Zentalis Announces Intermittent Azenosertib Monotherapy Dosing Nearly Doubles Efficacy Over Continuous Dosing

ORR of 36.8% in heavily pretreated platinum-resistant ovarian cancer and USC patients treated with intermittent dosing

Establishes monotherapy RP2D of 400 mg QD with 5:2 dosing schedule; New RP2D more than doubles exposure levels, maintains safety and improves tolerability with no treatment-related discontinuations

Company plans to update efficacy data from Phase 1 monotherapy dose optimization study and provide program timeline updates for three azenosertib Phase 2 monotherapy trials currently enrolling patients at the RP2D in the second half of 2023

Investor call at 8:00 a.m. ET today to review azenosertib monotherapy data supporting dose selection and chemotherapy combination data presented at ASCO

NEW YORK & SAN DIEGO, June 6, 2023 – 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 monotherapy recommended Phase 2 dose (RP2D) for azenosertib, the Company's potentially first-in-class WEE1 inhibitor. Based on encouraging Phase 1 dose optimization clinical data, the RP2D for azenosertib as a monotherapy is 400 mg daily (QD) on a 5 days on, 2 days off (5:2) weekly administration schedule. This intermittent dosing schedule more than doubled steady state drug exposure in comparison to continuous dosing, and achieved promising efficacy signals, while maintaining safety and improving tolerability.

"With this new optimized monotherapy dosing schedule for azenosertib, we believe we have unlocked the therapeutic potential of WEE1 inhibition, achieving monotherapy activity levels few oncology agents have been able to attain," said Kimberly Blackwell, M.D., Chief Executive Officer of Zentalis. "Having demonstrated favorable anti-tumor activity as both a monotherapy and in combination with chemotherapy, we are confident azenosertib has tremendous promise to help patients with difficult-to-treat cancers. With our focus on platinum-resistant ovarian cancer for azenosertib as a monotherapy and platinum-sensitive ovarian cancer for azenosertib in chemotherapy combinations, we have the potential to address the majority of ovarian cancer patients. We are committed to rapidly advancing our azenosertib clinical strategy, concentrating on the fastest paths to market to reach patients in need."

Summary of Phase 1 Monotherapy Dose Optimization Data:

As of April 24, 2023, a total of 127 heavily pretreated patients with advanced solid tumors were treated with monotherapy azenosertib at doses ≥ 300 mg at either continuous daily dosing or intermittent weekly administration schedules. Across all tumor types, 74 patients were treated with continuous dosing schedules and 53 patients were treated with intermittent dosing schedules.

- The confirmed objective response rate (ORR) was 36.8% (7/19) in the combined ovarian cancer and uterine serous carcinoma (USC) subgroups who received an intermittent dosing schedule, versus 19.2% (5/26) in those who received a continuous dosing schedule.
- Steady state exposure, as measured by AUC_{0-24}, more than doubled at the new intermittent RP2D, compared to AUC observed at 300 mg QD with continuous administration.
- Intermittent dosing maintained azenosertib safety and improved tolerability as compared to continuous dosing. Gastrointestinal, fatigue, and hematologic Grade 3 and 4 treatment-related adverse events (TRAEs) were comparable or favorable versus continuous dosing. No discontinuations due to TRAEs were observed in the intermittent cohorts.
- The Company is currently enrolling patients at the new RP2D in three ongoing Phase 2 trials evaluating monotherapy azenosertib in the following patient populations:
    - Cyclin E1+, platinum-resistant high-grade serous ovarian cancer
    - USC
    - PARP inhibitor-resistant and platinum-resistant ovarian cancer (new cohort of ongoing study)

"WEE1 inhibition by monotherapy azenosertib has the potential to address the significant unmet need in ovarian cancer and uterine serous carcinoma, where patients often have limited treatment options," said Funda Meric-Bernstam, M.D., Chair of the Department of Investigational Cancer Therapeutics -- the Phase 1 Program at The University of Texas MD Anderson Cancer Center, and a member of the Zentalis Scientific Advisory Board. "Today's data supporting the newly established monotherapy dose – which demonstrates promising efficacy and improved tolerability – coupled with data supporting the combination of azenosertib with chemotherapy, suggest that this promising molecule has potential to be a highly effective therapeutic tool to fight difficult-to-treat cancers."

Dr. Blackwell added, "These data sets underpin our broader strategy to expand options for patients in a broad array of tumor types."

Conference Call

The Company will host a webcast today at 8:00 a.m. ET to review the azenosertib Phase 1 monotherapy data supporting dose selection, as well as the positive azenosertib plus chemotherapy Phase 1b combination data presented at the 2023 ASCO Annual Meeting. The webcast will be accessible via the Investors page of Zentalis' website, www.zentalis.com. The archived webcast and presentation will be available on the Company's website after the event.

About Azenosertib

Azenosertib is a potentially first-in-class and best-in-class small molecule WEE1 inhibitor in development for the treatment of cancer. Inhibition of WEE1, a DNA damage response kinase, drives cancer cells into mitosis without being able to repair damaged DNA, resulting in cell death. Currently, there are no FDA-approved WEE1 inhibitors, and azenosertib has been designed for superior selectivity and pharmacokinetic properties. Azenosertib is being developed in therapeutic areas of high unmet need and is being evaluated as a monotherapy, in combination with chemotherapy, and in combination with molecularly targeted agents.

About Zentalis Pharmaceuticals

Zentalis® Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company discovering and developing small molecule therapeutics targeting fundamental biological pathways of cancers. Utilizing its Integrated Discovery Engine, the Company is developing a focused pipeline of potentially best-in-class oncology candidates, which include azenosertib (ZN-c3), a WEE1 inhibitor for advanced solid tumors, ZN-d5, a BCL-2 inhibitor for hematologic malignancies and related disorders, and a heterobifunctional degrader of BCL-xL for solid and hematological malignancies. 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 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 provide clinical data and program timeline updates, and the timing thereof; the potential for azenosertib to be first-in-class and best-in-class; the potential benefits of azenosertib; our belief that we have unlocked the therapeutic potential of WEE1 inhibition; our belief and confidence that azenosertib has tremendous promise to help patients with difficult-to-treat cancer; the potential addressable patient population of azenosertib, including the ovarian cancer patient population; our plans to rapidly advance our azenosertib clinical and regulatory strategy; the potential for azenosertib to address significant unmet need in ovarian cancer and USC; the potential for azenosertib to be a highly effective therapeutic tool to fight difficult-to-treat cancers; our broader strategy to expand options for patients in a broad array of tumor types; the potential benefits of the design of azenosertib; and the potential for our product candidates to be best-in-class. The terms "believe," "committed," "confident," "design," "encouraging," "plan," "potential," "promising," "strategy," "suggest," "to be," "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; 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.

Investor Contacts:
Adam D. Levy, PhD, MBA
alevy@zentalis.com

Emily White
Solebury Strategic Communications
ewhite@soleburystrat.com

Media Contact:
Danielle Cantey
Evoke Canale
danielle.cantey@evokegroup.com
(619) 826 4657