Zentalis Pharmaceuticals to Present Promising Results from Phase 1 Trial of Azenosertib and Gemcitabine in Relapsed or Refractory Osteosarcoma at 2024 American Society of Clinical Oncology Annual Meeting

May 23, 2024

Administration of azenosertib combined with gemcitabine was well tolerated and resulted in clinically meaningful increase in event-free survival compared to historical comparators

Results support further evaluation of azenosertib combined with gemcitabine in relapsed or refractory osteosarcoma through an investigator-initiated Phase 2 trial

NEW YORK and SAN DIEGO, May 23, 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 the presentation of final results from a Phase 1 trial of azenosertib and gemcitabine in relapsed or refractory (R/R) osteosarcoma at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago.

“We are pleased to report the final results from our Phase 1 trial evaluating azenosertib administered with gemcitabine in patients with relapsed or refractory osteosarcoma,” said Kimberly Blackwell, M.D., Chief Executive Officer of Zentalis. “Azenosertib was well tolerated and clinically active in combination with gemcitabine and a go-forward dose was identified. Most importantly, the event-free survival results demonstrate a tripling in the proportion of patients without progression or death at 18 weeks compared with historical control patients. These results support studying the combination in patients facing this aggressive cancer, which we expect will occur in an upcoming investigator-initiated Phase 2 trial. We also look forward to presenting additional data on azenosertib in gynecological malignancies later this year as our development path continues to progress on track.”

Data Highlights and Conclusions:

- 31 patients were enrolled in the study, of which 31 were evaluable for safety, 29 were evaluable for dose-limiting toxicities and 28 were evaluable for efficacy. The median age was 27 (range 12-76) and 21 patients (68%) were ≤39 years old. Patients received a median of 3 (range 1-9) prior therapies, including 10 patients (32%) who had previous treatment with gemcitabine.
- The 18-week event-free survival rate (EFS; time from treatment initiation until disease progression or death due to any cause) was 39% (11/28) across all dose levels. The EFS observed in the study compares favorably to historical cohorts with a similar patient population where a 16-week EFS of ~12% has been reported[1].
- The maximum tolerated dose (MTD) of azenosertib was determined to be 150 mg daily on a 5:2 schedule (5 days on, 2 days off) + gemcitabine 800 mg/m^2.
- At the MTD, the most frequent grade ≥3 adverse events (≥20%) included thrombocytopenia and lymphopenia (33% each); there were no grade 4 thrombocytopenia events or instances of febrile neutropenia at the MTD.
- Data support further investigation of azenosertib administered in combination with gemcitabine in patients with R/R osteosarcoma in an upcoming investigator-initiated Phase 2 trial.

[1] Lagmay JP, et al. J Clin Oncol. 2016;34(25):3031-3038.

“Historically, the management of relapsed and/or refractory osteosarcoma has been limited to cytotoxic chemotherapy and only recently, tyrosine kinase inhibitors, with suboptimal outcomes,” said Viswatej Avutu, M.D., Sarcoma Medical Oncology Service and Pediatric Sarcoma Team, Memorial Sloan Kettering Cancer Center, New York, NY. “Azenosertib provides promise as a novel class of drugs and offers hope for a well-tolerated and potentially efficacious treatment option that is desperately needed.”

Study Design
Phase 1 dose-finding study (NCT04833582) assessed azenosertib administered in combination with gemcitabine in patients ≥12 years of age. The primary endpoint was the incidence and severity of dose-limiting toxicities. Secondary endpoints included the incidence and severity of adverse events and EFS at 18 weeks per RECIST v1.1.

Poster Presentation Details:
The full abstract (#11525) is available here on the ASCO Congress portal.
Title: Phase 1 Results of the WEE1 Inhibitor, Azenosertib, in Combination With Gemcitabine in Adult and Pediatric Patients With Relapsed or Refractory Osteosarcoma.
Presenter: Dr. Viswatej Avutu, Sarcoma Medical Oncology Service and Pediatric Sarcoma Team, Memorial Sloan Kettering Cancer Center, New York, NY
Session Title: Poster Session – Sarcoma
Session Date and Time: June 1, 2024. 1:30-4:30 PM CDT

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 both New York and 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 our plans to present final results from a Phase 1 trial of azenosertib and gemcitabine in relapsed/refractory osteosarcoma at the 2024 American Society of Clinical Oncology Annual Meeting in Chicago; plans for an investigator-initiated Phase 2 trial evaluating azenosertib combined with gemcitabine in R/R osteosarcoma; our plans to present additional data on azenosertib in gynecological malignancies later in 2024; the potential for azenosertib to be first-in-class and best-in-class; the broad franchise potential of azenosertib; our plans with respect to the development of our product candidates, including azenosertib; and the potential benefits of azenosertib, including the potential benefits of the design thereof, the value potential of the asset, and the potential to improve outcomes for patients. The terms "continue," "expect," "look forward," "on track," "potential," "promise," "upcoming," "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 candidates; 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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