Zentalis Pharmaceuticals Announces First Patient Dosed in DENALI Part 2 Clinical Trial of Azenosertib in Patients with Cyclin E1+ PROC

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Phase 2 registration-intent trial enrolling Part 2a dose confirmation arms

Topline data from DENALI Part 2 anticipated by year end 2026 with the potential to support an accelerated approval, subject to FDA feedback

SAN DIEGO, April 28, 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 that the first patient has been dosed in Part 2 of the Phase 2 DENALI clinical trial (NCT05128825) of azenosertib in patients with Cyclin E1+ platinum-resistant ovarian cancer (PROC).

As previously disclosed, the Company aligned with the U.S. Food and Drug Administration (FDA) on the design of DENALI Part 2, which allows for seamless enrollment in the two parts of the trial:

- Part 2a is designed to confirm the primary dose-of-interest with a target enrollment of approximately 30 patients at each of two dose levels: 400mg QD 5:2 and 300mg QD 5:2 (intermittent daily dosing on a five days on, two days off dosing schedule).
- Part 2b is designed to enroll approximately 70 additional patients at the selected dose, which will be informed by the Part 2a results, subject to FDA feedback.

The Company expects to disclose topline data from DENALI Part 2 by year end 2026 and if successful, this trial has the potential to support an accelerated approval, subject to FDA review.

“Dosing the first patient in Part 2 of the DENALI study is an important milestone for Zentalis as we continue the clinical development of azenosertib,” said Ingmar Bruns, M.D., Chief Medical Officer of Zentalis. “We are proud that azenosertib is one step closer to our goal of addressing a tremendous unmet need. We are grateful to our patients and their families for participating in this trial, which has the potential to result in a treatment option for thousands of women diagnosed with Cyclin E1+ PROC.”

Previously disclosed clinical data from Part 1b of the DENALI study showed clinically meaningful results in patients with Cyclin E1+ PROC. As of the January 13, 2025 data cutoff, patients who were response-evaluable (n=43) had an objective response rate (ORR) of 34.9% and a median duration of response (mDOR) of 6.3 months. The mDOR is subject to change as there were patients with ongoing responses as of the cutoff date.

The data also established 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 protein based on its proprietary immunohistochemistry cutoff.

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 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 a treatment option for women with Cyclin E1+ PROC, our goal for azenosertib to address a tremendous unmet need; our anticipated milestones and the timing thereof, including the 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,” “opportunity,” “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 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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