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Corporate Presentation

January 2025

Nasdaq: ZNTL

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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.

Building Azenosertib Franchise in Gynecologic Cancers and Beyond

		INDICATION	TRIAL NAME + DEVELOPMENT APPROACH	Phase 1	Phase 1b	Phase 2	Phase 3
Azenosertib WEE1 Inhibitor	GYNECOLOGIC MALIGNANCIES	Platinum Resistant Ovarian Cancer	**DENALI (ZN-c3-005)** Monotherapy				
		PARPi Resistant Ovarian Cancer	**MAMMOTH (ZN-c3-006)** Azenosertib monotherapy, or with niraparib				GSK
		Uterine Serous Carcinoma	**TETON (ZN-c3-004)** Monotherapy, FDA Fast Track Designation				
		Platinum Resistant Ovarian Cancer	**ZN-c3-002** Azenosertib + multiple chemo backbones				
		Solid Tumors	**ZN-c3-001** Monotherapy				
	OTHER TUMOR TYPES	BRAF Mutant Colorectal Cancer	**ZN-c3-016** Azenosertib + encorafenib and cetuximab		Pfizer		
		Osteosarcoma	**ZN-c3-003** Azenosertib + gemcitabine				

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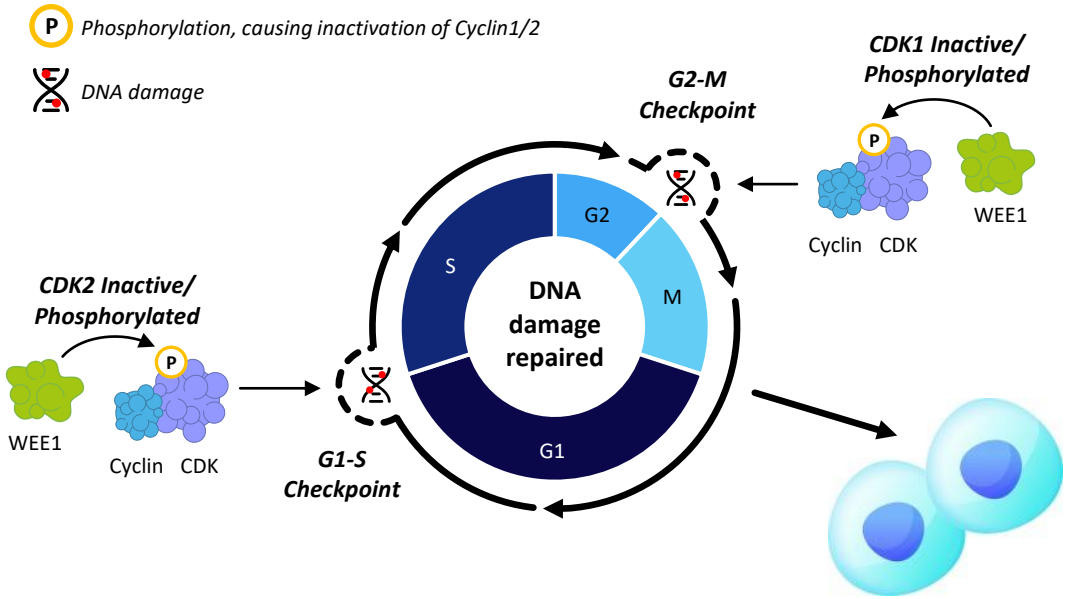
Azenosertib Mechanism of Action – Inhibitor of WEE1, Master Cell Cycle Regulator

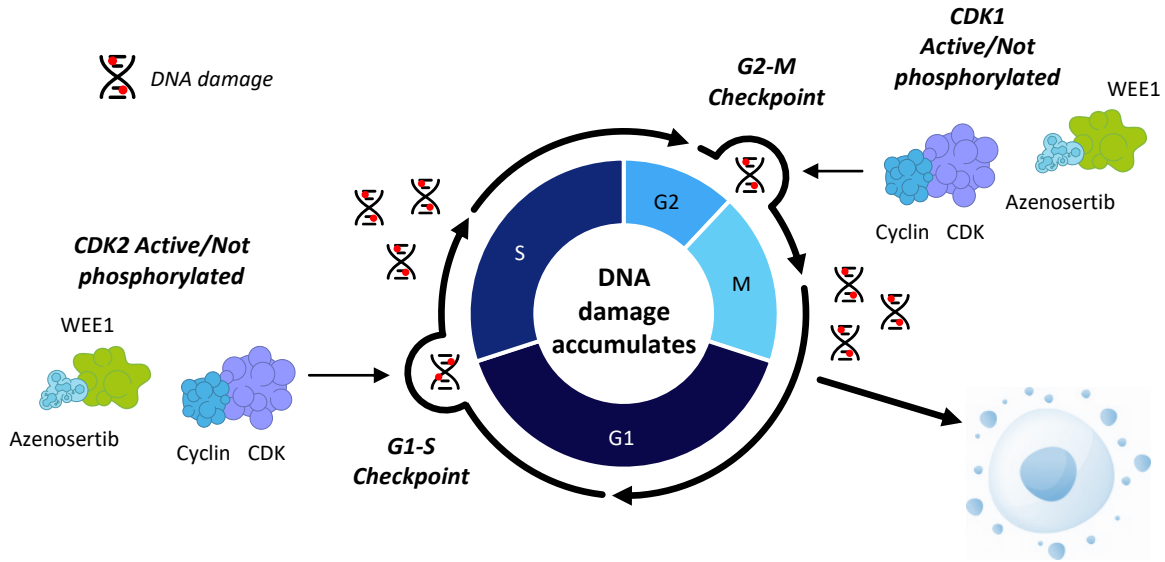
Normal Cell Cycle Regulation

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

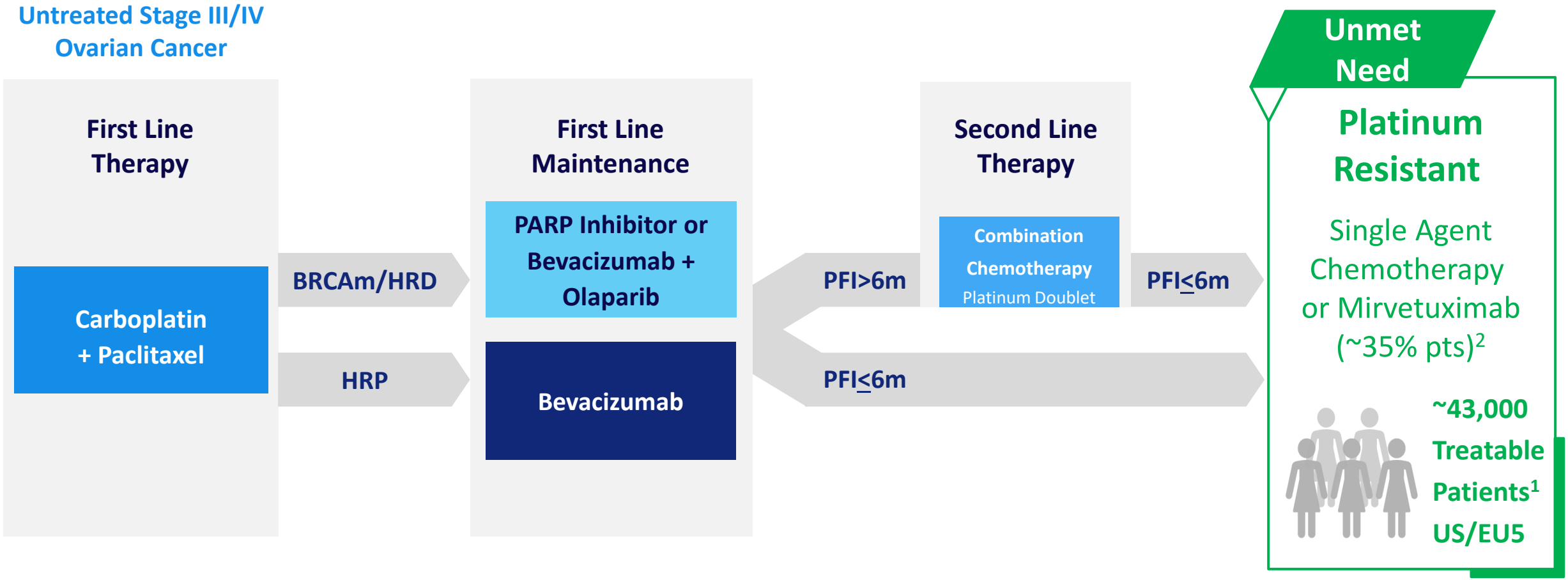


Cancer Cell and Azenosertib

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

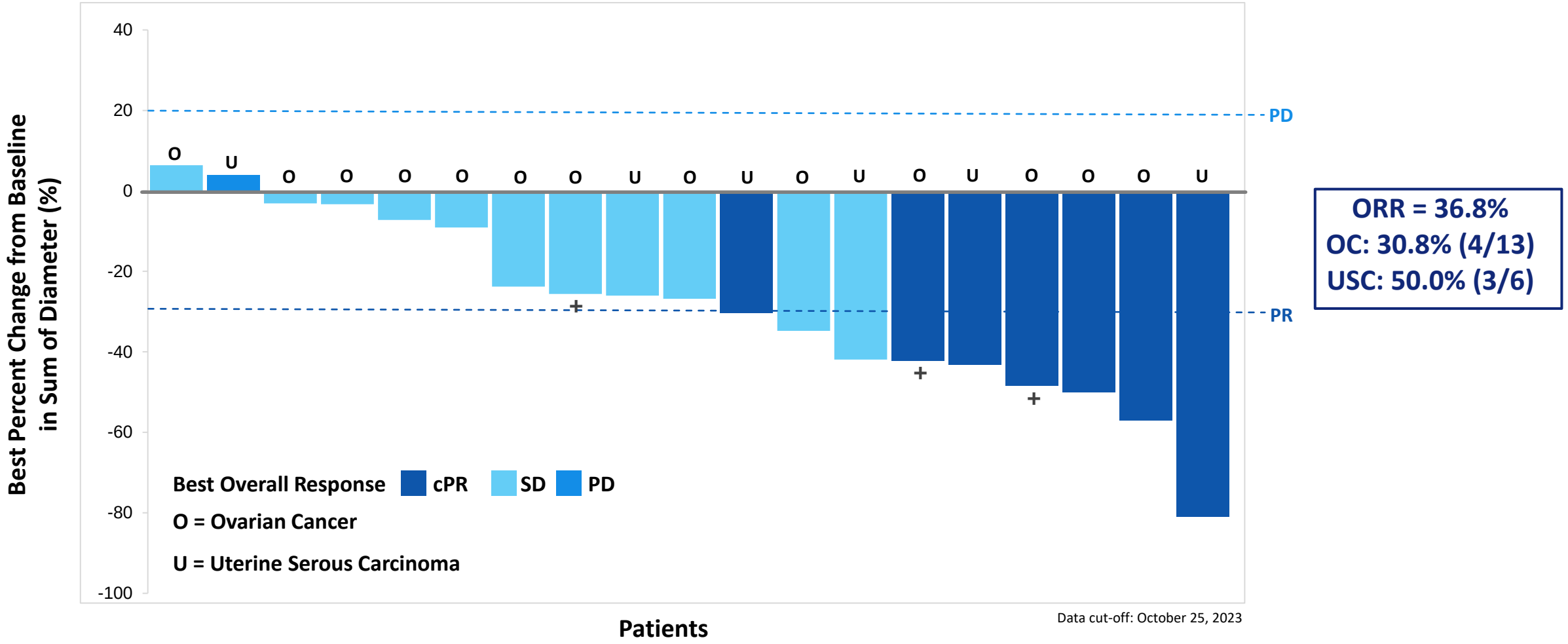


Platinum Resistant Ovarian Cancer: High Unmet Need Provides Opportunity for Azenosertib Monotherapy



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

Nov. 2023 Data Disclosure:
Objective Response Rate in Ovarian/USC Populations



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; cPR, confirmed partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate

Summary of Azenosertib Monotherapy Clinical Studies

Study ZN-c3-001

- Phase 1 dose-escalation monotherapy study in solid tumors
- **First site initiated:** 24 October 2019
- **Study sites:** 19 (US only)
- **Patients dosed:** 274
- **Status:** Fully enrolled
- **Results:** January 2025

Study ZN-c3-004: TETON

- Phase 2 monotherapy study in USC
- **First site initiated:** 8 July 2021
- **Study sites:** 54 (global)
- **Patients dosed:** 43 at continuous; 33 at intermittent
- **Status:** Recruiting
- **Results:** 1H26

Study ZN-c3-005: DENALI, Part 1b

- Phase 2 monotherapy study in PROC
- **First site initiated:** 5 December 2022
- **Study sites:** 58 (global)
- **Patients dosed:** 102
- **Status:** Fully enrolled; cohort 2 initiation paused
- **Results:** January 2025

Study ZN-c3-006: MAMMOTH

- Phase 1/2 monotherapy and niraparib combination study in PROC
- **First site initiated:** 8 December 2021
- **Study sites:** 22 (global)
- **Patients dosed:** 117 across all three cohorts
- **Status:** Fully enrolled
- **Results:** January 2025

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PROC, platinum-resistant ovarian cancer; USC, uterine serous carcinoma. Enrollment data is as of 17 June 2024

Recent Corporate Updates and Upcoming Disclosure

- Lifted partial clinical hold on azenosertib in Sep 2024
- Management and Board leadership changes in Nov 2024 to drive azeno to next stage of development
- Investor/Corporate and data update event in late January to discuss:
  - Ongoing review of existing data and clinical strategy
  - Monotherapy Data:
    - Topline results from 102 patients enrolled in Part 1b of the Phase 2 DENALI study of azenosertib monotherapy in platinum resistant high-grade serous ovarian cancer
    - Final results from patients treated at therapeutic doses in the Phase 1b ZN-c3-001 azenosertib monotherapy trial in solid tumors, including 69 PROC patients
    - Topline data from 61 patients in the monotherapy arm of the Phase 1/2 MAMMOTH trial of azenosertib as a monotherapy and in combination with PARP inhibitor (niraparib) in PARP-resistant PROC in partnership with GSK
  - Combination Data:
    - Initial data from Phase 1 ZN-c3-016 azenosertib + BEACON regimen (encorafenib + cetuximab) trial in BRAF mutant metastatic colorectal cancer in partnership with Pfizer
  - Design of registration-intent study
  - Corporate strategy and capital allocation

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