



NEWS RELEASE

ZENTALIS PHARMACEUTICALS PRESENTS UPDATED CLINICAL DATA AT THE SOCIETY OF GYNECOLOGIC ONCOLOGY 2025 ANNUAL MEETING ON WOMEN'S CANCER

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Azenosertib median duration of response (mDOR) updated to 6.3 months in the ongoing DENALI Part 1b clinical trial in patients with platinum-resistant ovarian cancer (PROC) and continues to demonstrate an objective response rate (ORR) of ~35% in response-evaluable patients

On track to initiate Part 2 of the ongoing DENALI clinical trial in 1H 2025, with registration-intent topline data anticipated by year end 2026

Company also presents preclinical combination data of azenosertib with microtubule inhibitor-based antibody drug conjugates (ADCs) demonstrating synergistic antitumor effects

SAN DIEGO, March 15, 2025 (GLOBE NEWSWIRE) -- Zentalis® Pharmaceuticals, Inc. (Nasdaq: ZNTL), a clinical-stage biopharmaceutical company developing a potentially first-in-class and best-in-class WEE1 inhibitor for patients with ovarian cancer and other tumor types, today announced updated clinical data from Part 1b of the ongoing DENALI clinical trial of azenosertib in patients with PROC in an oral presentation at the Society of Gynecologic Oncology (SGO) 2025 Annual Meeting on Women's Cancer.

DENALI Part 1b is a Phase 2 single-arm study that evaluated azenosertib monotherapy at the 400mg QD 5:2 dose (once daily, five days on, two days off, or the "intermittent schedule") in patients with PROC (n=102).

As of the January 13, 2025 data cutoff, patients with Cyclin E1+ PROC tumors who were response-evaluable (patients who had at least one scan after receiving azenosertib) demonstrated an ORR of 34.9% (15/43; 95% CI: 21.0 - 50.9). In the intent-to-treat patients with Cyclin E1+ PROC (patients who received at least one dose of azenosertib), the ORR was 31.3% (15/48; 95% CI: 18.7 - 46.3), and an mDOR of 6.3 months (95% CI: 2.7 - not estimable). The mDOR is subject to change since there were patients with ongoing responses as of the cutoff date.

The presentation also demonstrates Cyclin E1 protein overexpression, regardless of CCNE1 gene amplification, as a sensitive and specific predictive biomarker that can be used to identify patients who could potentially derive benefit from azenosertib. Zentalis estimates that about half of PROC patients overexpress Cyclin E1 based on its proprietary immunohistochemistry cutoff.

As of the January 13, 2025 data cutoff, the safety and tolerability profile was consistent with the safety and tolerability profile from the Company's January 29, 2025 investor event, which included data based off a cutoff date of December 2, 2024, with no new safety findings. Gastrointestinal toxicities and fatigue were found to be the most common treatment-related adverse events.

"The presentation of the updated DENALI Part 1b data at the SGO Annual Meeting supports our continued development of azenosertib," said Ingmar Bruns, M.D., Chief Medical Officer of Zentalis. "The clear anti-tumor activity and durable response observed highlights the potential of azenosertib to become an important treatment option for patients with Cyclin E1+ PROC. We are proud to have shared these data with many of the world's leading gynecologic oncologists at SGO as part of our continued commitment to patients living with PROC."

"Platinum-resistant ovarian cancer is one of the most challenging types of ovarian cancer to treat. Tumors overexpressing Cyclin E1 protein exhibit poorer outcomes after standard of care chemotherapy regimens," said Fiona Simpkins, M.D., Director of Clinical & Translational Gynecologic Oncology Research at the University of Pennsylvania, and lead principal investigator in the DENALI study. "Developing new therapies for this subset of ovarian cancer patients is urgently needed. DENALI Part 1b results are exciting as they show that the WEE1 inhibitor, azenosertib, is active in a Cyclin E1 biomarker selective population potentially addressing a clinical unmet need."

The Company is on track to initiate enrollment of DENALI Part 2 in the first half of 2025 and expects to disclose topline data from DENALI Part 2 by year end 2026. DENALI Part 2, if successful, has the potential to support an accelerated approval, subject to FDA review. Zentalis plans to treat the same patient population in a Phase 3 randomized confirmatory study, subject to FDA review, which the Company plans to enroll concurrently with DENALI Part 2b.

Tomorrow, the Company will also present preclinical data of azenosertib during a poster presentation at the SGO Annual Meeting. The poster data highlights synergistic effects and significantly improved tumor growth inhibition in *in vitro* and *in vivo* preclinical models using a combination of azenosertib and microtubule inhibitor-based ADCs. Together with the previous data that azenosertib synergized with TOPO1 inhibitor based ADCs, these results indicate that azenosertib could be used as a generalizable combination partner with ADCs for improving responses in patients with advanced solid tumors.

The oral presentation and poster can be accessed through the "Publications" section of the [Zentalis website](#).

About Azenosertib

Azenosertib is a novel, selective, and orally bioavailable inhibitor of WEE1 currently being evaluated as a monotherapy and combination 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.

About Zentalis Pharmaceuticals

Zentalis[®] Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company developing azenosertib (ZN-c3), a potentially first-in-class and best-in-class WEE1 inhibitor for patients with Cyclin E1+ platinum-resistant ovarian cancer (PROC). Azenosertib is being evaluated as a monotherapy and in combination across multiple tumor types in 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. The Company is also leveraging its extensive experience and capabilities to translate its science to advance research on additional areas of opportunity for azenosertib outside PROC. Zentalis has operations in San Diego.

For more information, please visit www.zentalis.com. Follow Zentalis on X/Twitter at [@ZentalisP](https://twitter.com/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, 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 of azenosertib, including the potential for azenosertib to become an important treatment option for patients with Cyclin E1+ PROC, the potential for azenosertib to address a clinical unmet need, and the potential for azenosertib to be used as a generalizable combination partner with ADCs for improving responses in patients with advanced solid tumors; our anticipated milestones and the timing thereof, including the anticipated timing of initiation of clinical trials and timing of clinical data disclosures; the potential to advance research on additional areas of opportunity for azenosertib outside PROC; the potential for azenosertib to be first-in-class and best-in-class; the potential for Cyclin E1 to serve as a sensitive and predictive biomarker that can be used to identify patients who could potentially derive benefit from azenosertib; our estimate of how many PROC patients overexpress Cyclin E1 based on our proprietary immunohistochemistry cutoff; and our planned clinical development strategy and regulatory strategy for azenosertib and the timing thereof, including plans for registration-intent studies and the potential for DENALI Part 2 to support an accelerated approval. The terms “anticipated,” “can,” “could,” “estimate,” “expect,” “intent,” “on track,” “opportunity,” “plan,” “potential,” 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 plans, including the costs thereof, of development of companion diagnostics; our substantial dependence on the success of our lead product candidate, azenosertib; 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.

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