NEWS RELEASE

Zentalis Pharmaceuticals Announces First Patient Dosed in ASPENOVA Phase 3 Trial of Azenosertib in Patients with Cyclin E1-Positive Platinum-Resistant Ovarian Cancer

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- Global Phase 3, randomized, controlled trial comparing azenosertib to standard-of-care chemotherapy now enrolling
- ASPENOVA designed as confirmatory study to support DENALI Phase 2 accelerated approval pathway, pending FDA feedback

SAN DIEGO, May 05, 2026 (GLOBE NEWSWIRE) -- Zentalis® Pharmaceuticals, Inc. (Nasdaq: ZNTL), a clinical oncology innovator advancing late-stage development of investigational first-in-class WEE1 inhibitor azenosertib as a biomarker-driven treatment approach for ovarian cancer, today announced that the first patient has been dosed in the Phase 3 ASPENOVA clinical trial (NCT07546500, GOG-3147, ENGOT-ov109, APGOT-OV27) evaluating azenosertib in patients with Cyclin E1-positive platinum-resistant ovarian cancer (PROC).

"Dosing the first patient in the ASPENOVA Phase 3 clinical trial represents a significant milestone in our development of azenosertib for patients with platinum-resistant ovarian cancer," said Ingmar Bruns, M.D., Chief Medical Officer of Zentalis. "With DENALI Part 2 progressing toward a year-end readout that may support accelerated approval and ASPENOVA now enrolling to evaluate azenosertib versus standard-of-care chemotherapy to support full approval, we are executing on a comprehensive development and regulatory strategy designed to bring this therapy to patients as quickly as possible. We are deeply grateful to the patients participating in this important trial and to our collaborators at The GOG Foundation, Inc. (GOG-F), ENGOT, and APGOT for their partnership in advancing this research."

"Cyclin E1-overexpressing ovarian cancers are associated with platinum-resistance and poor outcomes, representing a clinical unmet need," said Fiona Simpkins, M.D., Professor at the University of Pennsylvania Perelman School of Medicine and Lead Investigator for the ASPENOVA trial and GOG-F. "This biomarker has yet to be exploited therapeutically and azenosertib, a WEE1 inhibitor, is an oral, targeted treatment that is showing exciting activity in Cyclin E1-overexpressing ovarian cancer (SGO Annual Meeting, 2025). The biomarker-driven approach now being studied in this Phase 3 randomized

trial has the potential to identify patients most likely to benefit while sparing them from the inconvenience of intravenous regimens. On behalf of GOG Foundation, we are pleased to collaborate with Zentalis, ENGOT, and APGOT on this important trial for this underserved patient population."

ASPENOVA is a randomized, controlled Phase 3 trial designed to confirm the clinical benefit of azenosertib and support full approval as part of Zentalis' dual-track regulatory strategy. The company is pursuing accelerated approval based on the ongoing registration-intended DENALI Phase 2 trial, with a topline readout expected by year-end 2026, while simultaneously advancing ASPENOVA as the confirmatory study to satisfy FDA requirements for conversion to full approval. Both trials are evaluating azenosertib at 400mg once daily on a 5-days-on, 2-days-off schedule (400mg QD 5:2), the dose selected based on the DENALI Part 2a interim analysis announced in April 2026. The planned interim analysis showed a meaningful, clearly differentiated response rate at 400mg QD 5:2 over 300mg QD 5:2 and comparable safety profiles between the two dose groups.

The ASPENOVA trial is being conducted in collaboration with The GOG Foundation, Inc. (GOG-F), the European Network of Gynaecological Oncological Trial groups (ENGOT), and Asia-Pacific Gynecologic Oncology Trials Group (APGOT), reflecting the global clinical and scientific community's recognition of the significant unmet need in this patient population.

About ASPENOVA Clinical Trial
ASPENOVA (NCT07546500, GOG-3147, ENGOT-ov109) is a Phase 3 randomized, confirmatory clinical trial designed to support full approval of azenosertib in patients with Cyclin E1-positive platinum-resistant ovarian cancer (PROC). The trial is expected to enroll approximately 420 patients and compare azenosertib monotherapy at 400mg QD 5:2 to investigator's choice of standard-of-care single-agent chemotherapy (paclitaxel, pegylated liposomal doxorubicin [PLD], gemcitabine, or topotecan) in this biomarker-selected population. The primary endpoint is progression-free survival (PFS); key secondary endpoints include overall survival (OS) and overall response rate (ORR). The trial design was aligned with the U.S. Food and Drug Administration (FDA) to meet requirements for the accelerated approval pathway and potential conversion to full approval.

About DENALI Clinical Trial
DENALI is a multi-part Phase 2 registration-intended clinical trial (NCT05128825) studying azenosertib in PROC patients.

Part 1b enrolled patients with PROC regardless of Cyclin E1 protein expression, all treated at 400mg QD 5:2. Part 2 is prospectively enrolling PROC patients with Cyclin E1 protein overexpression based on Zentalis' proprietary immunohistochemistry cutoff.

Part 2, in total, is designed to support accelerated approval, pending study outcome and discussions with the FDA. The study design consists of the following parts:

- Part 2a: Dose confirmation evaluated two doses, 300mg QD 5:2 and 400mg QD 5:2, with approximately 30 patients enrolled per dose group. 400mg QD 5:2 was selected as the optimal monotherapy dose. Recruitment at the 300mg QD 5:2 dose level has been discontinued. All patients enrolled in Part 2a will contribute to the overall safety database submitted to the FDA.
- Part 2b: Enrollment expansion at the selected 400mg QD 5:2 dose up to approximately 100 patients, including patients at this dose in Part 2a. This cohort is currently enrolling.
- Part 2c: Broadening study population to include approximately 40 patients previously treated with a taxane-containing regimen for PROC. This cohort is currently enrolling.

Zentalis expects to complete enrollment in all cohorts of DENALI Part 2 (2a, 2b, 2c) and provide a

topline readout by year-end 2026.

For physician and patient information about the DENALI trial, please visit www.denalitrial.com.

About Azenosertib
Azenosertib is an investigational, potentially first-in-class, selective, and orally bioavailable inhibitor of WEE1 currently being evaluated in clinical studies in ovarian cancer and additional tumor types. WEE1 acts as a master regulator of the G1-S and G2-M cell cycle checkpoints, through negative regulation of both CDK1 and CDK2, to prevent replication of cells with damaged DNA. By inhibiting WEE1, azenosertib enables cell cycle progression, despite high levels of DNA damage, thereby resulting in the accumulation of DNA damage and leading to mitotic catastrophe and cancer cell death.

Azenosertib is in late-stage development as a potential treatment for Cyclin E1-positive platinum-resistant ovarian cancer (PROC). There is currently no approved treatment option specifically for this biomarker-selected population which comprises approximately 50% of PROC patients. Cyclin E1 protein overexpression has been established as a sensitive and specific predictive biomarker for identifying patients who could potentially derive benefit from azenosertib treatment, based on retrospective analysis of azenosertib studies in PROC. Validation of the Cyclin E1 companion diagnostic assay is ongoing in the DENALI and ASPENOVA trials.

Azenosertib has been granted Fast Track Designation by the U.S. FDA for the treatment of patients with Cyclin E1-positive platinum-resistant ovarian cancer. Fast Track Designation is intended to facilitate the development and expedite the review of therapies that have the potential to treat serious conditions and address unmet medical needs.

About Zentalis Pharmaceuticals

Zentalis is a clinical oncology innovator developing a treatment approach for ovarian cancer and multiple tumor types. Leveraging therapeutics development and biomarker expertise, Zentalis is advancing monotherapy and combination studies of its investigational first-in-class WEE1 inhibitor, azenosertib. Focused on translating WEE1 science into clinical practice, we aim to equip physicians with a targeted, non-chemo, orally available medicine that enhances treatment experience, choice, and outcomes. Our mission: to unburden cancer patients with more convenience and care.

For more information, please visit www.zentalis.com. Follow Zentalis 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, as amended. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including, but not limited to, statements regarding the potential for azenosertib to be first-in-class; the continued development of azenosertib; the clinical and therapeutic potential of azenosertib, including the potential for azenosertib to be an important treatment option for patients with ovarian cancer or other indications; the broad franchise potential of azenosertib; the Company's biomarker-driven strategy for azenosertib; the potential to advance research on additional areas of opportunity for azenosertib outside PROC; the Company's anticipated milestones and the timing thereof, including the anticipated timing of the topline readout from DENALI Part 2; and the Company's planned regulatory strategy for azenosertib and the timing thereof, including the potential for DENALI Part 2 to support an accelerated approval and the potential for ASPENOVA to support full approval. The terms "anticipate," "advance," "believe," "could," "design," "develop," "expect," "intent," "look forward," "may," "on track," "pending," "plan," "position," "potential," "runway," "strategy," "support," "target," and "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 substantial dependence on the success of azenosertib; our plans, including the costs thereof, of development of companion diagnostics; the outcome of preclinical testing and early trials may not be predictive of the success of later clinical trials; potential unforeseen events during clinical trials could cause delays or other adverse consequences; risks relating to the regulatory approval process or ongoing regulatory obligations; our product candidates may cause serious adverse side effects; the interim, initial, "topline," and preliminary data from our clinical trials may change as more patient data becomes available, and are subject to audit and verification procedures that could result in material changes in the final data; 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:
Aron Feingold
VP, Investor Relations & Corporate Communications
ir@zentalis.com

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