chief Executive Officer
Zentalis Pharmaceuticals

Carrie Brownstein, MD
Chief Medical Officer
Zentalis Pharmaceuticals

Funda Meric-Bernstam, MD
Chair of the Department of Investigational Cancer Therapeutics -- the Phase 1 Program at The University of Texas MD Anderson Cancer Center; Member, Zentalis Scientific. Advisory Board

Zentalis' Clinical Transformation Has Yielded Significant Progress

Purpose

- To develop **first in class** and **best in class** therapies against known cancer targets

Azenosertib meets all the criteria

- High potential, **validated target** in difficult-to-treat tumors
- WEE1 inhibitor designed to have **superior selectivity** and pharmacologic properties
- **Monotherapy activity** and favorable safety profile
- 400+ patients dosed to date

People

- Management team with **deep oncology experience**
- **Respected** scientific and clinical advisors
- Established partnerships with **Pfizer, GSK**

Promising Programs: BCL-2i and Degrader

- **Multiple opportunities** in hematologic malignancies
- 100+ patients dosed to date

Positioned to Execute and Deliver

Today's Call - Two Large Phase 1 Data Sets: Four Critical Take Home Messages Around Azenosertib

Monotherapy Dose Optimization Has Been Successful:

- **Confirmed ORR of 36.8% in heavily pre-treated platinum-resistant ovarian cancer and USC**
- **Improved tolerability** over other WEE-1 Inhibitor and highly comparable to Antibody Drug Conjugates

Combination With Single Agent Chemotherapy Improves Response Rates And Durability Over Chemotherapy Alone In Platinum-resistant/Refractory Ovarian Cancer:

- 50% ORR, 5.6 month DOR and a 7.4 month mPFS with paclitaxel
- 36% ORR, 11.4 month DOR and a 10.4 month mPFS with carboplatin

Comprehensive and Ongoing Development Strategy In Ovarian Cancer and USC:

- Phase 2 Monotherapy in USC (all patients)
- Phase 2 Monotherapy in platinum-resistant ovarian cancer
- Phase 1/2 Monotherapy or in combination/alternating with niraparib PARPi-resistant PROC
- Proposed Phase 3 Study in Cyclin E1+ platinum sensitive ovarian cancer
  - Chemotherapy + azenosertib followed by azenosertib monotherapy maintenance compared to doublet chemotherapy followed by placebo

zentalis

USC, Uterine Serous Carcinoma; ORR, Confirmed Objective Response Rate; DOR, Duration of Response; mPFS, Median Progression Free Survival.

AZENOSERTIB NEW INTERMITTENT MONOTHERAPY DOSE

Azenosertib Intermittent Monotherapy Dose Substantially Improves Antitumor Activity and Tolerability

Monotherapy Dose Selection: 400 mg intermittent (5 days on, 2 days off a week; 5:2)

Compared to prior dosing regimen (300 mg continuous), intermittent dosing led to:

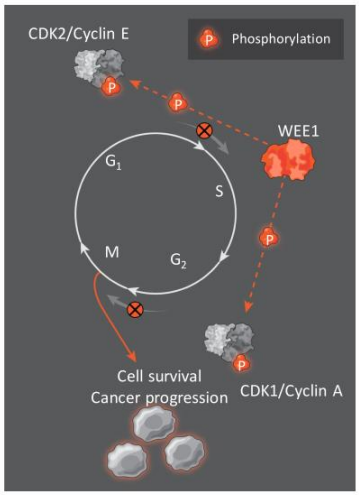
- More than a doubling of exposures
- A near doubling of response in both USC and HGSOC
  - Confirmed ORR of 36.8% in the patient population*
- Maintains or improves safety and tolerability

zentalis

*Response evaluable: have baseline measurable disease by RECIST 1.1, at least one post baseline scan, and received at least one dose of drug;
Abbreviations: 5:2, 5-days of treatment followed by 2-days off treatment; USC, Uterine Serous Carcinoma;
HGSOC, High Grade Serous Ovarian Cancer; ORR, objective response rate

Azenosertib Targets WEE1, a Critical Protein for Cancer Cell Survival

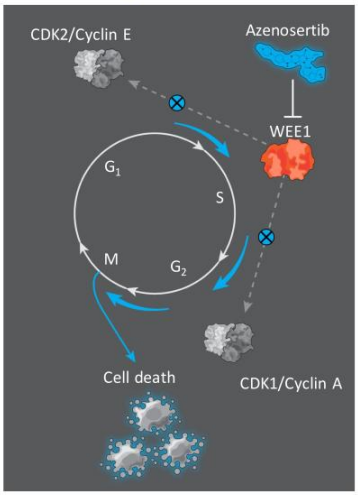
WEE1 activity in untreated cancer cell



- WEE1 phosphorylates CDK/Cyclin complexes to engage cell cycle checkpoints, allowing DNA repair to occur
- Azenosertib inhibits WEE1:
  - Leads to dephosphorylation of CDK 1 and 2, activating the cdk/cyclin complexes
  - Removes 2 cell cycle checkpoints: G1/S and G2/M
  - Cell cycle progresses without sufficient DNA repair
  - Cancer cells accumulate DNA damage, resulting in apoptosis and mitotic catastrophe

Azenosertib's MOA and early monotherapy clinical activity made dose optimization critical

Azenosertib blocks WEE1 resulting in cancer cell death



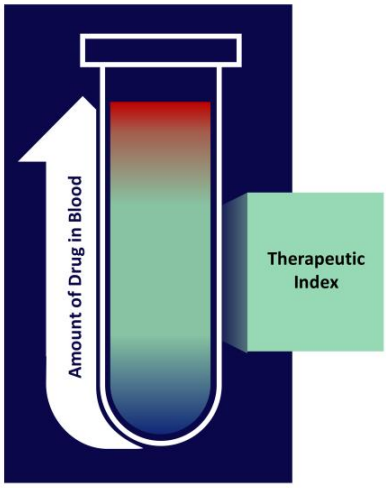
zentalis

Luserna di Rora, et al. 2020. J Hem Onc. 13:126. Elbaek et al. 2022. Cell Reports. 38:110261. Abbreviations: MOA, mechanism of action

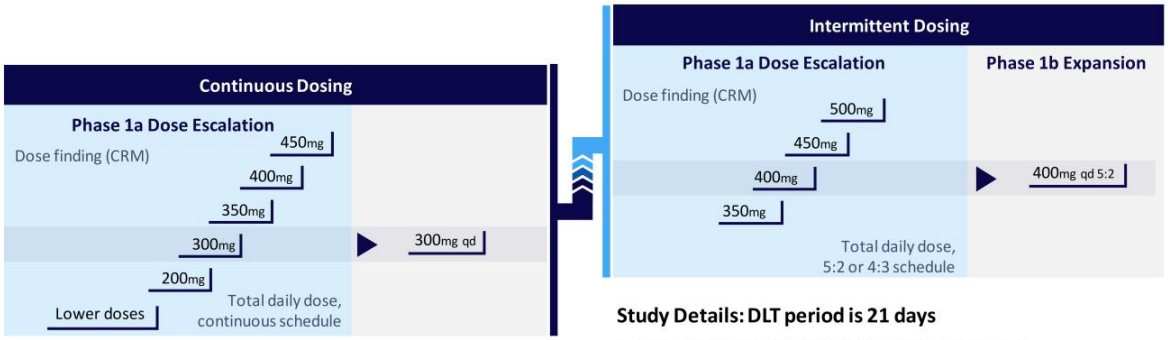
Finding The Optimal Dose of Azenosertib

300 mg continuous dose demonstrated favorable safety profile and antitumor activity, but preclinical models and clinical data suggested that intermittent dosing would allow for:

- Increased exposures at steady state
- Maintained or improved tolerability



Zentalis 001 Study: From First In Human to Dose Optimization



Study Details: DLT period is 21 days

- Tumor assessments (per RECIST 1.1) occur every 2 cycles (6 weeks)
- Protocol permits "Backfill" enrollment of additional patients at the highest previously cleared dose level

NCT04158336

Primary objectives: Safety, PK [Steady State Exposure (AUC_{0-24}) & Concentration Maximum (C_{max})]

zentalis

Abbreviations: CRM, continual reassessment method; qd, once 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; RECIST, response evaluation criteria in solid tumors; PK, pharmacokinetics; AUC, area under the curve

Zentalis 001: Heavily Pretreated Patients With Advanced Solid Tumors

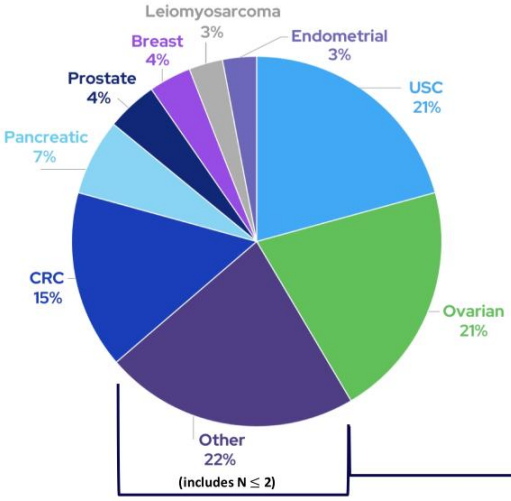
	Continuous N = 74	Intermittent N = 53	Total N = 127
Age			
Median	67	64	65
Range (Min-Max)	(41 - 81)	(35 - 83)	(35 – 83)
Measurable Disease (N, %)	70 (94.6)	53 (100)	123 (96.9)
ECOG PS (N, %)			
ECOG 0	20 (27.0)	18 (34.0)	38 (29.9)
ECOG 1	53 (71.6)	35 (66.0)	88 (69.3)
ECOG 2	1 (1.4)	-	1 (0.8)
Prior Lines of treatment			
Mean (range)	4.33 (1-18)	4.71 (1-10)	4.37 (1-18)
Prior Therapies (N, %)			
Prior PARPi	9 (12.2)	13 (24.5)	22 (17.3)
Prior experimental agent	30 (40.5)	19 (35.8)	49 (38.6)
Prior VEGF-inhibitor	42 (56.8)	31 (58.5)	73 (57.5)
Prior anti-PD1/PDL1	35 (47.3)	18 (34.0)	53 (41.7)

zentalis

Patients who received ≥300 mg; Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; PARPi, poly-ADP ribose polymerase inhibitor; VEGF, vascular endothelial growth factor; PD1/PDL1, programmed cell death protein 1/programmed death ligand 1

Data cut-off: April 24, 2023

Zentalis 001: Multiple Tumor Types, No Biomarker Stratification N=127



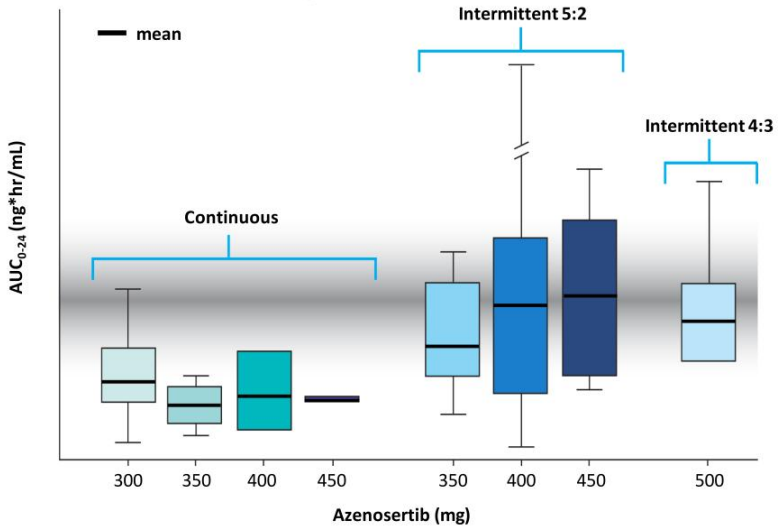
- Clear Cell RCC
- NSCLC
- Gastric Cancer
- Head and Neck SCC
- Anal SCC
- Melanoma
- SCLC
- Uterine stromal sarcoma
- Small cell ovarian
- Carcinosarcoma
- Adenoid cystic carcinoma
- Appendiceal

No biomarker, biopsy or prior therapy requirements for enrollment

zentalis

Patients who received ≥300 mg; Abbreviations: USC, uterine serous carcinoma; CRC, colorectal cancer; RCC, renal cell carcinoma; NSCLC, non-small cell lung cancer; SCC, squamous cell carcinoma; SCLC, small cell lung cancer

Intermittent Dosing Resulted In A Significant Increase In Steady State Exposure (AUC_{0-24})

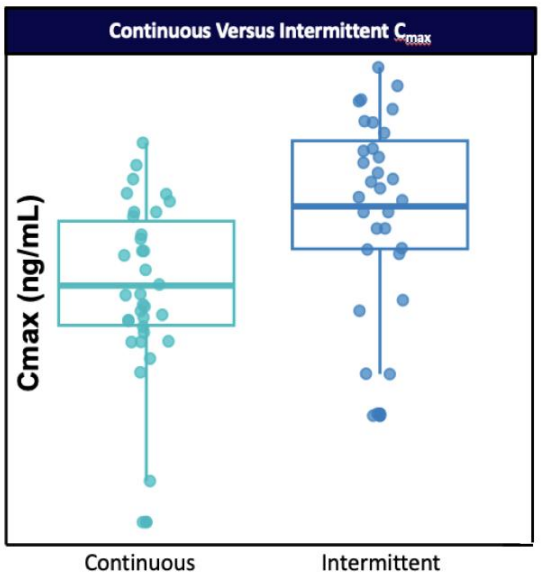


With intermittent dosing, more patients reach the projected target efficacious steady-state exposure (AUC_{0-24})

zentalis

Patients who received ≥300 mg; Collected at Day 12 after 3 consecutive days of dosing
Abbreviations: 5:2, 5-days of treatment followed by 2-days off treatment; AUC, area under the curve

Intermittent Dosing Achieves Higher Maximal Concentration (C_{max}) Levels



zentalis

Patients who received ≥300 mg;
Collected at Day 12 after 3 consecutive days of dosing

AZENOSERTIB MONOTHERAPY EFFICACY IN OVARIAN AND UTERINE SEROUS CARCINOMA

Zentalis 001: Patients With Uterine Serous Carcinoma And Ovarian Cancer After Multiple Prior Therapies

51 Patients Enrolled with Uterine Serous Carcinoma or High-Grade Serous Ovarian Cancer

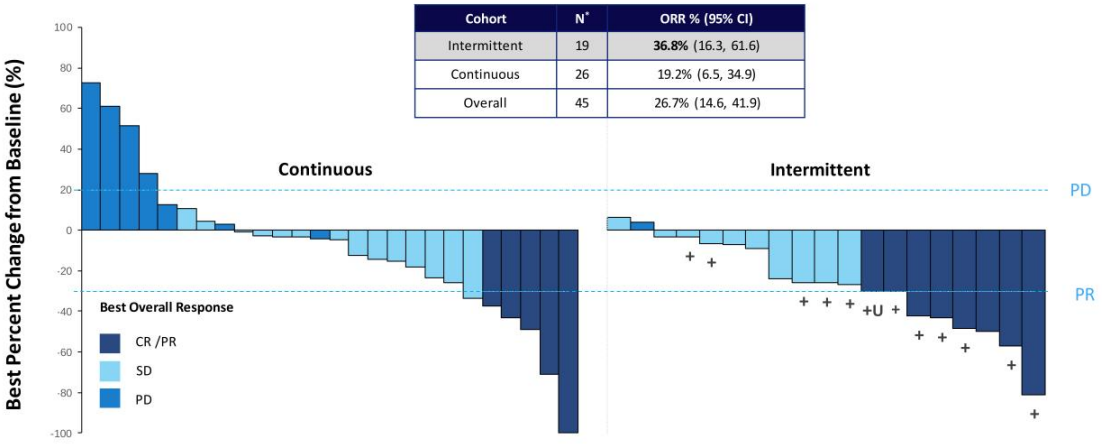
- Continuous and Intermittent dosing schedules
- Heavily Pretreated Group of Patients:

	USC N = 26	HGSOC N = 25
Prior Lines of treatment		
Mean (Range)	3.4 (1-9)	5.3 (1-18)
Platinum Resistant	26 (100%)	25 (100%)
Prior Therapies		
Prior PARPi	2 (7.7)	17 (68.0)
Prior experimental agent	5 (19.2)	7 (28.0)
Prior VEGF-inhibitor	19 (73.1)	21 (84.0)
Prior anti-PD1/PDL1	19 (73.1)	5 (20.0)

Patients who received ≥300 mg; Abbreviations: USC, uterine serous carcinoma; HGSOC, high-grade serous ovarian cancer
PARPi, poly-ADP ribose polymerase inhibitor; VEGF, vascular endothelial growth factor; PD1/PDL1, programmed cell death receptor 1/programmed death ligand 1

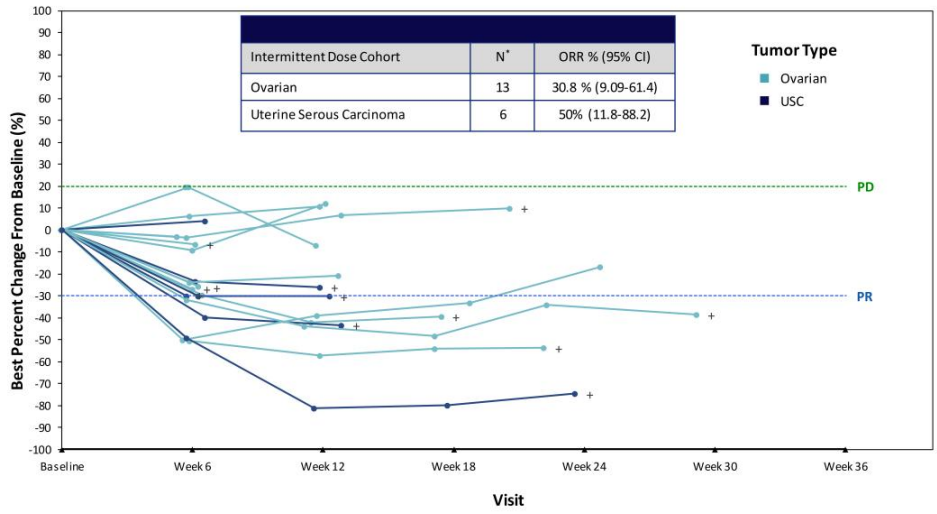
Azenosertib Intermittent Dosing Schedule Doubles Objective Response Rate In Ovarian/USC Populations

Cohort	N*	ORR % (95% CI)
Intermittent	19	**36.8%** (16.3, 61.6)
Continuous	26	19.2% (6.5, 34.9)
Overall	45	26.7% (14.6, 41.9)



*Response evaluable: have baseline measurable disease by RECIST 1.1, at least one post baseline scan, and received at least one dose of drug
Patients who received ≥300 mg. Abbreviations: USC, uterine serous carcinoma; CR, complete response; PR, partial response;
SD, stable disease; PD, progressive disease; ORR, objective response rate; CI, confidence interval; +: Patients remain on therapy at the time of data cut-off

Azenosertib Monotherapy Intermittent Dosing: 89% of Ovarian and USC Patients Had Target Lesion Reductions from their Baseline Scans



Intermittent Dose Cohort	N*	ORR % (95% CI)
Ovarian	13	30.8 % (9.09-61.4)
Uterine Serous Carcinoma	6	50% (11.8-88.2)

- 12/19 (63%) patients remain on therapy
- Median follow up of 4.4 months
- mPFS of 5.68 months (2.79, NR)
- 10/13 (77%) of ovarian cancer patients had received a prior PARP inhibitor

zentalis

*Response evaluable: have baseline measurable disease by RECIST 1.1, at least one post baseline scan, and received at least one dose of drug; Patients who received ≥300 mg.
Abbreviations: USC, uterine serous carcinoma; HGSOC, high-grade serous ovarian cancer SD, stable disease; PR, partial response; ORR, confirmed objective response rate; mPFS, median progression free survival; complete response; NR, Not reached, +: Patients remain on therapy at the time of data cut-off

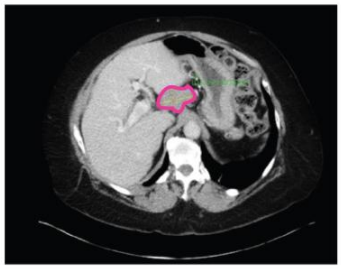
Azenosertib Patient Profile: Durable cPR In Cyclin E Amplified Platinum Resistant Ovarian Cancer

73-year-old female w/ HGSOC
CCNE1amp (Foundation)

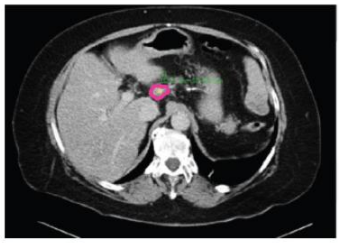
Prior lines of therapy:

1. Avelumab **(SD)**
2. Doxorubicin Liposomal **(PD)**
3. Topotecan/bevacizumab **(PD)**
4. Cyclophosphamide/bevacizumab **(unknown)**
5. XMT1536 (NaPi2b ADC) **(PR)**
6. APG115 (MDM2 inh) / Pembrolizumab **(SD)**
7. ABBV-155 (CD275 ADC) **(PD)**
8. NC318 (Siglec-15 mAB) **(SD)**
9. SM08502 (CLK inhibitor) **(PD)**
10. NBMBMX (HDAC8 inh) **(SD)**

Response	Treatment Length	Current Status
cPR (-71%)	**11** months	**Off** treatment



Baseline



12 weeks

zentalis

Abbreviations: cPR, confirmed partial response; HGSOC, high-grade serous ovarian cancer; SD, stable disease; PD, progressive disease; PR, partial response.

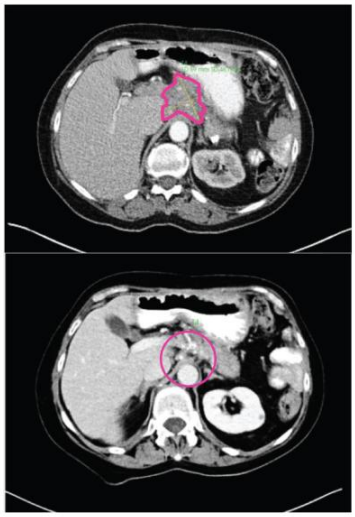
Azenosertib Patient Profile: Durable cPR In HRD+ PARPi Platinum Resistant Ovarian Cancer

64-year-old female
HGSOC; BRCA1m (Foundation)

Prior lines of therapy

1. Carbo/taxol/abraxane/bev/Olaparib **(PD)**
2. Pembrolizumab **(PD)**
3. NaPi2b targeting-ADC (XMT-1536) **(PD)**
4. Carbo/gem/bevacizumab **(PD)**
5. Pegylated doxorubicin **(PD)**
6. Topotecan **(PD)**
7. PABP-1 RNP (ATRC-101) **(PD)**

Response	Treatment Length	Current Status
cPR (-48%)	5 months	On treatment



Baseline

Target Lesion No Longer Visualized

zentalis

Abbreviations: cPR, confirmed partial response HGSOC, high-grade serous ovarian cancer; HRD+, homologous recombination repair deficiency; PARPi, poly-ADP ribose polymerase inhibitor; high-grade serous ovarian cancer; BRCA1m, BRCA1 mutant; PD, progressive disease

AZENOSERTIB MONOTHERAPY SAFETY IN PATIENTS FROM ZENTALIS 001

Intermittent Dosing Maintains Safety And Improves Tolerability Over Continuous Dosing

Treatment Related AEs, N (%)	Continuous (n=67)		Intermittent (n=27)		Total* (n=94)	
	All Grade	Grade 3/4	All Grade	Grade 3/4	All Grade	Grade 3/4
Gastrointestinal						
Nausea	46 (68.7)	2 (3.0)	9 (33.3)	-	55 (58.5)	2 (2.1)
Diarrhea	31 (46.3)	4 (6.0)	11 (40.7)	3 (11.1)	42 (44.7)	7 (7.4)
Vomiting	28 (41.8)	-	3 (11.1)	-	31 (33.0)	-
Decreased appetite	20 (29.9)	1 (1.5)	4 (14.8)	1 (3.7)	24 (25.5)	2 (2.1)
Dehydration	6 (9.0)	-	3 (11.1)	-	9 (9.6)	-
Fatigue	30 (44.8)	8 (11.9)	11 (40.7)	2 (7.4)	41 (43.6)	10 (10.6)
Hematologic						
Anemia	6 (9.0)	2 (3.0)	6 (22.2)	3 (11.1)	12 (12.8)	5 (5.3)
Thrombocytopenia	4 (6.0)	3 (4.5)	2 (7.4)	-	6 (6.4)	3 (3.2)
Neutropenia**	1 (1.5)	1 (1.5)	4 (14.8)	3 (11.1)	5 (5.3)	4 (4.3)

*Safety Evaluable Population: Received at least one dose of drug;
**No incidence of febrile neutropenia in either dosing group
Continuous 300, 350, 400; Intermittent 350 5:2 and 400 5:2
Treatment Related AEs > 10% and treatment related AEs of interest: All Tumor Types
Abbreviations: AE, adverse event

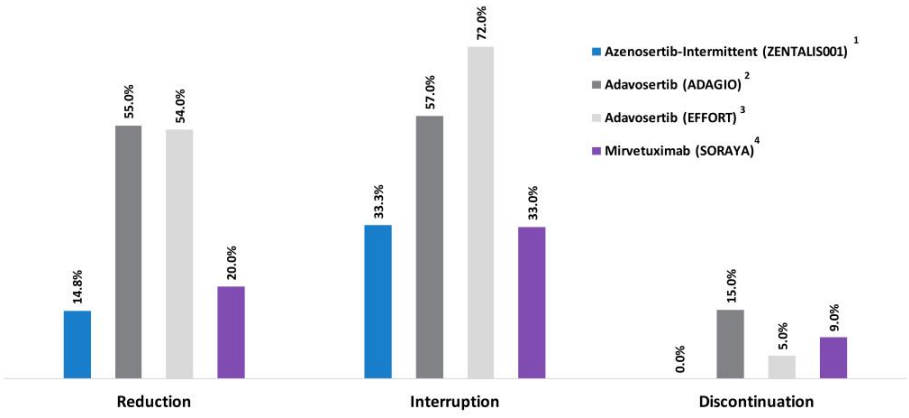
Azenosertib At Intermittent Schedules Reduces Dose Modifications And Serious Adverse Events

	Continuous N = 67	Intermittent N = 27	Total* N =94
Treatment Related AEs leading to, N (%):			
Dose reduction	19 (28.4)	4 (14.8)	23 (24.5)
Dose interruption	17 (25.4)	9 (33.3)	26 (27.7)
Discontinuation	4 (6.0)	-	4 (4.3)
Death	-	-	-
Treatment Related SAEs	5 (7.5)	-	5 (5.3)

zentalis

*Safety Evaluable Population: Received at least one dose of drug; Continuous 300, 350, 400; Intermittent 350 5:2 and 400 5:2
Abbreviations: SAEs, serious adverse events

Azenosertib: Tolerability* Compared To Adavosertib and Mirvetuximab



*Attributable to Treatment Related AEs. Not direct head-to-head comparisons.

1. ZENTALIS 001: data on file
2. (ADAGIO Study) Liu et. al. Presented at the Society of Gynecologic Oncology Annual Meeting, March 23–28, 2023
3. (EFFORT Study) Westin et. al. DOI: 10.1200/JCO.2021.39.15_suppl.5505 Journal of Clinical Oncology 39, no. 15_suppl (May 20, 2021) 5505-5505.
4. (SORAYA Study) Matulonis et al. DOI: 10.1200/JCO.22.01900 Journal of Clinical Oncology 41, no. 13 (May 01, 2023) 2436-2445.

zentalis

AZENOSERTIB MONOTHERAPY ONGOING STUDIES IN USC AND OVARIAN CANCER

Monotherapy Dose and Biomarker Enrichment Is Foundational To Our Clinical Strategy

Tumors with High Genomic Instability are Sensitive to Azenosertib

High genomic instability can be caused by:

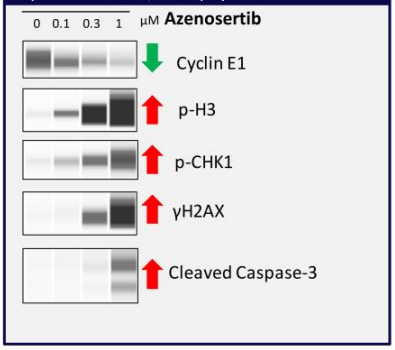
Cyclin E1+ Tumors

- Cyclin E1+ drives accelerated entry into S-phase through its partnership with CDK2
- Replication machinery is overloaded, resulting in genomic instability

Homologous Recombination Repair Defective (HRD+) Tumors

- Results in genomic instability through tumors inability to repair double stranded DNA breaks.

Azenosertib induces markers of DNA damage, replicative stress, and apoptosis*



*OVCAR3 Cyclin E1 positive cells, 16-hour treatment

zentalis

Zentalis 004 (TETON): Azenosertib Monotherapy In Women With ≥2L Advanced Uterine Serous Carcinoma

CURRENTLY ACCRUING- FDA Fast track designation

Key Eligibility: Recurrent or persistent USC; ≥1 prior platinum-based chemotherapy regimen; Prior HER-2 directed therapy for known HER-2+; Prior anti-PDL-1; Measurable disease; ECOG PS 0-1; No prior WEE1 inhibitor; No prior cell cycle checkpoint inhibitor.

NCT04814108

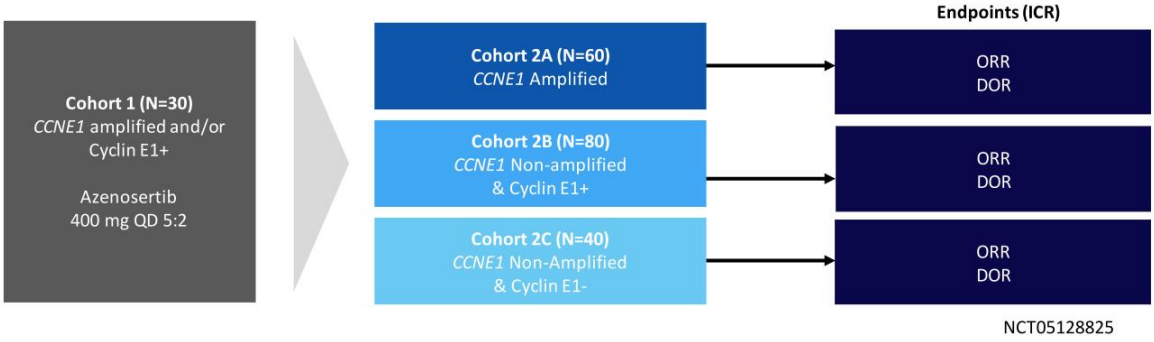
zentalis

Abbreviations: 2L, two lines; USC, uterine serous carcinoma; ECOG PS, Eastern Cooperative Oncology Group performance score; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; DOR, duration of response

Zentalis 005 (DENALI): Evaluating Impact of *CCNE1* Amplification and Cyclin E1+ in Platinum-Resistant High-Grade Serous Ovarian Cancer

CURRENTLY ACCRUING

Key Eligibility: High-Grade Serous Ovarian Cancer; ECOG PS 0-1; Platinum-resistant (excluding Platinum-refractory); 1-3 prior lines of chemotherapy; Measurable disease per RECIST v 1.1; Cyclin E1 IHC+ and/or CCNE1 amplified.



NCT05128825

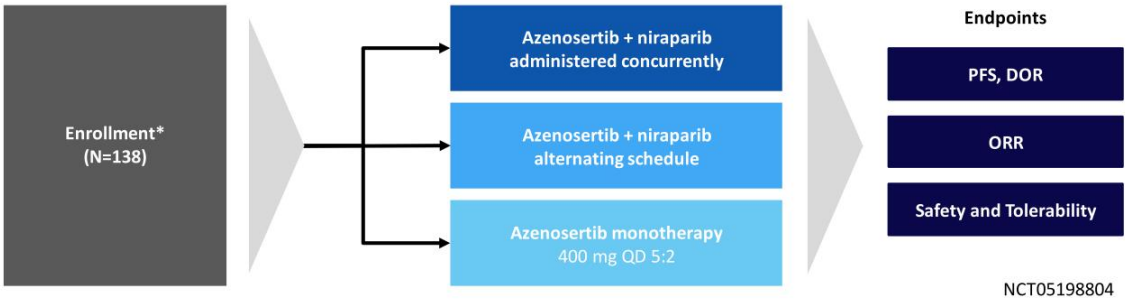
zentalis

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance score; RECIST, response evaluation criteria in solid t umors; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; DOR, Duration of Response; ICR, Independent Central Review

Zentalis 006 (MAMMOTH): Revised Phase 1/2 Study Of Azenosertib In Combination With Niraparib Or Alternating With Niraparib Or As A Monotherapy in Patients With PARP-resistant Ovarian Cancer

CURRENTLY ACCRUING

Key Eligibility: Recurrent high-grade epithelial ovarian, primary peritoneal, or fallopian tube cancer (serous, clear cell or endometrioid); 1 – 5 prior lines for advanced/metastatic disease; Relapsed within 6 months of platinum therapy (platinum resistant), progressed after taking at least 3 months of PARPi as maintenance treatment.



NCT05198804

* Enrollment Based on Slot Availability

zentalis

Abbreviations: PARPi, poly-ADP ribose polymerase inhibitor; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; PFS, progression free survival; ORR, objective response rate

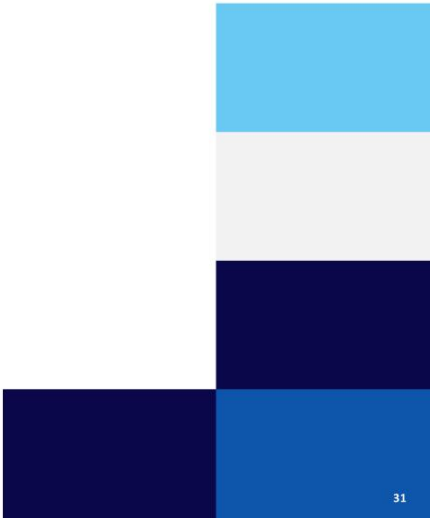
Azenosertib is Highly Active Agent in Ovarian Cancer and USC and has Favorable Safety Profile

- Recommended Phase 2 dose of 400 mg at 5:2 schedule selected based on clinical safety and efficacy

36.8% Confirmed Response Rate in Ovarian and Uterine Serous Carcinomas with intermittent dosing*

Majority of patients remain on intermittent treatment

- Update on monotherapy efficacy data, and clinical trial timelines in 2H23



zentalis

*Response evaluable patients (having received at least one scan)
USC, Uterine Serous Carcinoma

AZENOSERTIB CHEMOTHERAPY COMBINATIONS

Abstract #5513
Poster Bd #208

2023 ASCO ANNUAL MEETING

Correlation of Cyclin E1 expression and clinical outcomes in a Phase 1b dose-escalation study of Azenosertib (ZN-c3), a WEE1 inhibitor, in combination with chemotherapy (CT) in patients (pts) with platinum-resistant or refractory (R/R) epithelial ovarian, peritoneal, or fallopian tube cancer (EOC)

Joyce Liu[1], Siqing Fu[2], Gary Richardson[3], Zivko Vranjes[4], Tarek Meniawy[5], Catherine Shannon[6], Erika P. Hamilton[7], Stephanie Blank[8], Cara Mathews[9], Jasmina Alidzanovic[10], Rossitza Krasteva[11], Qing Shi[13], Olivier Harismendy[13], Mieke Ptaszynski[14], Shannon N. Westin[2], Funda Meric-Bernstam[2], Premal H.Thaker[15]

[1]Dana Farber Cancer Institute, Boston, MA [2]The University of Texas MD Anderson Cancer Center, Houston, TX; [3]Cabrini Hospital, Malvern, Australia; [4]University Clinical Center of Republic of Srpska, Bosnia and Herzegovina; [5]Linear Cancer Research, University of Western Australia, Perth, Australia; [6]Mater Hospital, Brisbane, Australia; [7]Tennessee Oncology, Sarah Cannon Research Institute, Nashville, TN; [8]Icahn School of Medicine at Mount Sinai, New York City, NY; [9]Women & Infants Hospital of Rhode Island, Providence, RI; [10]University Clinical Center Tuzla, Bosnia and Herzegovina; [11]Uni Hospital, Panagyurishte, Bulgaria; [13]Zentalis Pharmaceuticals, New York, NY; [14]Formerly Zentalis Pharmaceuticals, New York, NY; [15]Siteman Cancer Center, Washington University, St Louis, MO

zentalis

Azenosertib Is Active With Favorable Tolerability Profile in Combination with Chemotherapy

RP2D established for paclitaxel, carboplatin and PLD combinations

RP2D		
	Azenosertib	Chemotherapy
Paclitaxel	300 mg QD 5:2	80 mg/m^2 on D1, D8, D15 (28-day cycles)
Carboplatin	200 mg QD 5:2	AUC=5 on D1 (21-day cycles)
Gemcitabine	TBD*	TBD*
PLD	400 mg QD 5:2	40 mg/m^2 D1 (28-day cycles)

Main Takeaways

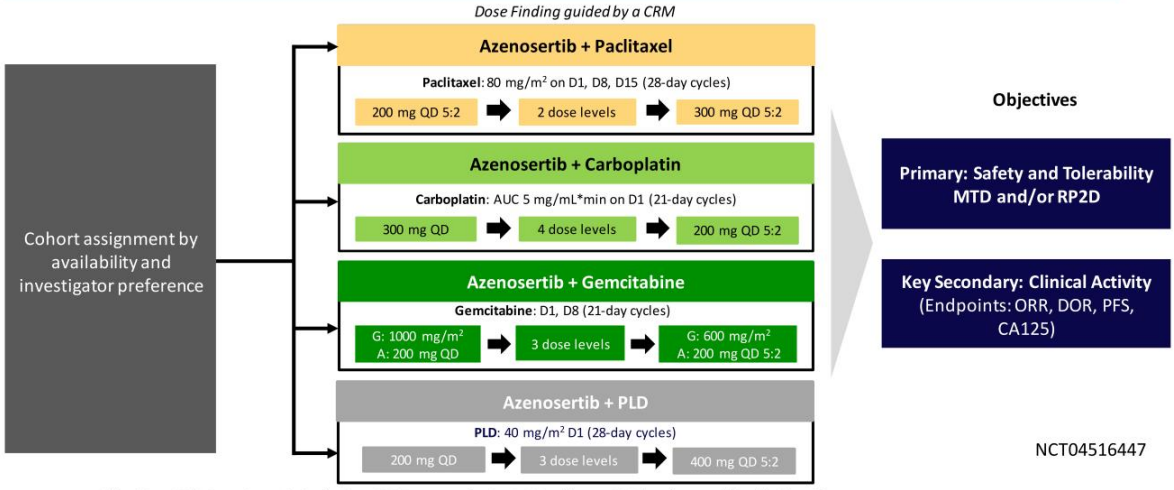
- Strong and durable efficacy signal across chemotherapy backbones
  - cORR of 34%; cDOR of 8.3 months; mPFS of 9.0 months (response evaluable=94)
- Cyclin E1 status predicts benefit of azenosertib addition to chemotherapy
  - Suggests azenosertib restores chemotherapy sensitivity in heavily pre-treated platinum- resistant ovarian cancer

zentalis

*Gemcitabine + Azenosertib has exciting and durable activity-a MTD has not been determined, further dose cohorts are ongoing.
Abbreviations: RP2D, recommended phase 2 dose; PLD pegylated liposomal doxorubicin; QD, once daily;
5:2, 5-days of treatment followed by 2-days off treatment; D, day; AUC, area under the curve; mg/mL*min

Phase 1b combination study to define RP2D dosing

Key Eligibility: High-Grade Serous Ovarian Cancer; ECOG Performance Status 0-2; Platinum-resistant/refractory; Up to 3 prior lines of chemotherapy; Measurable disease per RECIST v 1.1



NCT04516447

zentalis

Abbreviations: ; ECOG, Eastern Cooperative Oncology Group; RECIST, response evaluation criteria in solid tumors; 5:2, 5 -days of treatment followed by 2-days off treatment; CRM, continuous reassessment model; QD, once daily; D, day; AUC, area under the curve; G, gemcitabine; A, azenosertib; 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;

Patient Characteristics*

Characteristic		Azenosertib + Paclitaxel (N=26)	Azenosertib + Carboplatin (N=36)	Azenosertib + Gemcitabine (N=18)	Azenosertib + PLD (N=35)	Total (N=115)
Age, years	Median (Range)	61.5 (45-83)	61.0 (48-77)	62.5 (47-77)	56.0 (34-75)	61.0 (34-83)
Race and Ethnicity, N (%)	White	24 (92.3)	34 (94.4)	16 (88.9)	34 (97.1)	108 (93.9)
	Black or African-American	0	0	0	0	0
	Asian	1 (3.8)	1 (2.8)	1 (5.6)	1 (2.9)	4 (3.5)
	Other / NR	1 (3.8)	1 (2.8)	1 (5.6)	0	3 (2.6)
	Hispanic (Yes/No/NR)	1/25/0 (3.8/96.2/0)	0/34/2 (0/94.4/5.6)	1/17/0 (5.6/94.4/0)	1/33/1 (2.9/94.3/2.9)	3/109/3 (2.6/94.8/2.6)
ECOG Performance Status, N (%)	0	21 (80.8)	21 (58.3)	12 (66.7)	24 (68.6)	78 (67.8)
	1	5 (19.2)	15 (41.7)	6 (33.3)	11 (31.4)	37 (32.2)
Geographic Region, N (%)	US	6 (23.1)	10 (27.8)	10 (55.6)	5 (14.3)	31 (27.0)
	Europe	10 (38.5)	10 (27.8)	6 (33.3)	27 (77.1)	53 (46.1)
	Australia	9 (34.6)	15 (41.7)	1 (5.6)	3 (8.6)	28 (24.3)
	Korea	1 (3.8)	1 (2.8)	1 (5.6)	0	3 (2.6)
Platinum Status	Refractory, n (%)	5 (19.2)	9 (25.0)	3 (16.7)	7 (20.0)	24 (20.9)
Prior Lines of Therapy	1-2, n (%)	22 (84.6)	30 (83.3)	18 (100)	33 (94.3)	103 (89.6)
	3-4, n (%)	4 (15.4)	6 (16.7)	-	2 (5.7)	12 (10.4)
Prior PARP Inhibitor	n (%)	8 (30.8)	10 (27.8)	5 (27.8)	5 (14.3)	28 (24.3)
Prior Bevacizumab	n (%)	8 (30.8)	18 (50.0)	6 (33.3)	15 (42.9)	47 (40.9)

zentalis

*Safety Evaluable Population: Received at least one dose of drug.

Abbreviations: PLD, pegylated liposomal doxorubicin; NR, not reported; ECOG, Eastern Cooperative Oncology Group

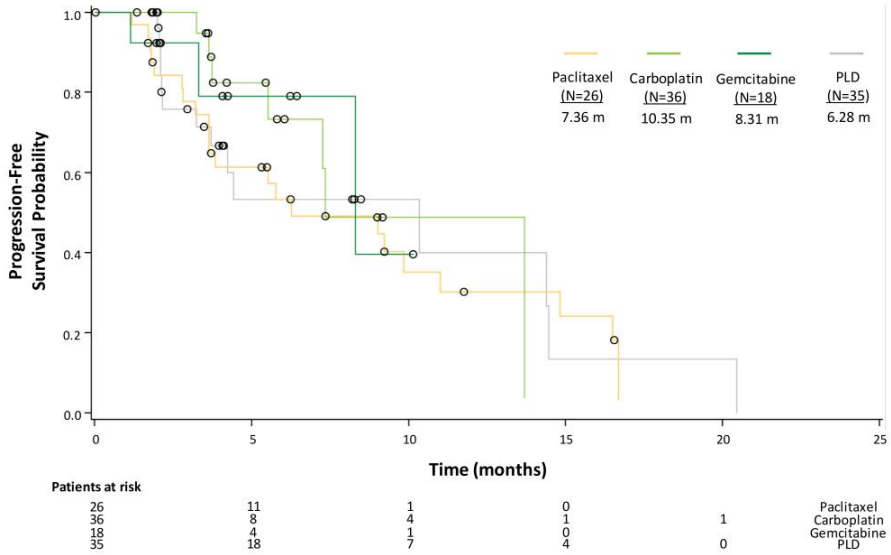
High Response of Azenosertib Doublets

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.
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

Kaplan-Meier Curves of Progression-Free Survival: Durable Responses



Patients at risk

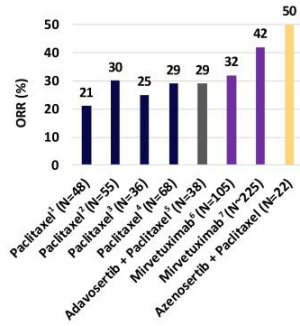
26	11	1	0		Paclitaxel
36	8	4	1	1	Carboplatin
18	4	1	0		Gemcitabine
35	18	7	4	0	PLD

zentalis

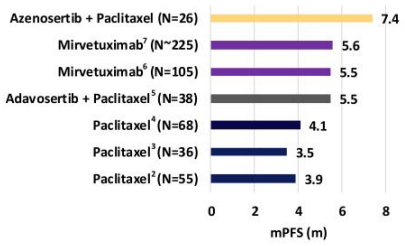
Abbreviations: PLD, pegylated liposomal doxorubicin; PFS, progression free survival; m, months.

The Activity of Azenosertib + Paclitaxel is Robust and Durable Compared to Historical Reports of Single Agent Paclitaxel, Adavosertib + Paclitaxel and Mirvetuximab in Platinum-Resistant Ovarian Cancer

Objective Response Rate (ORR)



Median Progression Free Survival (mPFS)

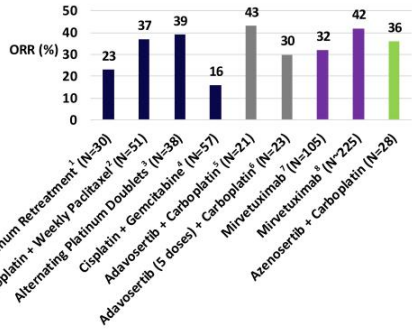


References: 1. Markman et al. Gynecol Oncol 2006;101:436-40. 2. AURELIA: Avastin USPI 3. MITO11: Pignata et al. Lancet Oncol 2015;16:561-68. 4. OCTOPUS: Banerjee et al. ESMO 2019. 5. GYN49: Moore et al. Clin Cancer Res 2022;28:36-44. 6. SORAYA: Matulonis et al. J Clin Oncol 2023;41:2436-45. 7. MIRASOL: Immunogen Press Release May 3, 2023.
Abbreviations: ORR, objective response rate; mPFS, median progression free survival; m, months. Not direct head-to-head comparisons.

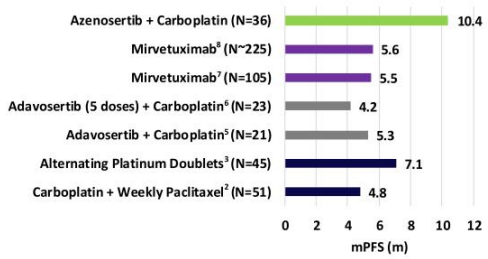
Data cut-off: April 10, 2023

The Activity of Azenosertib + Carboplatin is Robust and Durable Compared to Historical Reports of Single Agent Paclitaxel, Adavosertib + Paclitaxel and Mirvetuximab in Platinum-Resistant Ovarian Cancer

Objective Response Rate (ORR)



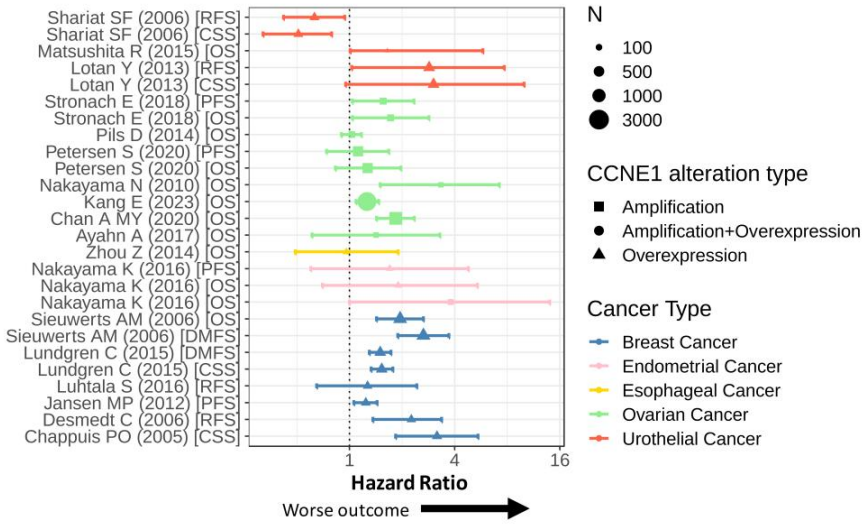
Median Progression Free Survival (mPFS)



References: 1. Leitao et al. Gynecol Oncol 2003;91:123-9. 2. CARTAXHY: Lortholary et al. Ann Oncol 2012;23:346-52. 3. Pectasides et al. Gynecol Oncol 2010;118:52-7. 4. Brewer et al. Gynecol Oncol 2006;103:446-50. 5. MK-1775-009: Leijen et al. J Clin Oncol 2016;34:4354-61. 6. GYN-49: Moore et al. Clin Cancer Res 2022;28:36-44. 7. SORAYA: Matulonis et al. J Clin Oncol 2023;41:2436-2445. 8. MIRASOL: Immunogen Press Release May 3, 2023.
Abbreviations: ORR, objective response rate; mPFS, median progression free survival; m, months. Not direct head-to-head comparisons.

Data cut-off: April 10, 2023

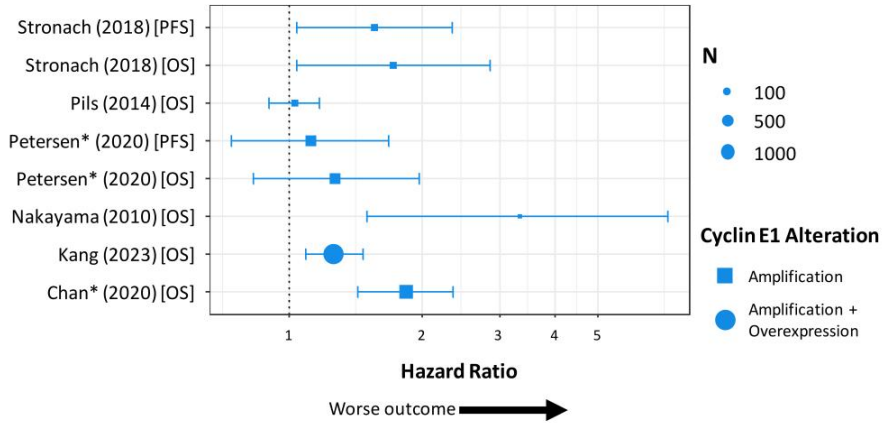
Patients With Cyclin E1+ Tumors Consistently Have Worse Outcomes On Chemotherapy



zentalis

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

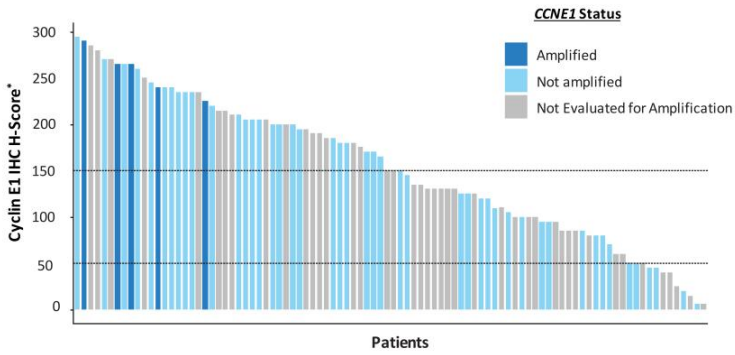


- 6 Studies; n=5404
- 4 Studies where timing of tissue collection was available-all were platinum sensitive tissue collected after ≤ 1 course of chemotherapy; 3533/5404 (65%)
- Other 2 Studies did not disclose timing of tissue collection

zentalis

*Timing of tissue collection was not disclosed. Abbreviations: PFS: progression free survival, OS; overall survival

Zentalis 002: Majority of Ovarian Cancers are Cyclin E1 +



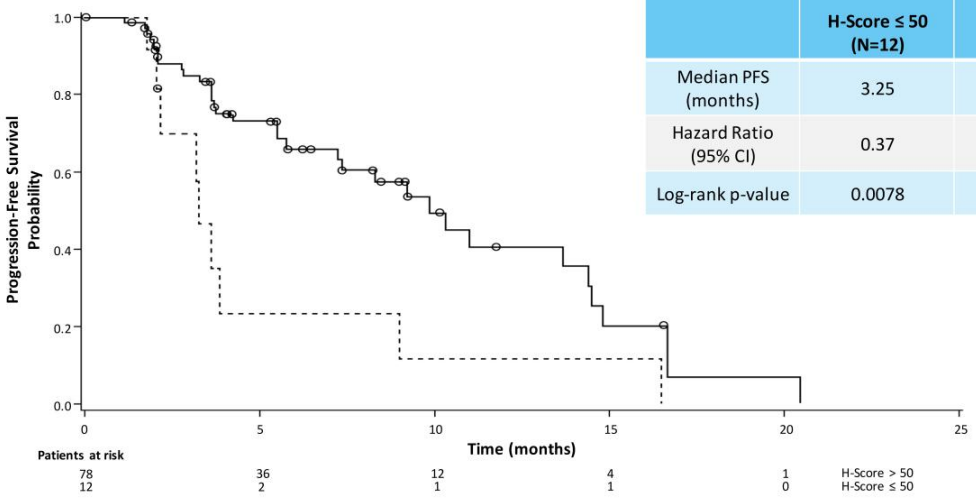
IHC H-Score*	>150	≤ 150 to > 50	≤ 50
CCNE1 Amplified	5	0	0
CCNE1 Not Amplified	25	15	6
Tissue Not Evaluated for Amplification	16	21	6

- H-score > 50 includes all *CCNE1* amplified tumors
- Prevalence of Cyclin E1-IHC+, H-score > 50 of all safety evaluable patients with tissue is 82/94 (**87**%);
- Prevalence of Cyclin E1+ in the response evaluable patients with tissue is 70/82 **(85%).**

zentalis

*H-scores calculated by multiplying the percentage of cells (0 to 100%) with intensity of Cyclin E1 expression (0 to 3); IHC: Immunohistochemistry
Safety evaluable: received at least one dose of drug; Response evaluable: have baseline measurable disease by RECIST 1.1, at least one post baseline scan, and received at least one dose of drug

Progression Free Survival is Significantly Improved in Cyclin E1+, Cohort compared to Cyclin E1- Independent of Chemotherapy Backbone



	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

*Response evaluable subjects are treated subjects with baseline measurable disease per RECIST version 1.1 and at least one post-baseline assessment.
Abbreviations: IHC, immunohistochemistry ; CI, confidence interval

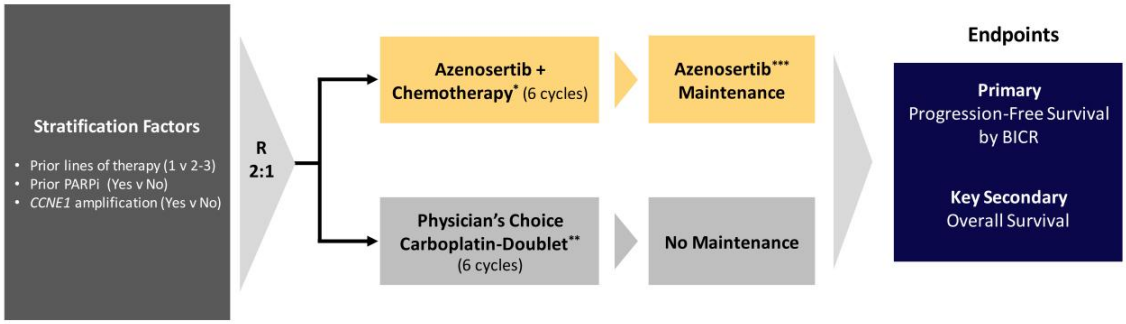
Treatment-related Adverse Events: All Doses Moving Forward Involve Intermittent Dosing

Treatment-Related Adverse Event ≥20% N (%)			Azenosertib + Paclitaxel (Continuous, N=7; Intermittent, N=19)		Azenosertib + Carboplatin (Continuous, N=22; Intermittent, N=14)		Azenosertib + Carboplatin (Continuous, N=14; Intermittent, N=8)		Azenosertib + Gemcitabine (Continuous N=8; Intermittent, N=10)		Azenosertib + PLD (Continuous N=27; Intermittent, N=8)		Total*** (Continuous, N=64; Intermittent, N=51)	
			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	C	5 (71.4)	5 (71.4)	9 (40.9)	7 (31.8)	4 (28.6)	3 (21.4)	7 (87.5)	6 (75.0)	19 (70.4)	17 (63.0)	40 (62.5)	35 (54.7)
		I	11 (57.9)	**5 (26.3)**	7 (50.0)	1 (7.1)	4 (50.0)	-	7 (70.0)	4 (40.0)	3 (37.5)	3 (37.5)	28 (54.9)	13 (25.5)
	Thrombo-cytopenia	C	4 (57.1)	2 (28.6)	16 (72.7)	11 (50.0)	11 (78.6)	6 (42.9)	8 (100.0)	5 (62.5)	9 (33.3)	2 (7.4)	37 (57.8)	20 (31.3)
		I	4 (21.1)	-	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	C	5 (71.4)	-	10 (45.5)	3 (13.6)	5 (35.7)	1 (7.1)	6 (75.0)	2 (25.0)	11 (40.7)	4 (14.8)	32 (50.0)	9 (14.1)
		I	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	C	4 (57.1)	-	15 (68.2)	1 (4.5)	10 (71.4)	1 (7.1)	5 (62.5)	-	16 (59.3)	2 (7.4)	40 (62.5)	3 (4.7)
		I	7 (36.8)	1 (5.3)	6 (42.9)	-	3 (37.5)	-	5 (50.0)	-	4 (50.0)	1 (12.5)	22 (43.1)	2 (3.9)
	Vomiting	C	3 (42.9)	1 (14.3)	8 (36.4)	-	6 (42.9)	-	1 (12.5)	-	11 (40.7)	2 (7.4)	23 (35.9)	3 (4.7)
		I	2 (10.5)	1 (5.3)	2 (14.3)	-	2 (25.0)	-	1 (10.0)	-	4 (50.0)	1 (12.5)	9 (17.6)	2 (3.9)
	Diarrhea	C	4 (57.1)	1 (14.3)	4 (18.2)	-	1 (7.1)	-	1 (12.5)	-	8 (29.6)	-	17 (26.6)	1 (1.6)
		I	6 (31.6)	1 (5.3)	5 (35.7)	-	3 (37.5)	-	6 (60.0)	-	2 (25.0)	-	19 (37.3)	1 (2.0)
Other	Fatigue	C	6 (85.7)	1 (14.3)	8 (36.4)	-	3 (21.4)	-	3 (37.5)	1 (12.5)	8 (29.6)	3 (11.1)	25 (39.1)	5 (7.8)
		I	8 (42.1)	2 (10.5)	5 (35.7)	1 (7.1)	4 (50.0)	-	6 (60.0)	2 (20.0)	2 (25.0)	-	21 (41.2)	5 (9.8)

Abbreviations: C, Continuous azenosertib dosing; I, Intermittent azenosertib dosing; MTD, maximum tolerated dose; PLD, pegylated liposomal doxorubicin
*All doses were at or below the MTD
A MTD for Gemcitabine + Azenosertib has not been determined, further dose cohorts are ongoing. * Safety evaluable: received at least one dose of drug

Proposed Randomized Phase 3 Trial Design of Azenosertib + Chemotherapy in Recurrent Platinum-Sensitive Ovarian Cancer that is Cyclin E1+

Key Eligibility: High-Grade Serous Ovarian Cancer; ECOG performance status 0-1; ≥1L Prior Line of Platinum-based chemotherapy; Platinum-Sensitive (Platinum-free interval ≥ 6 months); Prior Bevacizumab & PARPi if eligible and per regional standard of care; Cyclin E1 + (either *CCNE1* amplified and/or Cyclin E1 IHC-Positive)



*Paclitaxel or Carboplatin
**Paclitaxel or Pegylated Liposomal Doxorubicin
***Azenosertib, 400 mg QD 5:2
Abbreviations: ECOG, Eastern Cooperative Oncology Group; 1L, 1 line; PARPi, poly-ADP ribose polymerase inhibitor; IHC, immunohistochemistry; BICR, blinded independent central review.

Conclusions: Data Supports Dose and Advancement of Azenosertib-Chemotherapy Combination into Platinum-Sensitive Ovarian Cancer

RP2D established for paclitaxel, carboplatin and PLD combinations

RP2D		
	Azenosertib	Chemotherapy
Paclitaxel	300 mg QD 5:2	80 mg/m^2 on D1, D8, D15 (28-day cycles)
Carboplatin	200 mg QD 5:2	AUC=5 on D1 (21-day cycles)
Gemcitabine	TBD*	TBD*
PLD	400 mg QD 5:2	40 mg/m^2 D1 (28-day cycles)

Main Takeaways

- Strong and durable efficacy signal across chemotherapy backbones
- Cyclin E1 status predicts benefit of azenosertib addition to chemotherapy
  - Suggests azenosertib restores chemotherapy sensitivity in heavily pre-treated platinum-resistant ovarian cancer
- **Plans to initiate Phase 3 study of azenosertib in combination with chemotherapy in Cyclin E1+ platinum sensitive ovarian cancer**

zentalis

*Gemcitabine + Azenosertib has exciting and durable activity-a MTD has not been determined, further dose cohorts are ongoing.
Abbreviations: RP2D, recommended phase 2 dose; PLD pegylated liposomal doxorubicin; QD, once daily;
5:2, 5-days of treatment followed by 2-days off treatment; D, day; AUC, area under the curve; mg/mL*min

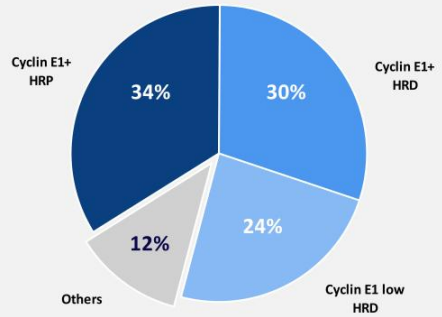
Potential to Transform Treatment Paradigm for Patients and Capture Significant Market Share in Ovarian Cancer

Azenosertib Monotherapy Potentially Addresses 88% Of High Grade Serous Ovarian Cancer

- Ongoing clinical programs address Cyclin E1+ and HRD+ patient populations
  - Opportunity is much larger than recently approved therapies
- Data support potential role for Azenosertib at every stage of metastatic therapy:
  - **Platinum sensitive**: combination with chemotherapy
  - **Platinum resistant**: monotherapy and combination with chemotherapy

Potential to transform standard of care

High Grade Serous Ovarian Cancer Patient Segments

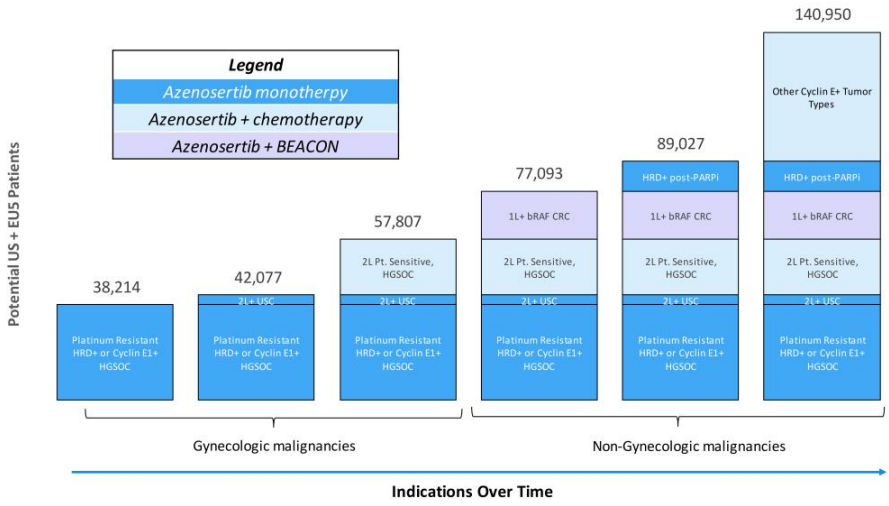


HRD: Homologous recombination deficient
HRP: Homologous recombination proficient

Sources:
1. HRD prevalence derived from **Konstantinopoulos**, et al *Cancer Discov* (2015)
2. CCNE1 amplification prevalence of ~20% reported in **Aziz** et al *Gynecol Oncol* (2018) and **TGCA Network** *Nature* volume 474 (2011)
3. Cyclin E1 expression and copy number extracted from the digital analysis of **Aziz** et al Figure 3A to infer full distribution of Cyclin E1 H-scores and overlap with CCNE1 amplification based on Cyclin E1 high definition of H-score >50
4. HRD prevalence and proportion of overlap with CCNE1 amplification from **Konstantinopoulos** et al, Figure 2
5. Total HGSOC incidence estimates (US, EU5) sourced from SEER and ECIS are 35, 388 individuals/year

zentalis

Addressable Patient Population More than Doubles as Franchise Expands to Non-Gynecological Malignancies



Source: Used 'drug-treatable' estimates from DRG Clarivate for all Ovarian, USC, CRC, Breast, Prostate and Pancreatic. For 'Other Cyclin-E1 driven solid tumors' used incidence reported by SEER and ECIS.
Cyclin E1 prevalence in platinum sensitive ovarian cancer derived from Petersen, et al CCNE1 and BRD4 co-amplification in high-grade serous ovarian cancer is associated with poor clinical outcomes, Gynecologic Oncology,Volume 157, Issue 2, 2020
Abbreviations: bRAF+ CRC: bRAF mutant Colorectal Cancer; HRD+: Homologous Recombinant Repair Deficiency; HGSOC: High Grade Serous Ovarian Cancer; 2L: Secon d Line
HRD+ Post PARPi tumor types: Prostate, Pancreas and Breast; Other Cyclin E+ Tumor Types include bladder, stomach, esophageal, lung squamous, lung adenocarcinoma, and breast cancer

Today's Conclusions: Great Progress in Advancing Azenosertib's Potential to Transform Cancer Care

Azenosertib monotherapy RP2D dose: 400 mg intermittent (5 days on, 2 days off a week; 5:2)

- Increased exposures with intermittent dosing led to an ORR of 36.8% in Ovarian Cancer and USC
- Strong safety profile: no treatment-related discontinuations
- Majority of patients remain on therapy; update in 2H23

Solid efficacy with multiple chemotherapy combinations

- Significant improvements in ORR and mPFS over chemotherapy alone or chemotherapy + adavosertib
- Opportunity to use Cyclin E+ as biomarker to identify patients who would benefit from azenosertib addition to chemo

Comprehensive Clinical Strategy

- All lines of therapy for ovarian cancer, both as a monotherapy and in combination with chemotherapy
- Post-pembro (≥2 L) therapy for USC
- Clinical trial timelines to be updated in 2H23

zentalis

Abbreviations: RP2D, recommended Phase 2 dose; ORR, confirmed objective response rate; HGSOC, High Grade Serous Ovarian Cancer; USC, Uterine Serous Carcinoma of the Endometrium; 2H23, second half of 2023; mPFS, media progression free survival

Our Thanks And Deepest Appreciation To All Patients, Caregivers, Families, And Investigators

zentalis

Question & Answer Session

Kimberly Blackwell, MD
Chief Executive Officer
Zentalis Pharmaceuticals

Carrie Brownstein, MD
Chief Medical Officer
Zentalis Pharmaceuticals

Funda Meric-Bernstam, MD
Chair of the Department of Investigational Cancer Therapeutics -- the Phase 1 Program at The University of Texas MD Anderson Cancer Center; Member, Zentalis Scientific. Advisory Board

Backup: Data Breakdown for ASCO Disclosures

N, ORR (%)	Azenosertib + Paclitaxel	Azenosertib + Carboplatin	Azenosertib + Gemcitabine	Azenosertib + PLD	Total
Efficacy Evaluable in Abstract*	9/18 (50.0)	9/27 (33.3)	2/14 (14.3)	5/35 (14.3)	25/94 (26.6)
Efficacy Evaluable ASCO Poster Data Cut**	11/26 (42.3)	10/29 (34.5)	5/18 (27.8)	6/35 (17.1)	32/104 (30.8)
Response Evaluable on ASCO Poster**	11/22 (50.0)	10/28 (35.7)	5/13 (38.5)	6/31 (19.4)	32/94 (34.0)

Definitions:

- **Efficacy evaluable:** received at least 1 dose of study drug, measurable disease at baseline
- **Response evaluable:** received at least one dose of study drug, measurable disease at baseline AND at least one follow-up scan

*Data Cut Off of January 17, 2023
**Data Cut Off of April 10, 2023
Reasons for 21 patients not being evaluable: No post-baseline scan yet (n=11); AE (n=4); Subject decision (n=4); Withdrawal of consent (n=1); Clinical progression (n=1)

zentalis