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): November 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 2.02 Results of Operations and Financial Condition.

On November 6, 2023, Zentalis Pharmaceuticals, Inc. (the “Company”) announced its financial results for the quarter ended September 30, 2023 and commented on certain business updates. The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K (this "Current Report") and is incorporated herein by reference.

Item 7.01 Regulation FD Disclosure.

Beginning on November 6, 2023, spokespersons of the Company plan to present the information in the Corporate Presentation furnished as Exhibit 99.2 to this Current Report and incorporated herein by reference at conferences and in meetings with investors and analysts.

The information in Items 2.02 and 7.01 of this Current Report (including Exhibits 99.1 and 99.2 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 Exchange Act or the Securities Act of 1933, as amended, whether made before or after the date hereof, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

The following exhibits relating to Items 2.02 and 7.01 shall be deemed to be furnished, and not filed:

ExhibitNo.	Description
99.1	Press Release issued on November 6, 2023
99.2	Corporate Presentation, dated November 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: November 6, 2023

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

Exhibit 99.1

Zentalis Pharmaceuticals Reports Third Quarter 2023 Financial Results and Operational Updates

Updated data from azenosertib monotherapy study with longer follow up shows 37% ORR and mPFS of 6.5 months in heavily pretreated ovarian and uterine serous carcinoma patients

Azenosertib programs on track for first NDA submission in a gynecologic malignancy in 2026

Sharing key clinical milestones through 2026 for azenosertib and ZN-d5

$517 million cash balance as of September 30, 2023, with projected cash runway into 2026

Chief Translational Officer, Mark Lackner, Ph.D., to succeed Co-Founder, Kevin Bunker, Ph.D., as Chief Scientific Officer

NEW YORK and SAN DIEGO — November 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 financial results for the quarter ended September 30, 2023, and highlighted recent corporate accomplishments.

“We are executing on our fast-to-market strategy for our potentially first-in-class and best-in-class WEE1 inhibitor, azenosertib, while also laying the groundwork for the franchise opportunity we see for azenosertib across multiple tumor types,” said Kimberly Blackwell, M.D., Chief Executive Officer of Zentalis. “Azenosertib continues to show very encouraging monotherapy anti-tumor activity, safety and tolerability in both ovarian cancer and uterine serous carcinoma. We are executing our clinical strategy to advance this high-potential asset to patients with ovarian cancer and uterine serous carcinoma as quickly as possible and expand into additional indications where WEE1 inhibition has the potential to improve outcomes for patients. By focusing our team and resources on the advancement of azenosertib, Zentalis is targeting the submission of the first NDA for azenosertib in a gynecologic malignancy in 2026.”

“This quarter we are also executing on our succession plan for Chief Scientific Officer, which will see our Chief Translational Officer, Mark Lackner, succeed our co-founder, Kevin Bunker, at the end of the year” said Dr. Blackwell. “Kevin’s passion for discovering promising oncology drugs is a cornerstone of our culture and led to four of our product candidates advancing into the clinic, including azenosertib. I want to thank Kevin for his immense contributions to Zentalis and to the cancer patients we serve.”

“Since joining Zentalis last year, Mark has put together a talented translational team and has spearheaded our biomarker enrichment strategies for azenosertib,” continued Dr. Blackwell. “Mark’s appointment as Chief Scientific Officer sees our translational and discovery efforts brought under a single umbrella, which puts us in a strong position as we continue to advance azenosertib through the clinic while supporting robust preclinical drug discovery efforts.”

Program Updates and Highlights

- **Azenosertib monotherapy program.** Today, the Company announced an updated analysis of the ongoing Phase 1 clinical trial of azenosertib as a monotherapy in solid tumors (ZN-c3-001), which continued to show anti-tumor activity with intermittent dosing. In the same population of 19 platinum resistant or refractory ovarian cancer and uterine serous carcinoma (USC) patients that were included in the data reported on June 6, 2023, the objective response rate (ORR) was 37%.

Median follow-up has increased by nearly 5 months and the median progression free survival (mPFS) has increased to 6.5 months. With additional safety-evaluable patients and follow-up since June, azenosertib continues to demonstrate a favorable safety and tolerability profile that is similar to or better than approved ovarian cancer products, supporting its continued advancement

- **Azenosertib development strategy.** Azenosertib is currently being evaluated in more than 10 ongoing and planned clinical trials as a monotherapy and in combinations with compelling scientific rationales across a broad array of tumor types. The Company is on track to submit its first New Drug Application (NDA) for azenosertib in a gynecologic malignancy in 2026. The Company has revised its strategy in platinum sensitive ovarian cancer (PSOC) and plans to evaluate azenosertib in PSOC in the first-line (1L) maintenance setting in the clinic. This strategy allows for the opportunity to benefit a larger segment of patients with ovarian cancer and fill a gap in the treatment paradigm since the standard of care in the 1L maintenance setting is evolving and fewer options are available. The Company plans to provide additional details on this trial in the second half of 2024, and anticipates initiating enrollment in 2025.

- **Presentation at the American Association for Cancer Research (AACR) Special Conference: Ovarian Cancer.** In October, the Company presented a poster presentation titled "Cyclin E1 Positive Staining Is Frequent and Independent of Prior Platinum Treatment in High Grade Serous Ovarian Cancer" at the AACR Special Conference: Ovarian Cancer in Boston. To review the data in more detail, click here.

- **ZN-d5 + azenosertib in relapsed or refractory acute myeloid leukemia (R/R AML).** Zentalis is the only company known to have both a WEE1 inhibitor, azenosertib, and a BCL-2 inhibitor, ZN-d5, in clinical development. The Company is evaluating the combination of these promising product candidates in a Phase 1/2 trial in heavily pretreated patients with R/R AML based on strong preclinical data demonstrating highly synergistic anti-leukemia activity of this combination. The Company updated guidance for sharing initial data from this trial to the second half of 2024.

- **ZN-d5 in relapsed or refractory light chain amyloidosis (R/R AL amyloidosis).** Dose escalation is complete in the Phase 1 trial of ZN-d5 as a monotherapy in R/R AL amyloidosis. A preliminary efficacy signal was observed in patients with R/R AL amyloidosis with a hematologic response rate of 40% in patients treated with at least 400 mg daily of ZN-d5. ZN-d5 was well tolerated with few treatment-related adverse events. The proposed monotherapy dose has been identified as 800 mg daily. The Company does not plan to develop ZN-d5 further for this indication in order to focus its resources on the azenosertib franchise opportunity, including the azenosertib + ZN-d5 combination.

Corporate Highlight

- Today, the Company announced that Mark Lackner, Ph.D., Chief Translational Officer, Head of Biomarker Strategy, will succeed co-founder, Kevin Bunker, Ph.D., as Chief Scientific Officer at the end of the year. Dr. Bunker will continue his service to the Company as an advisor following the transition. Dr. Lackner joined Zentalis in October 2022. Prior to Zentalis, Dr. Lackner served as Senior Vice President, Head of Biology and Translational Sciences at IDEAYA Biosciences, where he successfully led biology efforts contributing to three small molecule development candidates and established a strong translational team that led to the discovery of a novel combination biomarker strategy. Previously, Dr. Lackner worked at Genentech for over a decade, holding multiple roles of increasing responsibility that culminated in serving as the Head of Genentech Oncology Early Stage Biomarker Group. During this tenure, he led multiple

research teams in developing and incorporating predictive biomarker strategies across all phases of clinical trials and managed a diverse biomarker portfolio spanning targeted therapies, immuno-oncology agents and antibody drug conjugates.

Anticipated Upcoming Milestones

- 1H 2024
  - Final results of Phase 1 azenosertib + chemotherapy (gemcitabine) trial in osteosarcoma (ZN-c3-003)
- 2H 2024
  - Final results of Phase 1b azenosertib monotherapy trial in solid tumors (ZN-c3-001)
  - Topline data from Phase 1/2 azenosertib + PARP inhibitor (niraparib) and azenosertib monotherapy trial in platinum resistant ovarian cancer in partnership with GSK (MAMMOTH, ZN-c3-006)
  - Initial data from Phase 1 azenosertib + BEACON regimen (encorafenib + cetuximab) trial in BRAF mutant metastatic colorectal cancer in partnership with Pfizer (ZN-c3-016)
  - Initial data from Phase 1 of azenosertib + ZN-d5 trial in R/R AML (ZN-d5-004C)
  - Additional details on planned clinical trial of azenosertib in PSOC in the 1L maintenance setting
- 1H 2025
  - Topline data from Phase 2 azenosertib monotherapy trial in platinum resistant high-grade serous ovarian cancer (DENALI, ZN-c3-005)
- 2H 2025
  - Topline data from Phase 2 azenosertib monotherapy trial in recurrent or persistent USC (TETON, ZN-c3-004)
- 2025
  - Initiate clinical trial of azenosertib in PSOC in the 1L maintenance setting.
- 2026
  - First NDA for azenosertib in a gynecologic malignancy

Third Quarter 2023 Financial Results

- **Cash and Marketable Securities Position**: As of September 30, 2023, Zentalis had cash, cash equivalents and marketable securities of $516.6 million. The Company believes that its existing cash, cash equivalents and marketable securities as of September 30, 2023 will be sufficient to fund its operating expenses and capital expenditure requirements into 2026.

- **Research and Development Expenses**: Research and development (R&D) expenses for the quarter ended September 30, 2023 were $46.8 million, compared to $42.2 million for the quarter ended September 30, 2022. The increase of $4.6 million was primarily attributable to $3.2 million of costs shared with Zentera in the prior period, a $2.6 million increase related to personnel expenses, of which $1.4 million related to non-cash stock-based compensation expense, and $0.8 million related to consulting costs. These increases were partially offset by decreases of $1.3 million and $0.7 million in facility expenses and clinical expenses, respectively.

- **General and Administrative Expenses:** General and administrative (G&A) expenses for the quarter ended September 30, 2023 were $16.0 million, compared to $12.0 million during the quarter ended September 30, 2022. This increase of $4.0 million was primarily attributable to a $2.9 million increase in personnel expenses, of which $2.2 million related to non-cash stock-based compensation expense, and a $1.1 million increase related to facilities and outside services.

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 clinically differentiated small molecule therapeutics targeting fundamental biological pathways of cancers. The Company's lead product candidate, azenosertib (ZN-c3), is a potentially first-in-class and best-in-class WEE1 inhibitor for advanced solid tumors and hematologic malignancies. Azenosertib is being evaluated as a monotherapy and in combination across multiple clinical trials and has broad franchise potential. In clinical trials, azenosertib has been well tolerated and has demonstrated anti-tumor activity as a single agent across multiple tumor types and in combination with several chemotherapy backbones. As part of its azenosertib clinical development program, the Company is exploring enrichment strategies targeting tumors of high genomic instability, such as Cyclin E1 positive tumors and homologous recombination deficient tumors. 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 X/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 the potential for azenosertib to be first-in-class and best-in-class; the potential for the Company to execute on its fast-to-market strategy for azenosertib; the potential to build a meaningful franchise around azenosertib; opportunities with azenosertib across multiple tumor types; our plans to submit an NDA for azenosertib in a gynecologic malignancy and the timing thereof; our plans to evaluate azenosertib in PSOC in the 1L maintenance setting in the clinic, and the timing thereof; the potential for azenosertib to benefit a larger segment of patients with ovarian cancer and fill a gap in the treatment paradigm; our plans with respect to the development of our product candidates, including azenosertib and ZN-d5; our plans and timing for the initiation of and the release of data from our clinical trials and our ability to meet other key milestones; the potential benefits of azenosertib, including the potential benefits of the design thereof, the value potential of the asset, and the potential to improve outcomes for patients; our plans to execute on a succession plan for our Chief Scientific Officer; and the Company's cash runway. The terms "anticipate," "believe," "continue," "designed," "milestone," "on track," "opportunity," "plan," "potential," "projected," "promising," "strategy," "support," "target," "to," "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; our substantial dependence on the success of our 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; 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.

Contact:

Katie Beach Oltsik
Evoke Canale
Katherine.Beach@evokegroup.com

Zentalis Pharmaceuticals, Inc.
Condensed Consolidated Statements of Operations
(Unaudited)
(In thousands, except per share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Operating Expenses				
Research and development	$ 46,765	$ 42,181	$ 138,033	$ 132,118
Acquired in-process research and development	—	—	45,568	—
General and administrative	15,953	12,012	47,986	43,415
Total operating expenses	62,718	54,193	231,587	175,533
Operating loss	(62,718)	(54,193)	(231,587)	(175,533)
Other Income (Expense)				
Investment and other income, net	7,209	1,905	15,769	2,755
Net loss before income taxes	(55,509)	(52,288)	(215,818)	(172,778)
Income tax expense (benefit)	31	(159)	(466)	(109)
Loss on equity method investment	—	2,371	16,014	9,460
Net loss	(55,540)	(54,500)	(231,366)	(182,129)
Net loss attributable to noncontrolling interests	(12)	(99)	(92)	(294)
Net loss attributable to Zentalis	$ (55,528)	$ (54,401)	$ (231,274)	$ (181,835)
Net loss per share outstanding, basic and diluted	$ (0.79)	$ (0.96)	$ (3.64)	$ (3.56)
Common shares used in computing net loss per share, basic and diluted	70,612	56,807	63,601	51,098

Zentalis Pharmaceuticals, Inc.
Selected Condensed Consolidated Balance Sheet Data
(Unaudited)
(In thousands)

	As of September 30, 2023	As of December 31, 2022
Cash, cash equivalents and marketable securities	$ 516,637	$ 437,371
Working capital [1]	469,346	395,286
Total assets	585,715	539,310
Total liabilities	103,818	105,286
Total Zentalis equity	$ 481,897	$ 434,024

[1] The Company defines working capital as current assets less current liabilities.

Exhibit 99.2

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Corporate Presentation

November 2023

Nasdaq: ZNTL

Forward Looking Statements and Disclaimer

Zentalis Pharmaceuticals, Inc. ("we," "us," "our," "Zentalis" or the "Company") cautions that this presentation (including oral commentary that accompanies this presentation) contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding potential for azenosertib (ZN-c3) to be first-in-class and best-in-class; the franchise potential of azenosertib; the potential applicability of azenosertib to a broad array of tumor types, including in combination with molecularly targeted agents; the potential timing of filing our first New Drug Application for azenosertib; potential for azenosertib to have real impact for patients; our positioning to execute; our projected cash runway; our development approach for our product candidates; planned clinical trials for our product candidates, including our strategy with respect to azenosertib in platinum sensitive ovarian cancer; the potential that we are generating registrational data; the potential of azenosertib to address large unmet need across a broad array of tumor types; the potential for studies to be registrational; potential paths to registration; the potential and suitability of azenosertib to address tumors with high genomic instability; the opportunity for azenosertib in first-line maintenance in homologous repair proficient platinum sensitive ovarian cancer; the opportunity for a monotherapy approval of azenosertib in platinum resistant ovarian cancer; our strategy for azenosertib development, including in platinum sensitive ovarian cancer; the potential for azenosertib to provide prolonged benefit for the greatest number of ovarian cancer patients in the first-line maintenance setting; the potential for CCNE1 amplification and Cyclin E1 IHC as potential patient enrichment strategies; the opportunity to address unmet need in relapsed or refractory acute myeloid leukemia by combining azenosertib and ZN-d5; building the azenosertib franchise, including that the franchise opportunity for azenosertib more than doubles as it expands beyond gynecologic malignancies; the potential unmet need in a particular indication and/or patient population; potential for generating datasets with value-creating potential; potential for combinations including our product candidates and the potential benefits thereof; our potential positioning for success with the azenosertib franchise; the potential benefits of the designs of our product candidates; the target profiles and potential benefits of our product candidates and their mechanisms of action, including as a monotherapy and/or in combination; the market opportunities for and market potential of our product candidates, including the number of potential patients per year; the timing and content of our anticipated milestones, including the timing of initiation of clinical trials and disclosure of clinical data, as well as statements that include the words such as "anticipate," "building," "estimate," "expect," "may," "milestone," "opportunity," "plan," "positioned," "potential," "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.

Advancing Azenosertib

First-in-class WEE1 Inhibitor with Broad Franchise Potential

Highly Specific Agent Targeting WEE1

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

Real Impact for Patients

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

Blockbuster Opportunity

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

Positioned to Execute

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

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

Building Azenosertib Franchise in Gynecologic Cancers and Beyond

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

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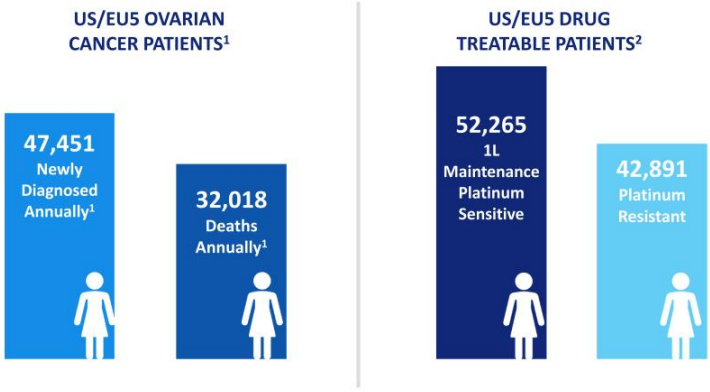
Ovarian Cancer is the Leading Cause of Death Across Gynecologic Cancers and Remains a Significant Unmet Need

New therapeutic strategies are needed

- Approximately 80% of women with advanced stage disease who respond to first-line chemotherapy will relapse[3]
- Single agent chemotherapy response for heavily pretreated platinum resistant/refractory ovarian cancer is 10-15%[3]

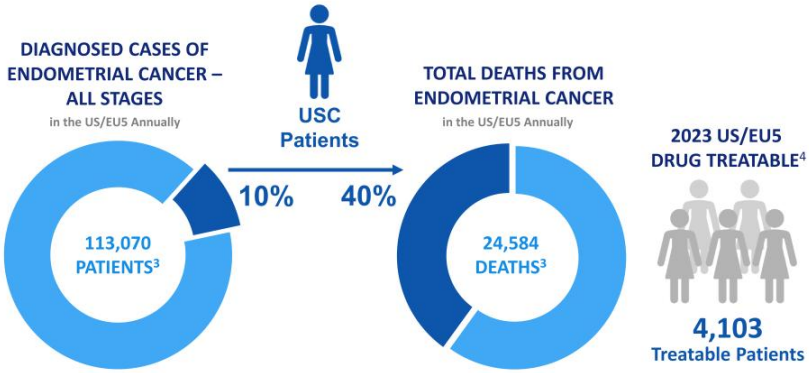


1 American Cancer Society Ovarian Cancer Key Statistics 2023, ECIS and SEER 2023; 2 Figures represent Company estimates of U.S. patients in 2023 with conditions covered by the Company's targeted indications and are dependent upon regulatory approvals; Source: IQVIA, DRG Clarivate, Kantar Health; 3 NCI Int J Gynaecol Obstet. 2021 Oct; 155(Suppl 1): 61–85. Abbreviation: 1L, first line

Uterine Serous Carcinoma Represents High Unmet Medical Need

Uterine Serous Carcinoma Comprises 10% of Endometrial Cancer But is the Subgroup with the Highest Mortality

- Uterine serous carcinoma (USC), a subtype of endometrial cancer, represents approximately **10% of all endometrial cases**[1]
- USC accounts for nearly **40% of all endometrial cancer-related deaths**[1]
- Chemotherapy resistant with single agent **chemotherapy response rate of ~15%** in heavily pretreated patients[2]



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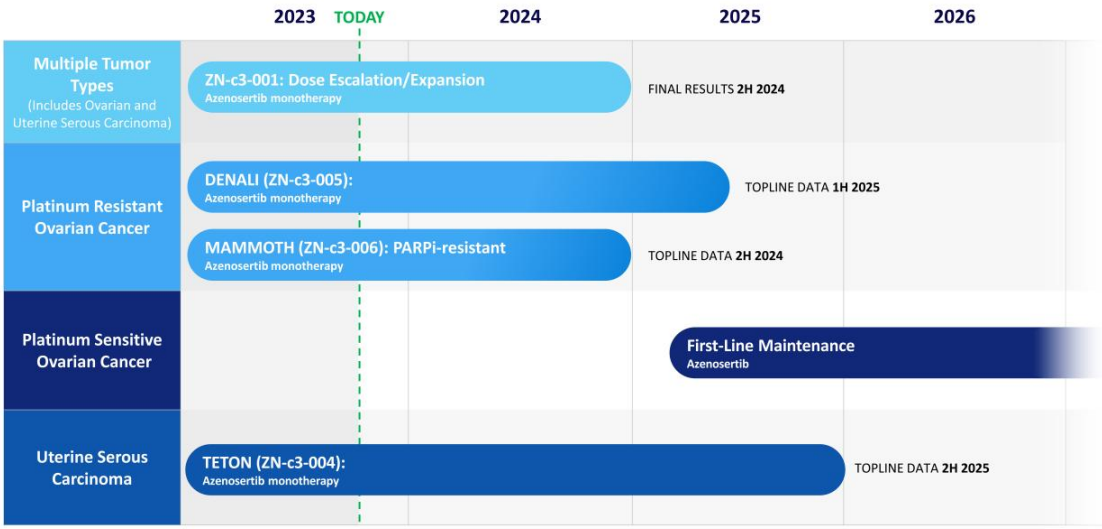
1 Monk B, et al. Gynecologic Oncology 2022;164:325-332; 2 Ferriss JS, et al. International Journal of Gynecologic Cancer 2021;31:1165-1174; 3 American Cancer Society Ovarian Cancer Key Statistics 2023 ECIS and SEER 2023;
4 Figures represent Company estimates of U.S. patients with conditions covered by the Company's targeted indications and are dependent upon regulatory approvals; Source: IQVIA, DRG Clarivate, Kantar Health

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



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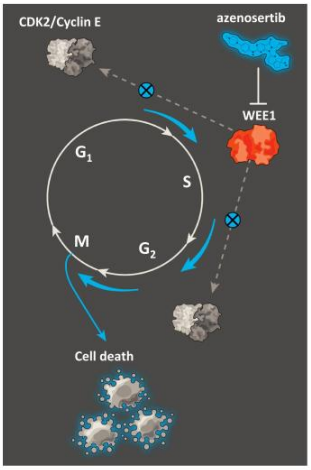
Abbreviations: 1H, first half; 2H, second half

Azenosertib's Mechanism of Action Causes Accumulation of DNA Damage Leading to Cancer Cell Death

- Azenosertib **dephosphorylates CDK1 and CDK2** which abrogates G1-S and G2-M cell cycle checkpoints, accelerating cell cycling[1]
- **Acceleration of cell cycling** does not allow for adequate DNA repair[1,2]
- **DNA damage** increases and accumulates[1,2]
- Cancer cell undergoes **mitotic catastrophe**[1,2]

Clinically active as a single agent in tumors with high genomic instability, such as ovarian and uterine serous carcinoma



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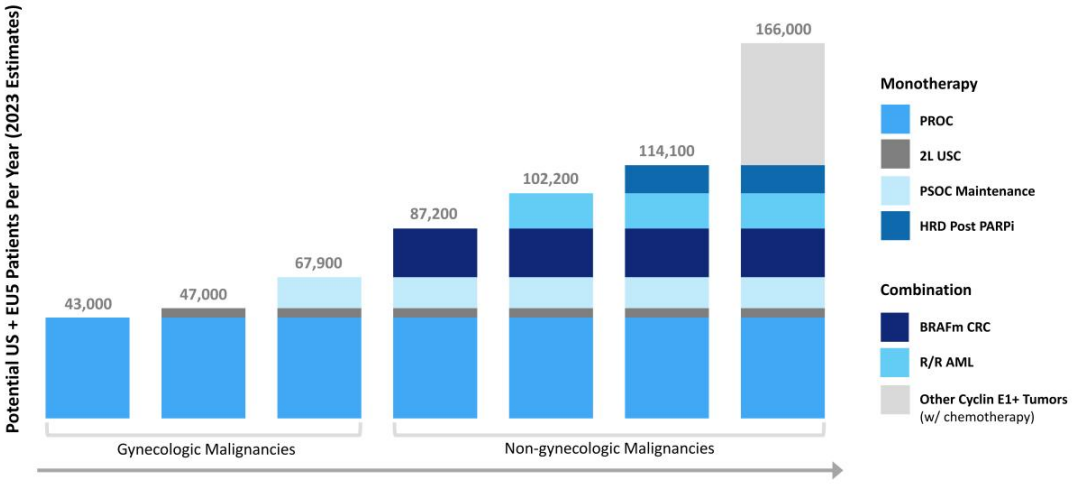
1 Ghelli Luserna di Rorà A, et al. J Hematol Oncol 2020;13:126; 2 Elbæk CR, et al. Cell Rep 2022

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



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

Azenosertib Monotherapy Updated Results

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

Longer Follow Up Improves Duration of Benefit

Strong Safety and Tolerability of Azenosertib Monotherapy

CORPORATE CALL
June 6, 2023

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

UPDATED DATA
Nov 6, 2023

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

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

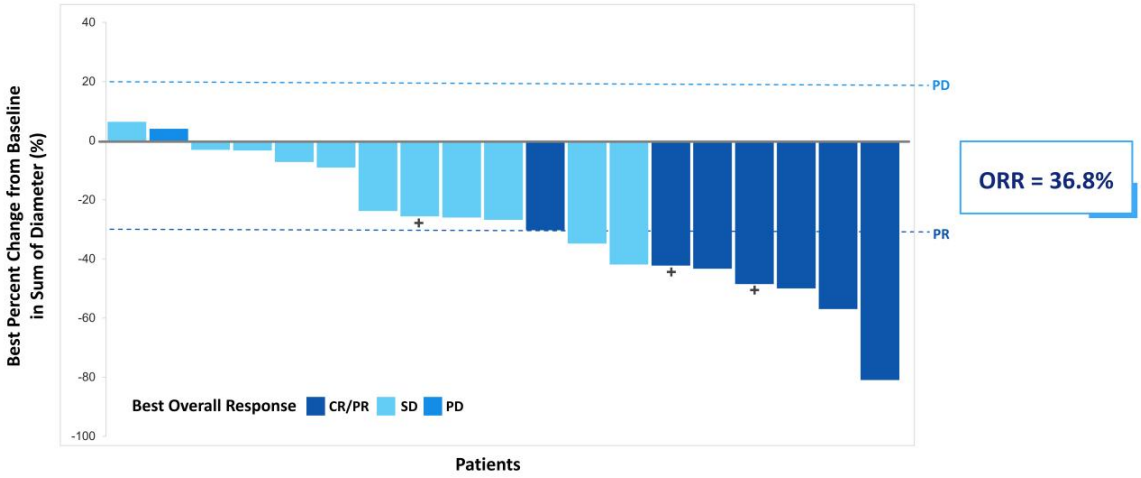
Intermittent Monotherapy Patient Population Was Heavily Pretreated and Treatment Refractory

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

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

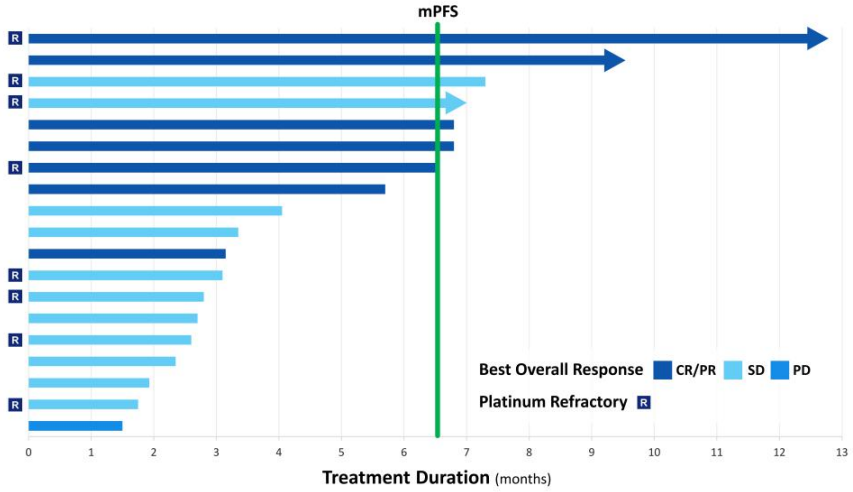
Monotherapy Azenosertib Results in a 37% Confirmed Response Rate

In Both Platinum Resistant Ovarian Cancer and Uterine Serous Carcinoma



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

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



mPFS of 6.5 months

Median follow up of 9.2 months, compared to 4.4 months as of June 2

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

Data cut-off: October 25, 2023

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

Treatment Related AEs, n (%)

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

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

No cases of febrile neutropenia or sepsis

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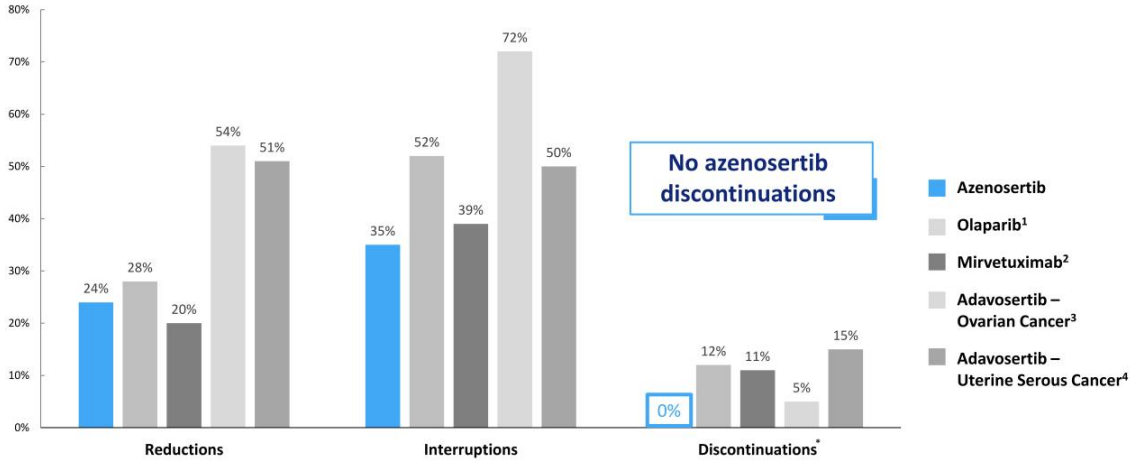
*Safety Evaluable Population (All tumor types; n=46) as of Sept 27, 2023 versus n=27 reported on June 6, 2023 corporate call: Received at least one dose of drug; Intermittent 350 5:2 and 400 5:2; Treatment Related AEs > 10% for entire trial and treatment related AEs of interest. Abbreviations: AE, adverse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

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



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

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

Monotherapy Conclusions

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

MONOTHERAPY EFFICACY
37% confirmed ORR

IMPROVED mPFS of 6.5 MONTHS
With longer follow-up

EXCELLENT TOLERABILITY & SAFETY
Consistent or better than other available agents

DEFINITIVE DATA
Supports differentiation from other clinical WEE1 inhibitors

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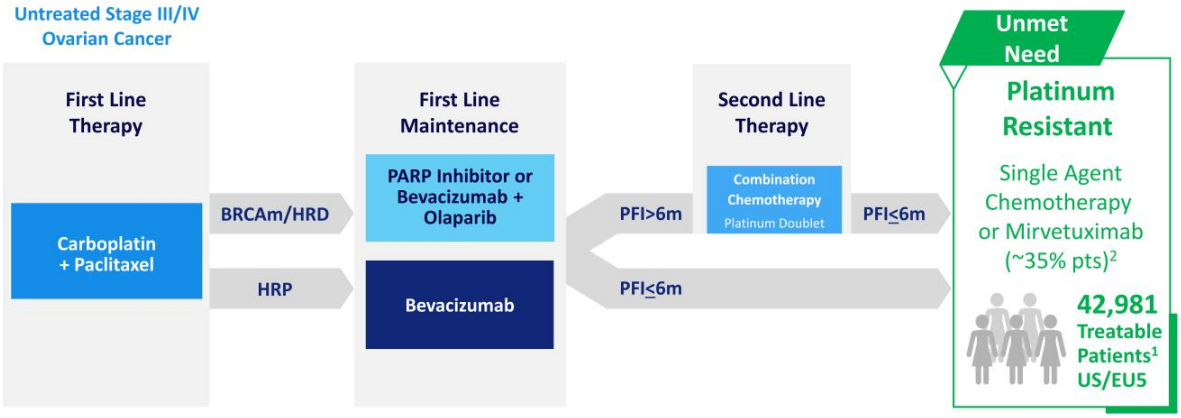
Abbreviations: ORR, objective response rate; mPFS, median progression free survival; Comparisons to other agents are not head-to-head.

Multiple Ongoing Phase 2 Trials of Azenosertib

Potential Paths to Registration in Ovarian Cancer and Uterine Serous Carcinoma

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



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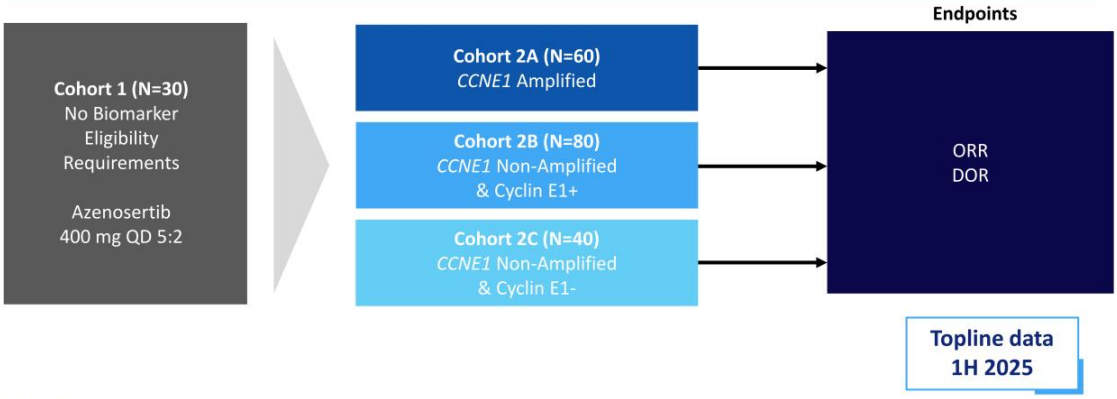
1 Figures represent Company estimates of U.S. and EU5 patients with conditions covered by the Company's targeted indications; Source: IQVIA, DRG Clarivate;
2 Matulonis U. JCO 2023 41:13:2436-2445; Abbreviations: BRCAm, BRCA mutant; HRD, homologous-recombination repair deficient; HRP, homologous-recombination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

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

CURRENTLY ACCRUING

Key Eligibility: 1-5 prior lines of therapy in Cohort 1 (1-4 prior lines in Cohort 2)



Topline data 1H 2025

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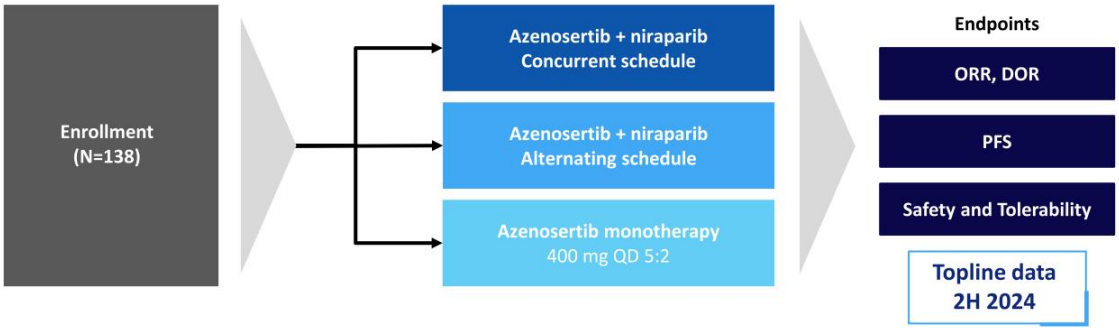
Abbreviations: QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; DOR, Duration of Response; 1H, first half

NCT05128825

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

CURRENTLY ACCRUING

Key Eligibility: 1-5 prior lines of therapy; platinum-resistant, progressed while receiving an approved PARP inhibitor



NCT05198804

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Abbreviations: PARP, poly-ADP ribose polymerase; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate DOR, duration of response; PFS, progression free survival; 2H, second half

New Treatment Options Needed in 2L+ Uterine Serous Carcinoma

Stage IV
or Recurrent USC

1L Carboplatin + Paclitaxel +
Pembrolizumab/Dostarlimab

Unmet Need

2L+ Single-Agent
Chemotherapy

4,103
Treatable
Patients[1]
US/EU5

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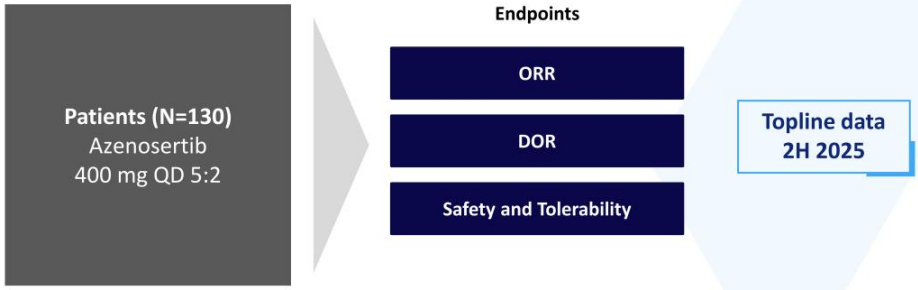
1 Figures represent Company estimates of U.S. patients with conditions covered by the Company's targeted indications and are dependent upon regulatory approvals; Source: IQVIA, DRG Clarivate, Kantar Health;
Abbreviations: 2L+, second line maintenance plus; USC, uterine serous carcinoma; 1L, first line

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

CURRENTLY ACCRUING - FDA Fast Track Designation

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



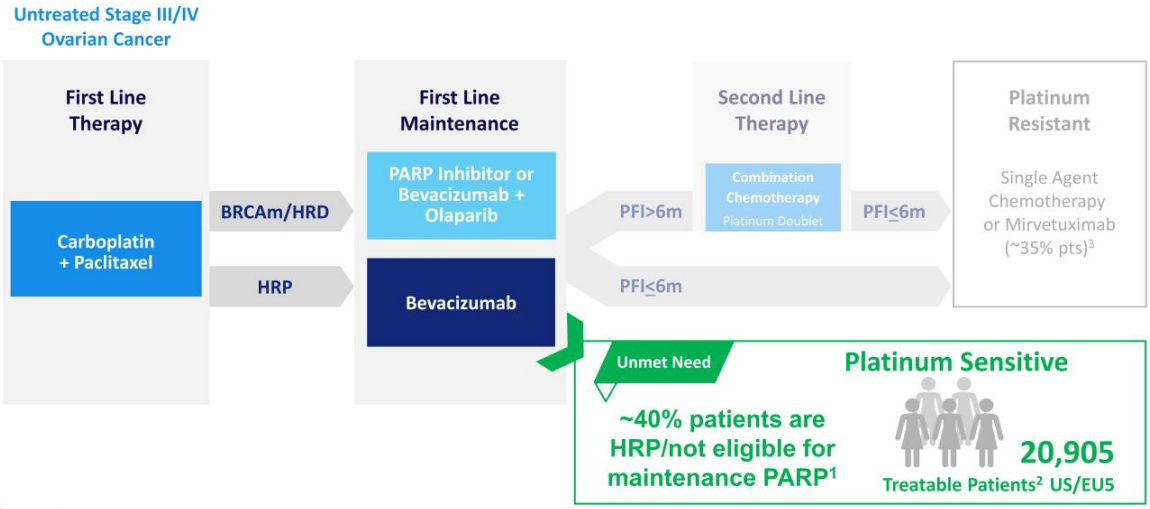
Abbreviations: 2L, two lines; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; ORR, objective response rate; DOR, duration of response; 2H, second half; The FDA granted Fast Track designation in November 2021 to azenosertib in patients with advanced or metastatic USC who have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

NCT04814108

Azenosertib in Platinum Sensitive Ovarian Cancer Revised Strategy

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

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



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

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

2x as **many patients**

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

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

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

40% of **1L maintenance patients**

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

Azenosertib uniquely positioned for success in maintenance setting

Oral non-chemotherapy agent
Clear global regulatory pathways

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

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

Additional trial details in 2H 2024

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

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

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

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

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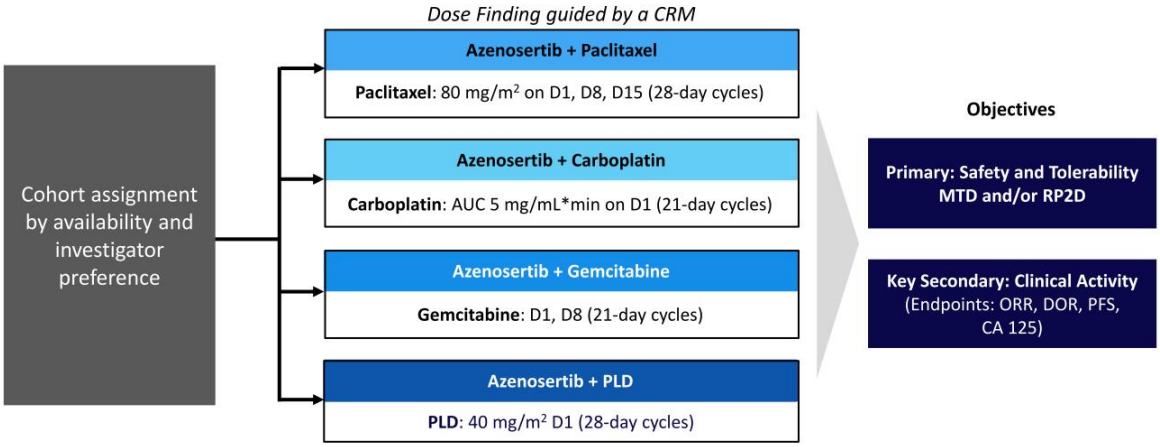
Azenosertib Combination with Chemotherapy

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

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

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



NCT04516447

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

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

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

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

Azenosertib* in Combination with Chemotherapy Demonstrates Favorable Safety Profile

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

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

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

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

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

Targeting Tumors with High Genomic Instability Using Azenosertib

Multiple Mechanisms Leading to Genomic Instability Enhance Sensitivity to Azenosertib

High Genomic Instability[1] Can be Caused By:

Cyclin E1+ Activation

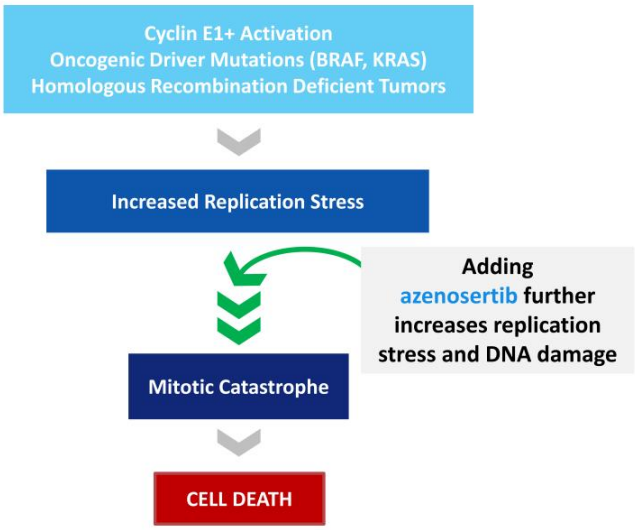
- Activation of Cyclin E1/CDK2 increases cell proliferation, resulting in higher replication stress and contributing to genomic instability

Tumors with Oncogenic Driver Mutations[2]

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

Homologous Recombination Deficient Tumors[3]

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



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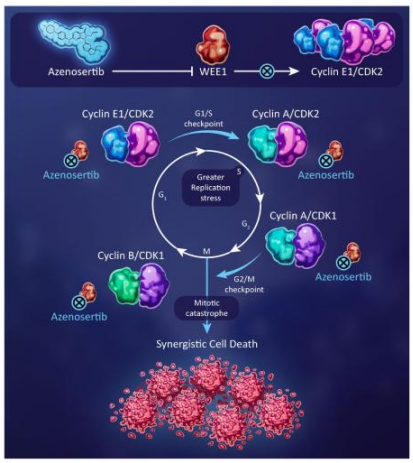
1 Fagundes R, et al. Front Cell Dev Biol. 2021; 2 Stewart MD, Oncologist. 2022; 3 Zhang, J, et al. Genes 2016; Abbreviations: BRAF, V-Raf Murine Sarcoma Viral Oncogene Homolog B; KRAS, Kirsten rat sarcoma viral oncogene homolog

Tumors with *CCNE1* Amplification or Cyclin E1 Positivity are Highly Sensitive to Azenosertib



Azenosertib Treated Cyclin E1^{high} Cancer Cell

- *CCNE1* gene amplification is a common oncogenic driver in many solid tumors, including high grade serous ovarian carcinomas[1]
- Both *CCNE1* gene amplification and protein expression have been associated with chemotherapy resistance and poor patient outcomes[2]
- Cyclin E1 overexpression, which can also occur in the absence of *CCNE1* gene amplification, increases CDK2 activity and accelerates G1/S transition[3, 4]
- Cyclin E1 overexpression results in replication stress and renders cells more dependent on the WEE1 G2/M cell cycle checkpoint[3, 4]

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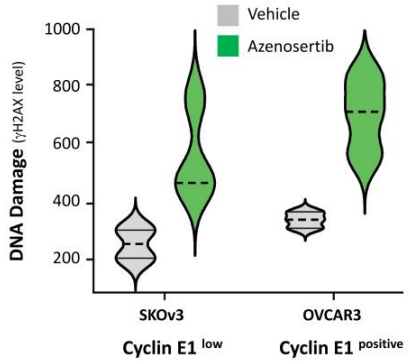
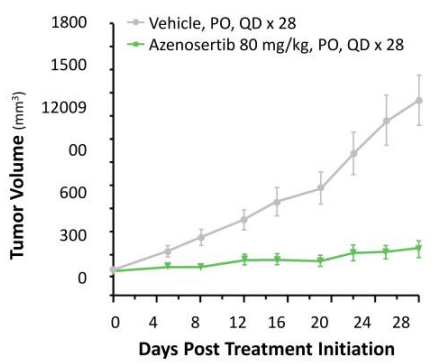
1 Etemadmoghadam D, et al. Proc Natl Acad Sci U S A. 2013; 2 Zhao H, et al. J Cancer. 2018; 3 Ma, et al. Cancer Res 2023 83 (7_Supplement): 2153; 4 Kok, YP et al. Oncogenesis 9, 88 2020

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



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



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

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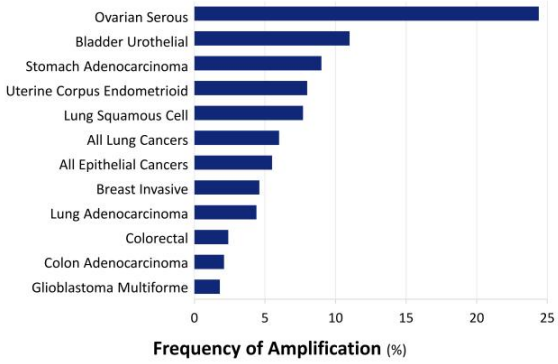
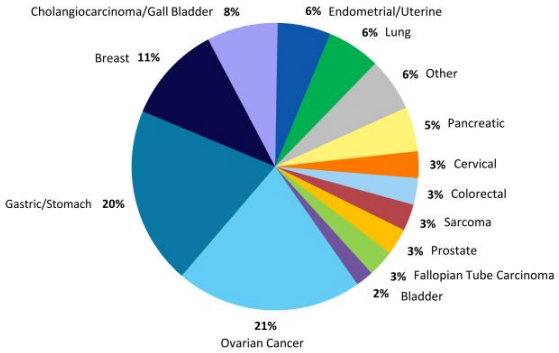
Ma, et al. Cancer Res (2023) 83 (7_Supplement): 2153; Abbreviations: PO, orally; QD, daily

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

TCGA Pan Cancer Analysis (6547 samples)[1]



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



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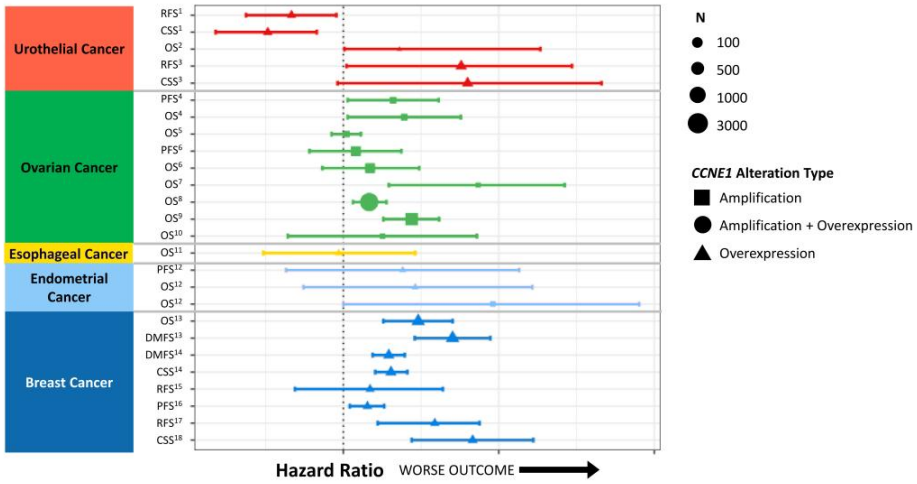
1 Etemadmoghadam D., et al. Proc Natl Acad Sci USA 2013; 2 Yao, S., et al. Sci Rep 12, 8701 2022

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

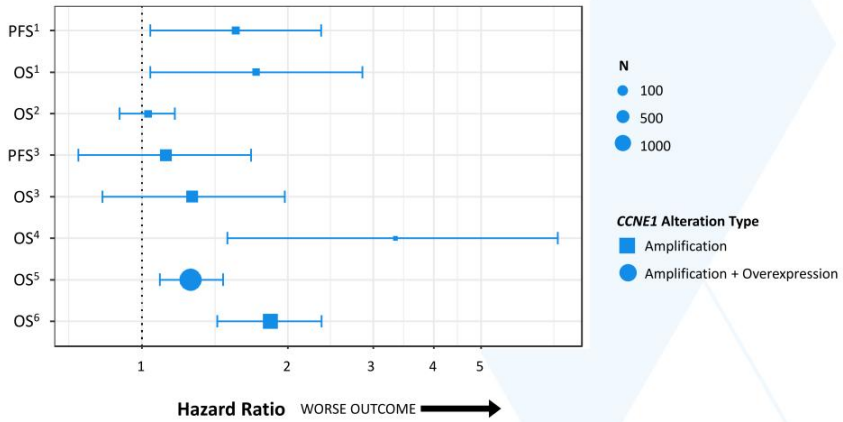


1 Shariat SF, et al. Human Path. 2006; 2 Matsushita R, et al. British J Cancer 2015; 3 Lotan Y, et al. Euro Assoc Urology 2013; 4 Stronach E, et al. Mol Cancer Res 2018; 5 Pils D, et al. Euro J Cancer 2014;
6 Petersen S, et al. Gynecol Oncol 2020; 7 Nakayama N, et al. Cancer 2010; 8 Kang E, et al. Cancer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

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

6 Studies; n=5,404

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



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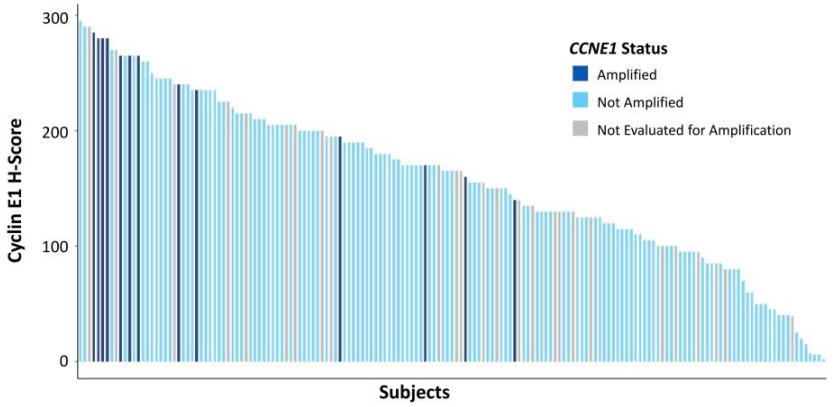
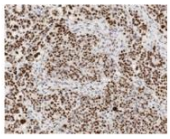
1 Stronach, et al. Mol Cancer Res 2018;16:1103-11; 2 Pils, et al. Eur J Cancer 2014;50:99-110; 3 Peterson, et al. Gynecol Oncol 2020;157:405-10; 3 Nakayama, et al. Cancer 2010;116:2621-34; 5 Kang, et al. Cancer 2023;129:697-713; 6 Chan, et al. J Pathol Clin Res 2020;6:252-62; *Timing of tissue collection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

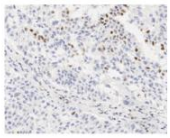
Analysis of Zentalis Clinical Trial Samples Confirms Cyclin E1 Protein Expression is High in the Majority of Ovarian Cancers



Cyclin E1⁺ by IHC



Cyclin E1⁻ by IHC



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

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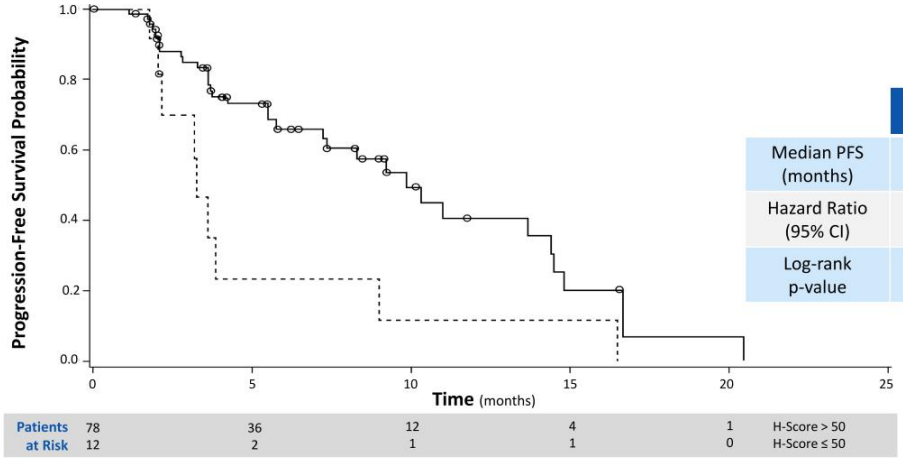
*H-scores calculated by multiplying the percentage of cells (0 to 100%) with intensity of Cyclin E1 expression (0 to 3).
Harismendy, et al. Presented at the AACR Special Conference in Cancer Research: Ovarian Cancer. October 5 - 7, 2023 - Boston, MA; Abbreviations: HGSOC, high-grade serous ovarian cancer;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

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



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

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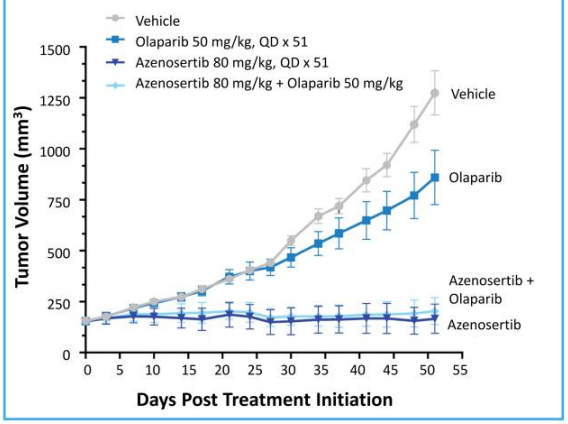
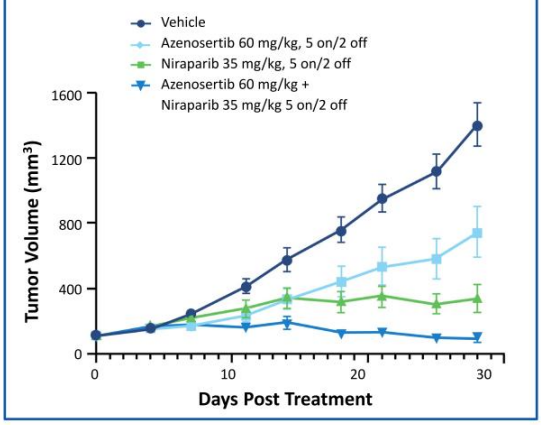
H-scores calculated by multiplying the percentage of cells (0 to 100%) with intensity of Cyclin E1 expression (0 to 3); Liu JF., et al. Journal of Clinical Oncology 41, no. 16_suppl (June 01, 2023) 5513-5513;
Abbreviations: CI, confidence interval; PFS, progression free survival

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

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



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



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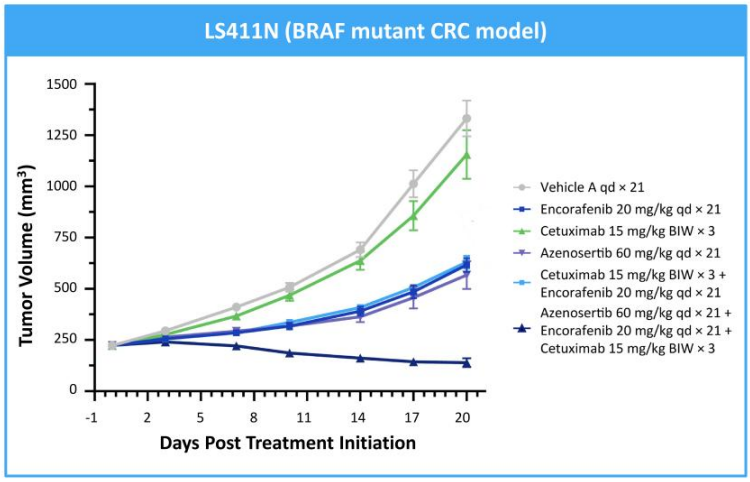
Zentalis data on file; Abbreviations: PARP, poly-ADP ribose polymperase; HRD, homologous recombination repair deficient; PARPi, PARP inhibitor; CDX, cell line derived xenograft; PDX, patient derived xenograft; TNBC, triple-negative breast cancer

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



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

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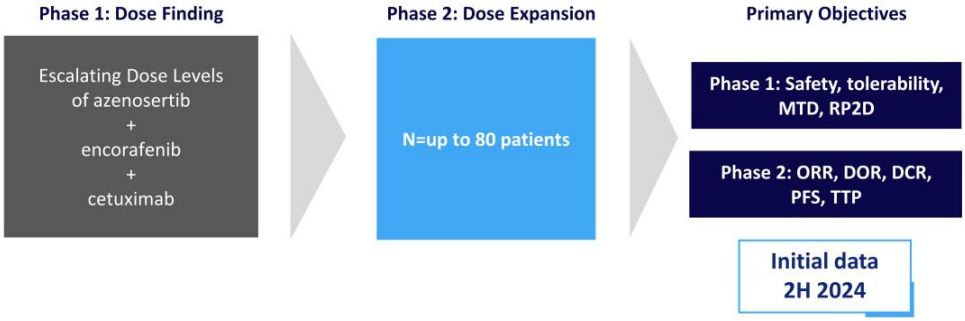
Zentalis Data on File; 1. Kotsantis P, et al. Cancer Discov. 2018. Abbreviations: BRAF, V-Raf Murine Sarcoma Viral Oncogene Homolog B; CRC, colorectal cancer; EGFR, epidermal growth factor receptor

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

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



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

NCT05743036

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

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

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

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

2 Azenosertib has monotherapy activity in multiple HRD models

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

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

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

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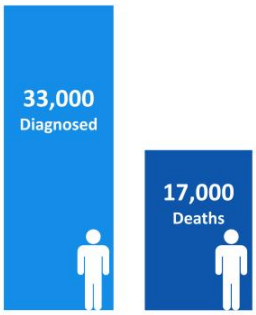
Abbreviations: IHC, immunohistochemistry; PARP, poly-ADP ribose polymerase; BRAF, V-Raf Murine Sarcoma Viral Oncogene Homolog B; EGFR, epidermal growth factor receptor; HRD, homologous recombination repair deficient

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

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

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

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



2023 US/EU5 Drug Treatable[2]

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

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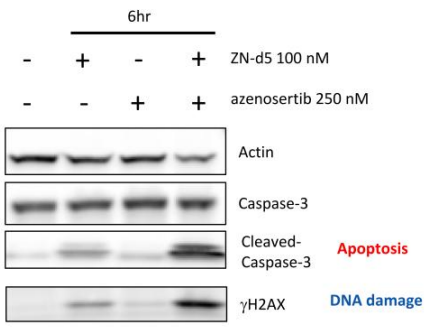
1. American Cancer Society. Cancer Facts & Figures 2023, SEER and ECIS. 2 Figures represent company best estimates based on US patients with conditions covered by the companies target indication. Sources DRG Clarivate, Kantar Health 3 Shimony, S, et al. Am J Hematol. 2023; 98(3): 502-526; 4 Maiti A,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

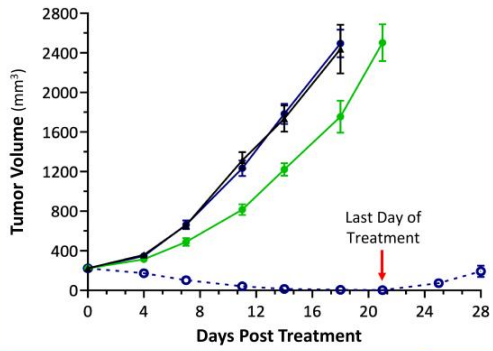
Combination of ZN-d5 and Azenosertib Results in Enhanced Apoptosis, DNA Damage and Synergistic Anti-Tumor Activity in an AML Model

HL-60 (in vitro)



Synergistic effects seen at sub-efficacious doses of both agents

HL-60 (in vitro)



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

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

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

Newly Diagnosed: Front Line → Maintenance → Relapsed/Refractory

Unmet Need

1st Relapse Chemo/SCT Ineligible: Without Actionable Mutation

~10,500
treatment eligible

2nd Relapse: After Mutation Directed Therapy

~4,500
treatment eligible

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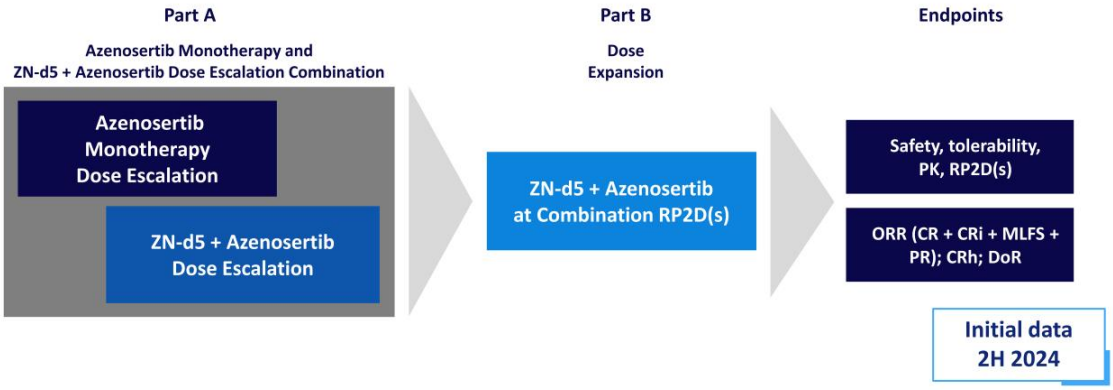
Adapted from Heuser, Y. et. Al. Annals of Oncology 31 (6) 697-712 2020; Abbreviations: AML, acute myeloid leukemia; SCT, stem cell transplant

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

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



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

Executing on the Franchise Potential of Azenosertib

2023 Milestones Achieved

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

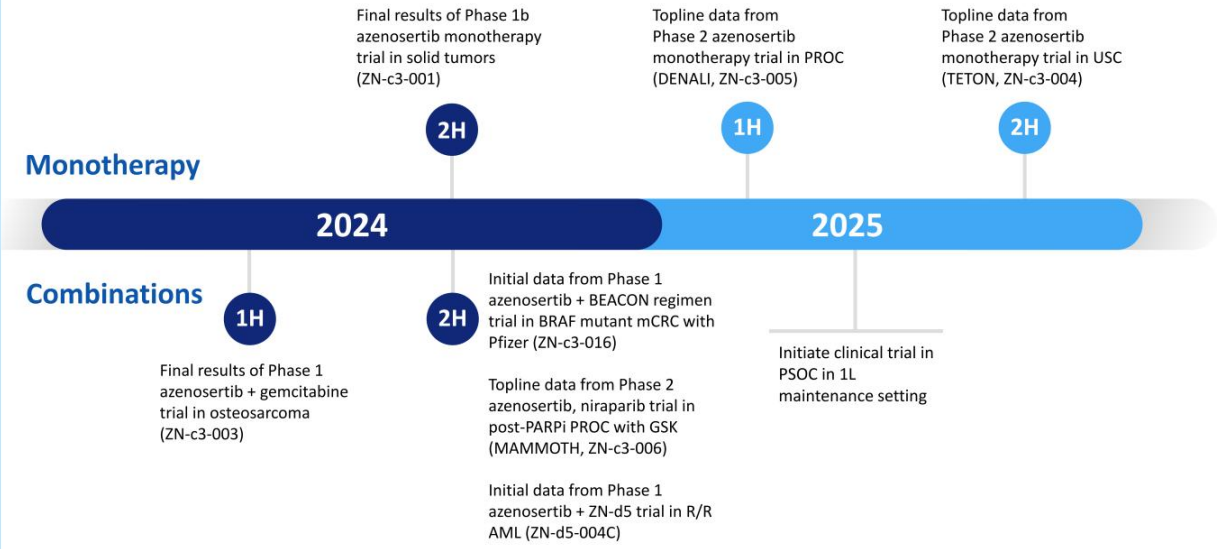
ZN-d5 BCL-2 Inhibitor

- ✓ 2H 2023 — Provide interim clinical data and declare RP2D for Phase 1/2 monotherapy trial in amyloidosis
- 2H 2023 Revised to 2H 2024 — Provide preliminary data from clinical trial of azenosertib + ZN-d5 in relapsed/refractory acute myeloid leukemia

Discovery

- ✓ 2023 — Advance ongoing research on protein degrader programs of undisclosed targets

Upcoming Clinical Milestones



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

Zentalis is Positioned for Success with Azenosertib Franchise

Potentially First- and Best-in-Class WEE1 Inhibitor

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

Clinical Strategy Supports Blockbuster Opportunity

- Planned trial as 1L maintenance in ovarian cancer offers potential to benefit greatest number of patients
- Expanding to a broad array of tumor types in combination with targeted agents

Multiple Near-Term Value Inflection Points

- Readouts from 3 Phase 2 trials over next 18-24 months in addition to other data updates
- Potential first NDA in 2026
- Supported by strong cash balance and runway into 2026

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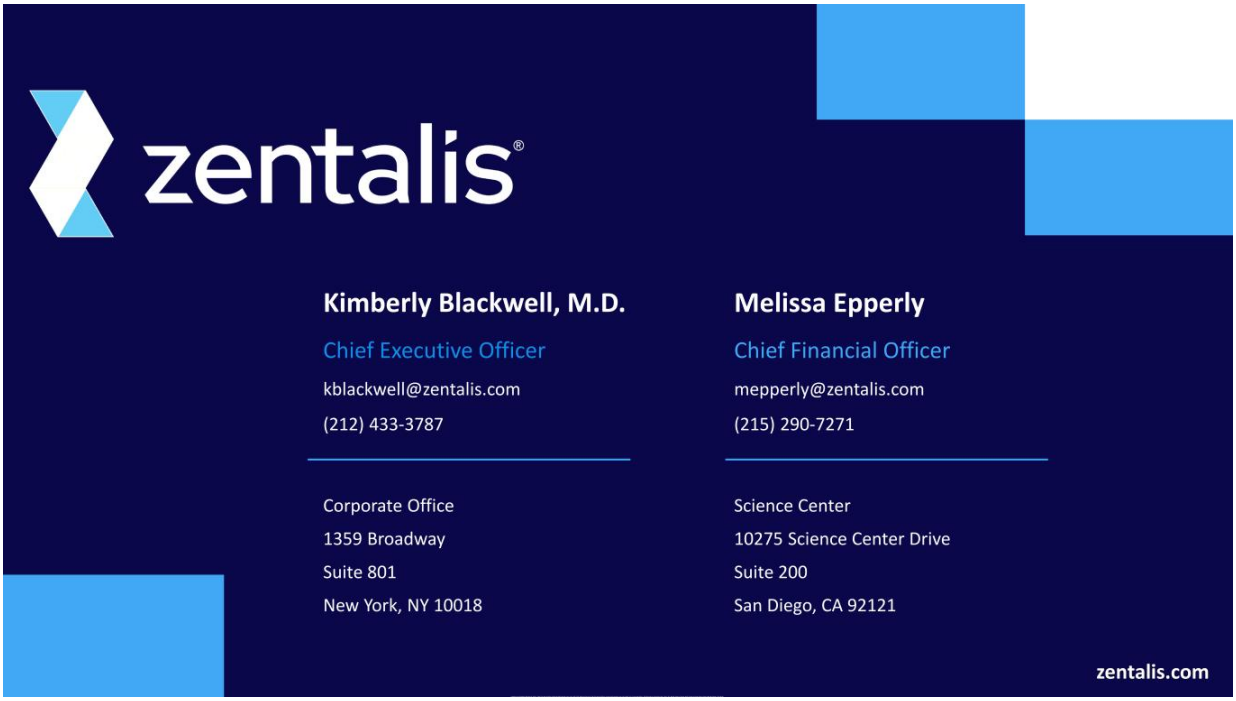
Abbreviations: mPFS: median progression free survival; ORR, objective response rate; mPFS, median progression free survival; USC, uterine serous carcinoma; 1L, first line NDA, New Drug Application; Statements comparing azenosertib to other agents, not head-to-head comparisons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