



NEWS RELEASE

ZENTALIS PHARMACEUTICALS TO PRESENT PRECLINICAL AZENOSERTIB DATA AT ESMO 2024

2024-09-09

Azenosertib shows synergistic anti-tumor effects in combination with topoisomerase I (TOP1) inhibitor-based antibody drug conjugates

SAN DIEGO, Sept. 09, 2024 (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 company will present preclinical data from its selective WEE1 inhibitor azenosertib at the European Society of Medical Oncology (ESMO) 2024 Congress, occurring September 13-17 in Barcelona, Spain.

"The confluence of DNA damage induced by TOP1 inhibitors and cell cycle deregulation and genomic instability induced by azenosertib provides a mechanistic rationale for this combination, as well as more broadly with antibody drug conjugates (ADCs) utilizing these inhibitors as payloads," said Mark Lackner, PhD, Chief Scientific Officer. "The preclinical data demonstrated this synergistic effect and suggest that azenosertib in combination with ADCs could be an important therapeutic approach in treating patients with advanced solid tumors."

Presentation Details:

Poster #35P: The Selective WEE1 Inhibitor Azenosertib Shows Synergistic Antitumor Effects in Combination with Topoisomerase I Inhibitor-Based Antibody-Drug Conjugates

Presenter: Jianhui Ma, Zentalis Pharmaceuticals

Poster Display Date: Sunday, September 15, 2024

Data in the abstract showed that the combination of azenosertib with TOP1 inhibitors demonstrated significant synergistic effects in all cell lines tested. In HER2+ breast cancer animal models, those treated with the combination of azenosertib plus trastuzumab deruxtecan (T-Dxd) resulted in 50% of animals showing complete tumor regression (CR), compared with no CRs in monotherapy arms. Significant combination effects were also observed in a HER2+ ovarian model and a HER2-low breast cancer model. These data suggest that azenosertib significantly improves the anti-tumor effect of TOP1 inhibitors as well as ADCs with TOP1 inhibitor payload and that the combination could be a generalizable therapeutic approach for improving responses to ADCs in patients with advanced solid tumors.

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 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 and hematologic malignancies. 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, homologous recombination deficient 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](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. 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 benefits of azenosertib in combination with ADCs as a therapeutic approach. The terms "could" 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 ability to resolve the ongoing partial clinical hold on azenosertib; 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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