Zentalis Pharmaceuticals Announces Azenosertib Fast Track Designation and Virtual Corporate Event to Present Updated Data from Azenosertib Clinical Studies

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Azenosertib Fast Track Designation granted for Cyclin E1 positive patients by U.S. Food and Drug Administration (FDA)

Manuscript focused on role of Cyclin E1/CDK2 activation predicting sensitivity to azenosertib published in npj Precision Oncology

Corporate event to be held on January 29, 2025 to provide updates on azenosertib clinical data, development and regulatory path

SAN DIEGO, Jan. 09, 2025 (GLOBE NEWSWIRE) -- Zentalis® Pharmaceuticals, Inc. (Nasdaq: ZNTL), a clinical-stage biopharmaceutical company discovering and developing clinically differentiated small molecule therapeutics targeting fundamental biological pathways of cancers, today announced that the FDA has granted Fast Track Designation to azenosertib for the treatment of patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer (PROC) who are positive via Cyclin E1 immunohistochemistry for protein levels. The FDA grants investigational medicines Fast Track Designation to facilitate the development and expedite the review of medicines that demonstrate the potential to treat serious conditions and fill an unmet medical need.

"Zentalis is sharply focused on our goal of bringing azenosertib to patients with gynecological malignancies," said Ingmar Bruns, Chief Medical Officer. "The FDA's decision to grant Fast Track Designation for azenosertib in Cyclin E1 positive ovarian cancer patients underscores the unmet medical need in this patient population which has historically been associated with resistance to chemotherapy and poor patient outcomes. This designation provides meaningful benefits, including those that may expedite the regulatory review of this product candidate in this patient population. We look forward to sharing updated azenosertib clinical data and a regulatory update, including plans for registration-intent studies, at our corporate event on January 29."

In addition, this week *npj Precision Oncology* published a paper from Zentalis researchers highlighting the role of Cyclin E1/CDK2 activation in predicting sensitivity to azenosertib.

"The data in this manuscript provide functional and mechanistic demonstration that preclinical models with high levels of Cyclin E1 activation are particularly sensitive to azenosertib inhibition, along with supporting clinical data from select patients enrolled in azenosertib clinical studies," said Mark Lackner, Chief Scientific Officer. "We believe these data support a biomarker-directed strategy to identify patients most likely to benefit from azenosertib."

Corporate Event
On January 29, 2025, at 8:00am ET Zentalis will host a webcast to present data from its studies of azenosertib in PROC and provide a regulatory and development update, including the following:

- Topline results from 102 patients enrolled in Part 1b of the Phase 2 DENALI study (ZN-c3-005) 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 (ZN-c3-006) trial of azenosertib as a monotherapy and in combination with PARP inhibitor (niraparib) in PARP-resistant PROC in partnership with GSK
- Presentation of design of registration-intent study and a regulatory update
- Initial data from the Phase 1 ZN-c3-016 azenosertib + BEACON regimen (encorafenib + cetuximab) trial in BRAF mutant metastatic colorectal cancer in partnership with Pfizer

Additional information on the corporate webcast, including registration links and dial in information, will be posted to the Investors & Media section of www.zentalis.com.

About Azenosertib
Azenosertib is a novel, selective, and orally bioavailable inhibitor of WEE1 currently being evaluated as a monotherapy and in 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 cycling of cells with damaged DNA. By inhibiting WEE1, azenosertib enables cell cycle progression in the presence of high levels of DNA damage, thereby resulting in the further 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 discovering and developing clinically differentiated small molecule therapeutics targeting fundamental biological pathways of cancers. The Company's lead product candidate, azenosertib (ZN-c3), is a potentially first-in-class and best-in-class WEE1 inhibitor for advanced solid tumors. Azenosertib is being evaluated as a monotherapy and in combination across multiple 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 and in combination with several chemotherapy backbones. As part of its azenosertib clinical development program, the Company is exploring enrichment strategies targeting tumors of high genomic instability, such as Cyclin E1 positive tumors and tumors with oncogenic driver mutations. The Company is also leveraging its extensive experience and capabilities across cancer biology and medicinal chemistry to advance its research on protein degraders. 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. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including statements regarding the potential of azenosertib; our plans to hold a corporate event and provide updates on clinical data, development and regulatory path, including the timing and content thereof; the potential of azenosertib to treat serious conditions and fill an unmet medical need; the potential for Fast Track Designation to provide meaningful benefits, including those that may expedite the regulatory review of azenosertib in the applicable patient population; our belief that data support a biomarker-directed strategy to identify patients most likely to benefit from azenosertib; the potential for azenosertib to be first-in-class and best-in-class; the broad franchise potential of azenosertib; and our plans with respect to the development of our product candidates, including azenosertib. The terms "believe," "goal," "likely," "look forward," "may," "plan," "potential," "support," "to be," 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 any diagnostic tools; 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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