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Azenosertib Clinical Development Update

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Azenosertib Clinical Development Update

FDA has placed three clinical studies of azenosertib (ZN-c3-001, ZN-c3-004/TETON, and ZN-c3-005/DENALI) on a partial clinical hold following two drug-related Grade 5 events (deaths) which occurred in the first half of 2024, on the DENALI monotherapy study in platinum-resistant ovarian cancer (PROC).

- Patients on these studies may continue to receive azenosertib; enrollment of new patients is currently paused.
- Patient safety has always been Zentalis' top priority and will continue to be.
- Company is working with the FDA to resolve the partial hold as soon as possible to continue the monotherapy development of azenosertib.
- Today, we will review all treatment-related Grade 5 events that have occurred across our azenosertib development protocols.

Azenosertib has been in clinical development since 2019, with almost 800 patients having received the drug to date through multiple clinical studies. Zentalis continues to believe that, based on available safety and efficacy data, azenosertib has significant potential to benefit patients facing cancer.

ZN-c3-001, DENALI (Cohort 1b), and MAMMOTH (ZN-c3-006) have completed accrual, and results of these studies will be disclosed in the second half of 2024.

Summary of Monotherapy Azenosertib 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:** 2H24

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:** Patient accrual paused
- **Results:** 2H25

Study ZN-c3-005: DENALI, Cohort 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:** 2H24

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:** 116 across all three cohorts
- **Status:** Fully enrolled
- **Results:** 2H24

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

Grade 5 Treatment-Related Events in Zentalis-Sponsored Solid Tumor Studies

Monotherapy

Disease	Study	Study Treatment	Event
HGSOC	DENALI (ZN-c3-005)	Azeno 400 mg QD 5:2	Neutropenia (sepsis)
HGSOC	DENALI (ZN-c3-005)	Azeno 400 mg QD 5:2	Pancytopenia (presumed sepsis)
HGSOC	MAMMOTH (ZN-c3-006)	Azeno 350 mg QD 5:2	Neutropenia (sepsis)
USC	TETON (ZN-c3-004)	Azeno 400 mg QD 5:2	Hypovolemic shock, thrombocytopenia
USC	ZN-c3-001	Azeno 175 mg BID 5:2	Pancytopenia, bowel perforation

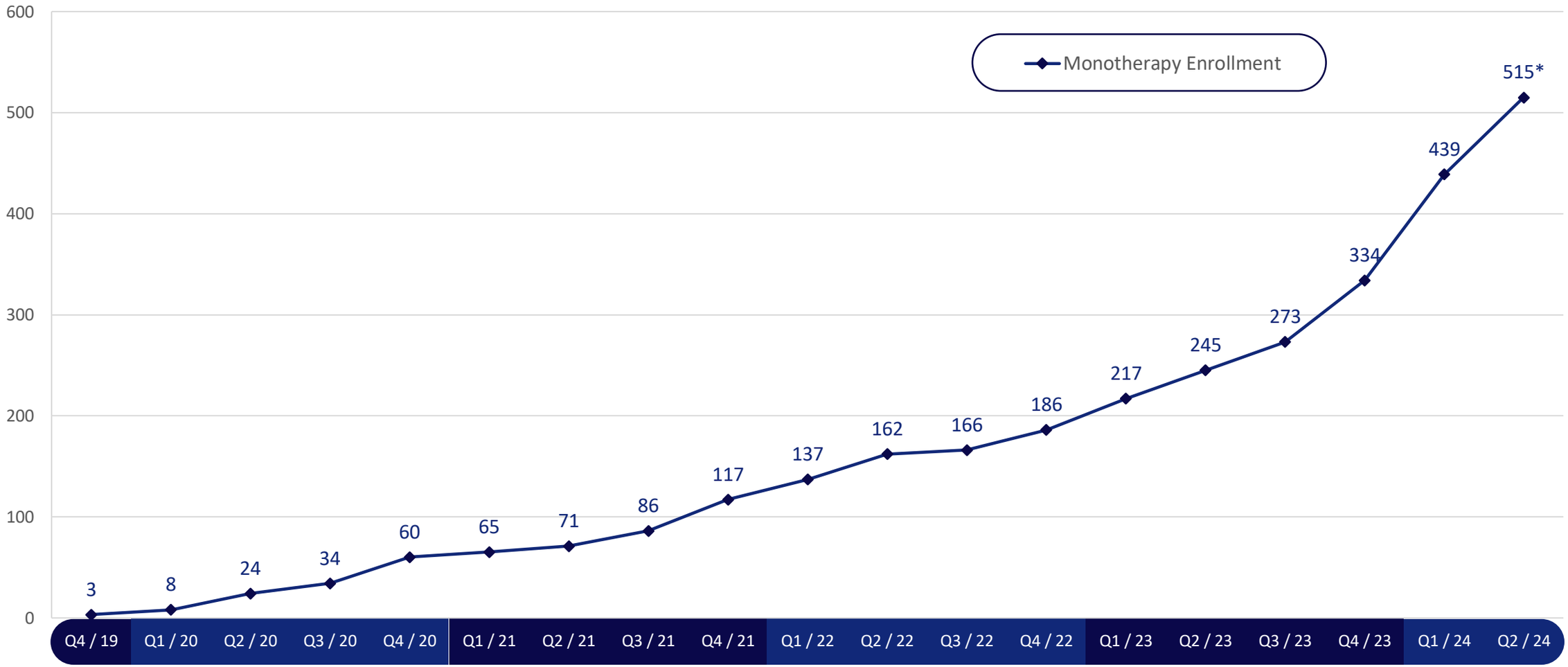
Combination Therapy

Disease	Study	Study Treatment	Event
HGSOC	ZN-c3-002 Chemo Combo	Azeno 200 mg QD Paclitaxel 80 mg/m2 IV QW	Sepsis
HGSOC	ZN-c3-002 Chemo Combo	Azeno 200 mg QD PLD 40 mg/m^2 IV Q4W	Acute respiratory distress syndrome Drug-induced liver injury
CRC BRAF V600	ZN-c3-016	Azeno 400 mg QD Encorafenib 75 mg PO QD Cetuximab 860 mg IV Q2W	Neutropenia Listeria sepsis

Abbreviations: HGSOC, high-grade serous ovarian cancer; USC, uterine serous carcinoma; CRC, colorectal cancer; QD, once daily; 5:2, 5-days of treatment followed by 2-days off treatment; PO, by mouth; BID, twice daily; QW, weekly; Q4W, every four weeks; Q2W, every two weeks; IV, intravenous.

There have been two additional deaths in patients treated with azenosertib. One on a non-Zentalis sponsored study (Zentera study 002A, China) of patient with ovarian cancer on azenosertib 200 mg qd and paclitaxel 80 mg/m2 qw who died of intestinal perforation in 2022, and a non-solid tumor (Acute Myelogenous Leukemia) patient (Zn-004c) who died of aspergillosis.

Exponential Increase in Azenosertib Monotherapy Enrollment Over the Past Year



*More than 200 patients who have been enrolled at a dose of 400 mg 5:2.

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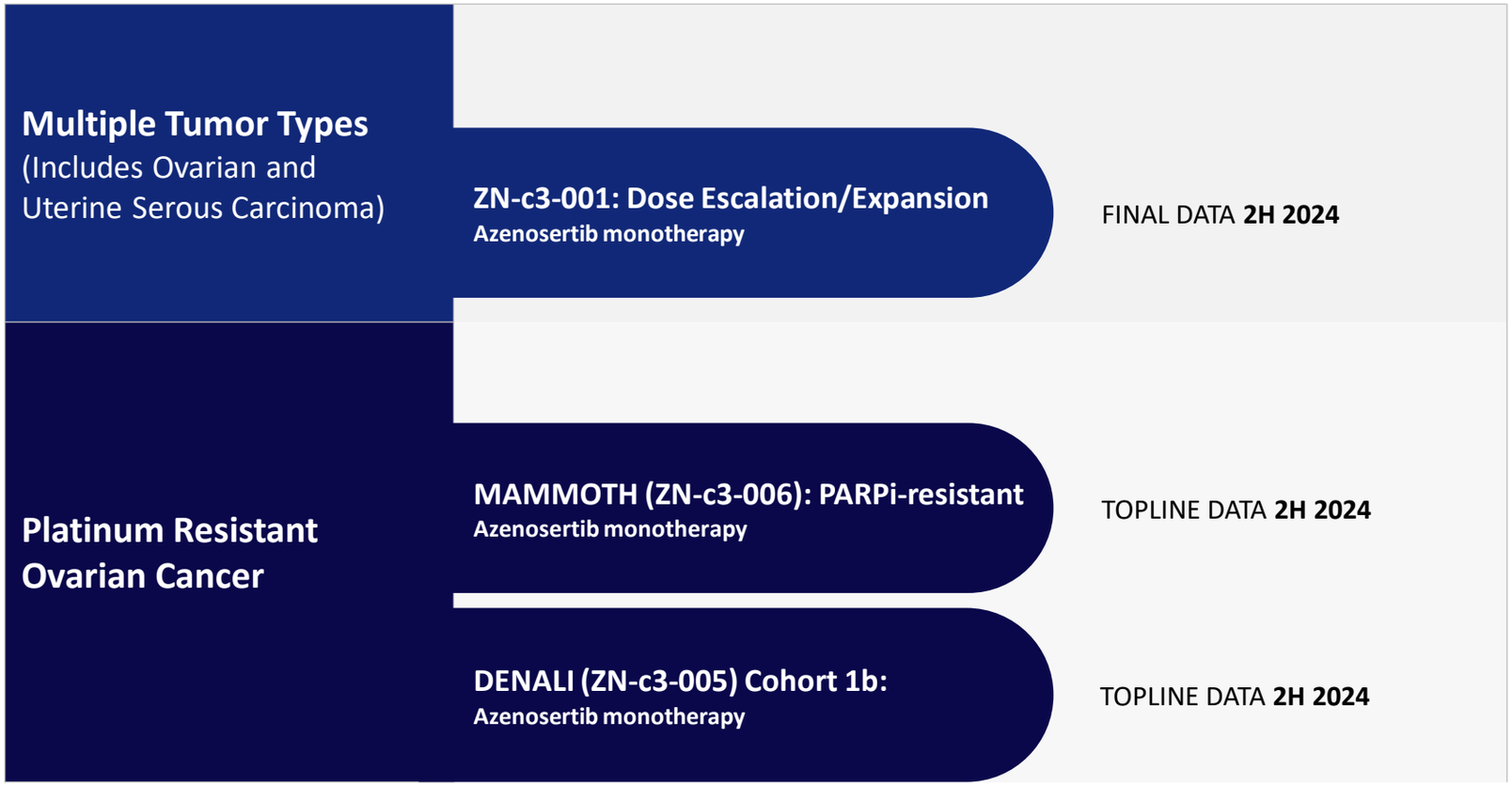
Zentalis On Track to Report Data from Three Azenosertib Monotherapy Datasets by Year End



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

Q&A