



NEWS RELEASE

ZENTALIS PHARMACEUTICALS SHARES UPDATED CLINICAL DATA DEMONSTRATING MEANINGFUL AZENOSERTIB ACTIVITY IN CYCLIN E1+, PLATINUM-RESISTANT OVARIAN CANCER

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Results from DENALI Part 1b show an Objective Response Rate (ORR) of ~35% in response-evaluable, heavily-pretreated patients with Cyclin E1+ platinum-resistant ovarian cancer (PROC)

Across monotherapy cohorts in key clinical studies, well-characterized safety and tolerability profile shows no new safety signals

Company aligned with FDA on seamless study design for DENALI Part 2 in patients with Cyclin E1+ PROC; study expected to begin 1H 2025

Topline data from registration-intent DENALI Part 2 anticipated by year end 2026

Management to host conference call today at 8:00 am ET

SAN DIEGO, Jan. 29, 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 presented updated azenosertib monotherapy clinical data from its ZN-c3-001, MAMMOTH and DENALI studies and shared details on future clinical development and potential registration plans for patients with Cyclin E1+ platinum-resistant ovarian cancer (PROC). Results from the combination cohorts of MAMMOTH and from the ZN-c3-016 study in colorectal cancer were also disclosed today.

"We are excited to outline a clear path for Zentalis to bring azenosertib to patients with Cyclin E1+ PROC," said Ingmar Bruns, M.D., Chief Medical Officer. "In a patient population with a clear unmet medical need, the monotherapy data showed a meaningful and consistent improvement in responses as compared to historical data from current monotherapy chemo standard of care, across multiple studies, in heavily-pretreated patients at the 400mg QD 5:2 intermittent dose. The results demonstrate a median duration of response of approximately 5.5 months that continues to mature with patients

remaining on therapy. In addition, with over 350 patients treated at clinically active monotherapy doses (total daily dose $\geq 300\text{mg}$) across our studies, we have observed a well-characterized safety profile and no new safety signals since our last report. Our data have also confirmed Cyclin E1 overexpression as a predictor of sensitivity to azenosertib monotherapy in PROC, and we intend to pursue further development in this patient population.”

“We are very pleased with the azenosertib results obtained to date and believe we have a clear path to advancing this product candidate to patients,” said Julie Eastland, Chief Executive Officer. “Notably, approximately 50% of patients with PROC are Cyclin E1+, and we believe that the therapeutic and commercial opportunity in this population, which tends to be especially treatment-refractory, is substantial. Looking ahead at continued azenosertib development, we believe that DENALI Part 2, if successful, has the potential to support an accelerated product approval, subject to FDA feedback. Together with the corporate restructuring announced yesterday that extended our cash runway into late 2027, well beyond the anticipated topline data readout from DENALI Part 2, Zentalis is well-positioned to execute on our goal to bring azenosertib to patients as quickly as possible.”

The Company plans to present the following at the corporate event:

DENALI Part 2 Study Design

The Company has aligned with the U.S. Food and Drug Administration (FDA) on the design of its DENALI Part 2 study in patients with Cyclin E1+ PROC, which allows for seamless enrollment across Parts 2a and 2b: Part 2a is designed to confirm the primary dose-of-interest, 400mg QD 5:2 (intermittent daily dosing on a five days on, two days off schedule), with a target enrollment of approximately 30 patients at each of two dose levels: 400mg QD 5:2 and 300mg QD 5:2. Part 2b is designed to enroll approximately 70 patients at a single dose, the selection of which will be informed by the Part 2a results, with the final Part 2b dose selection and endpoints subject to FDA feedback. The Company plans to initiate enrollment of DENALI Part 2 in the first half of 2025 and 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.

Azenosertib Clinical Results

ZN-c3-001

ZN-c3-001 is a Phase 1, dose-escalation study that evaluated azenosertib monotherapy in solid tumors across continuous and intermittent dosing schedules.

ZN-c3-001 is fully enrolled (n=274). As of the December 2, 2024 data cutoff, results from ZN-c3-001 showed encouraging ORR and median duration of response (mDOR) at a total daily dose level $\geq 300\text{mg}$ in patients with Cyclin E1+ PROC who were dosed at an intermittent schedule (n=23). In these patients, an ORR of 34.8% (8/23; 95% CI: 16.4-57.3) and an mDOR of 5.2 months (95% CI: 2.8, 6.9) were observed. Full efficacy results at a total daily dose level $\geq 300\text{mg}$ across biomarker status and tumor types will be shared in the presentation.

In the ZN-c3-001 study, as of the December 2, 2024 data cutoff, azenosertib was shown to be tolerable at a total daily dose level $\geq 300\text{mg}$ (n=193) across all tumor types and regardless of biomarker status, with no Grade 3+ gastrointestinal treatment-related adverse events (TRAEs) observed and low rates of Grade 3+ hematological toxicity, with the majority of hematological toxicity events being Grade 3. There was also a low rate of TRAEs leading to discontinuation (n=10, 5.2%). There was one previously reported treatment-related Grade 5 event in the study (n=1, 0.5%). Additional safety results at clinically active dose levels across tumor types will be shared in the presentation.

MAMMOTH (ZN-c3-006)

MAMMOTH is a multi-arm study that evaluated azenosertib monotherapy and in combination with

niraparib in patients with PARP-inhibitor resistant ovarian cancer.

MAMMOTH is fully enrolled. In the monotherapy arm of the study (n=61), patients who were PARPi refractory were treated with azenosertib at the 300mg QD 5:2 or 400mg QD 5:2. As of the December 2, 2024 data cutoff, among Cyclin E1+ patients treated at the primary dose-of-interest, 400mg QD 5:2 (n=16), an ORR of 31.3% (5/16; 95% CI: 11.0 - 58.7) and an mDOR of 4.2 months (95% CI: 3.0 - not estimable) were observed. The upper end of the mDOR confidence interval was not estimable due to the small number of patients and events. Efficacy results across dose levels and biomarker status will be shared in the presentation.

As of the December 2, 2024 data cutoff, in the monotherapy arm of the MAMMOTH study at both 300mg QD 5:2 and 400mg QD 5:2 regardless of biomarker status, similar rates of treatment-related serious adverse events (SAEs) were observed across dose levels. There was a low rate of treatment-related Grade 3+ hematological toxicity with the majority being Grade 3 events. There was a low rate of TRAEs leading to treatment discontinuation 5.6% in the 400mg arm (n=2). There was one previously reported treatment-related Grade 5 event in the study (n=1, 1.6%). Additional safety results across dose levels will be shared in the presentation.

In the combination arms of the study, where azenosertib was dosed on a concurrent or alternating schedule with niraparib, although no new safety signals were observed, efficacious exposures of azenosertib were not reached, and the Company is not proceeding further with development of the combination with niraparib.

DENALI (ZN-c3-005) Part 1b

DENALI Part 1b is a single-arm study that evaluated azenosertib monotherapy at the 400mg QD 5:2 dose in patients with PROC (n=102). Tissue collection for biomarker assessment was mandated in the study and upon a retrospective analysis, approximately 50% of the patients were Cyclin E1+ per the Company's proprietary cutoff.

As of the December 2, 2024 data cutoff, in patients with Cyclin E1+ PROC tumors who were response-evaluable (patients who had at least one scan after receiving azenosertib), an ORR of 34.9% (15/43; 95% CI: 21.0 - 50.9) was observed. 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). As of the December 2, 2024 data cutoff, the mDOR for the intent-to-treat population was still maturing and was approximately 5.5 months (95% CI: 2.7 – not estimable).

As of the December 2, 2024 data cutoff, a safety and tolerability profile broadly consistent with ZN-c3-001 and MAMMOTH monotherapy was observed. There were two previously reported treatment-related Grade 5 events in the study (n=2, 2.0%). Additional safety results will be shared in the presentation.

ZN-c3-016

ZN-c3-016 is a Phase 1/2 study that evaluated azenosertib in combination with encorafenib and cetuximab in patients with metastatic BRAF V600E mutant colorectal cancer in collaboration with Pfizer.

The dose-finding phase of the ZN-c3-016 study is fully enrolled (n= 44). 34 patients were BRAF-inhibitor naïve and 10 had previously been treated with a BRAF-inhibitor. Topline results as of the November 25, 2024 data cutoff can be found in the appendix of the presentation. While the results in BRAF inhibitor naïve patients were encouraging, the Company decided not to advance into the dose expansion phase of the study due to resource prioritization and an evolving treatment landscape.

Corporate Event Details

On January 29, 2025, at 8:00am ET Zentalis will host a virtual corporate event to present data from its studies of azenosertib and provide a regulatory update. Access to a live webcast of this event, as well as an archived recording, will be available under the “[Events & Presentations](#)” tab on the Investors & Media section of the Company’s [website](#). Analysts who wish to join the teleconference and participate in Q&A should register [here](#).

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; our plans to hold a corporate event and present clinical data and provide a development and regulatory update, including the timing and content thereof; 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; our anticipated cash runway; the potential for azenosertib to be first-in-class and best-in-class; the broad franchise potential of azenosertib; the potential of azenosertib to address an unmet need in patients with Cyclin E1+ PROC and our plans to pursue further development in this patient population; our belief that we have a clear path to advance azenosertib to patients; the planned design of our clinical trials, including target enrollment numbers; the potential for Cyclin E1 to serve as a predictor for sensitivity to azenosertib; the therapeutic and commercial opportunity for azenosertib; the potential for DENALI Part 2 to support an accelerated approval for azenosertib; our positioning to execute; 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 accelerated approval. The terms “anticipated,” “ahead,” “believe,” “design,” “excited,” “expect,” “further,” “future,” “goal,” “intent,” “opportunity,” “path,” “plan,” “potential,” “promising,” “target,” 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.

Statements such as "compared to historical data" indicate that no head-to-head clinical trial has been conducted evaluating azenosertib against the indicated therapies. Notable differences exist between the Company's trial designs, conditions under study and subject characteristics as compared to the evaluated third party results and caution should be exercised when comparing data across these studies.

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