NEWS RELEASE

Zentalis Pharmaceuticals To Present Azenosertib Preclinical Data in Triple-Negative Breast Cancer and Real-World Analysis of Unmet Need in Cyclin E1-Positive Ovarian Cancer at AACR 2026

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- Preclinical data show encouraging activity of azenosertib combinations in ADC-resistant TNBC, supporting the potential for pipeline expansion beyond ovarian cancer
- Real-world data demonstrate Cyclin E1-positive ovarian cancer patients have significantly worse outcomes, independent of CCNE1 gene amplification status, reinforcing the potential for azenosertib to address the unmet need for these patients

SAN DIEGO, April 17, 2026 (GLOBE NEWSWIRE) -- Zentalis® Pharmaceuticals, Inc. (Nasdaq: ZNTL), a clinical oncology innovator advancing late-stage development of investigational first-in-class WEE1 inhibitor azenosertib as a biomarker-driven treatment approach for ovarian cancer, today announced data from two posters being presented at the 2026 American Association for Cancer Research (AACR) Annual Meeting, taking place April 17-22, 2026, in San Diego, CA. The data show encouraging preclinical activity of azenosertib in triple-negative breast cancer (TNBC) and highlight the poor prognosis of Cyclin E1-positive ovarian cancer patients with currently available treatments in a real-world data analysis.

Compelling Preclinical Activity in Triple-Negative Breast Cancer with Azenosertib

"The preclinical data in triple-negative breast cancer being presented at AACR showed that azenosertib combinations can induce complete tumor responses in a model resistant to emerging ADC therapies, supporting the potential to broaden the impact of azenosertib beyond ovarian cancer," said Julie Eastland, Chief Executive Officer of Zentalis. "This includes potential development of azenosertib through differentiated combination strategies with antibody-drug conjugates (ADCs) and chemotherapy. As ADCs advance toward first-line use in TNBC, effective post-ADC treatment strategies represent a growing unmet need that azenosertib combinations may be uniquely positioned to fill. Our data suggest azenosertib may achieve this through multiple mechanisms – possibly resensitizing tumors to chemotherapy, enhancing the responses to ADC, and extending the duration of response – which is an exciting potential future direction for our pipeline."

Preclinical evidence supports azenosertib as a therapeutic strategy in TNBC:

- TNBC cell lines showed higher Cyclin E1 expression and greater sensitivity to WEE1 inhibition compared to other breast cancer cell lines
  - Azenosertib monotherapy demonstrated meaningful antitumor activity across a diverse panel of 12 TNBC *in vivo* xenograft models (42-99% tumor growth inhibition)
- In a patient-derived xenograft model of TNBC with clinical resistance to sacituzumab govitecan, an approved topoisomerase 1 inhibitor (TOPO1i) ADC, azenosertib + enfortumab vedotin (EV):
  - Induced complete responses in 7 of 8 mice (87.5%); 5 mice did not progress after treatment discontinuation
  - Prevented tumor progression in 8 of 8 mice for more than 52 days compared to 100% progression observed within 30 days with EV alone
  - Drove deep tumor regression in mice models refractory to sacituzumab govitecan or trastuzumab deruxtecan with large tumor volumes (average ~900mm^3)
- Combinations of azenosertib with TOPO1i-payload ADCs (sacituzumab govitecan, datopotamab deruxtecan, or trastuzumab deruxtecan) enhanced both depth and duration of response compared to ADC monotherapy in ADC-naïve models
- Azenosertib + paclitaxel restored substantial sensitivity to paclitaxel in a model resistant to both paclitaxel and TOPO1i ADCs (51% tumor growth inhibition vs. 16% with paclitaxel alone)

Cyclin E1 Protein Overexpression Characterizes Ovarian Cancer Patients with Poor Prognosis

"The real-world data being presented at AACR provide important validation that Cyclin E1-positive ovarian cancer patients face a particularly challenging disease trajectory with standard-of-care therapies," said Ingmar Bruns, M.D., Chief Medical Officer of Zentalis. "The consistency of worse outcomes across independent cohorts and multiple treatment settings underscores the significant unmet need in this population. These findings provide important context for Zentalis' registration-intended DENALI and ASPENOVA studies, which are evaluating WEE1 inhibition with azenosertib monotherapy as a targeted approach for the Cyclin E1-positive population that currently has limited effective treatment options."

Real-world data from two independent cohorts (Tempus Lens Ovarian cancer dataset and Zentalis' historical clinical trials) consistently demonstrated that Cyclin E1-positive ovarian cancer patients experience worse clinical outcomes:

- After first-line treatment, Cyclin E1-positive patients, with or without CCNE1 gene amplification, had shorter time to next treatment compared to Cyclin E1-negative patients (13.2 months and 14.9 months, respectively, compared to 19.5 months, p=0.002)
- Cyclin E1-positivity is associated with a trend toward reduced clinical benefit from standard-of-care PROC treatments

AACR Poster Details

Title: “WEE1 Inhibition as a Therapeutic Strategy in Triple-Negative Breast Cancer: Evaluating Single Agent and Combination Activity of Azenosertib in Preclinical Models”
Abstract Number: 2012
Date/Time: Monday, April 20, 2026, 2:00 p.m. - 5:00 p.m. PDT
Presenting Author: Alexandra Levy, MS

Title: “Real-World Treatment Patterns and Outcomes Reveal Distinct Clinical Trajectories of Patients with Cyclin E1-Positive Ovarian Cancer”

Abstract Number: 1708
Date/Time: Sunday, April 19, 2026, 2:00 p.m. - 5:00 p.m. PDT
Presenting Author: Jinkil Jeong, PhD

The posters can be accessed on the Supporting Publications page of the Zentalis website.

About Azenosertib
Azenosertib is an investigational, potentially first-in-class, selective, and orally bioavailable inhibitor of WEE1 currently being evaluated in 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.

Azenosertib is in late-stage development as a potential treatment for Cyclin E1-positive platinum-resistant ovarian cancer (PROC). There is currently no approved treatment option specifically for this biomarker-selected population which comprises approximately 50% of PROC patients. Cyclin E1 protein overexpression has been established as a sensitive and specific predictive biomarker for identifying patients who could potentially derive benefit from azenosertib treatment, based on retrospective analysis of azenosertib studies in PROC. Validation of the Cyclin E1 companion diagnostic assay is ongoing in the DENALI and ASPENOVA trials.

Azenosertib has been granted Fast Track Designation by the U.S. FDA for the treatment of patients with Cyclin E1-positive platinum-resistant ovarian cancer. Fast Track Designation is intended to facilitate the development and expedite the review of therapies that have the potential to treat serious conditions and address unmet medical needs.

About Zentalis Pharmaceuticals
Zentalis is a clinical oncology innovator developing a treatment approach for ovarian cancer and multiple tumor types. Leveraging therapeutics development and biomarker expertise, Zentalis is advancing monotherapy and combination studies of its first-in-class WEE1 inhibitor, azenosertib. Focused on translating WEE1 science into clinical practice, we aim to equip physicians with a targeted, non-chemo, orally available medicine that enhances treatment experience, choice, and outcomes. Our mission: to unburden cancer patients with more convenience and care.

For more information, please visit www.zentalis.com. Follow Zentalis 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 continued development of azenosertib; the clinical and therapeutic potential of azenosertib; the potential for azenosertib to be first-in-class; the potential benefits of azenosertib, including the potential for azenosertib to be an important treatment option for patients with ovarian cancer, triple negative breast cancer or other indications, the mechanisms through which azenosertib may fill unmet needs, and the ability of azenosertib combinations to induce complete tumor responses; the unmet need for treatments in ovarian cancer, triple negative breast cancer or other indications; the broad franchise potential of azenosertib; the Company's biomarker-driven strategy for azenosertib; the future direction of our pipeline, including the potential for pipeline expansion; and our participation in poster presentations. The terms "anticipate," "advance," "believe," "design," "develop," "encouraging" "expect," "future," "intent," "look forward," "may," "on track," "plan," "position," "potential," "runway," "strategy," "target," "upcoming,"

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 substantial dependence on the success of azenosertib; our plans, including the costs thereof, of development of companion diagnostics; the outcome of preclinical testing and early trials may not be predictive of the success of later clinical trials; potential unforeseen events during clinical trials could cause delays or other adverse consequences; risks relating to the regulatory approval process or ongoing regulatory obligations; our product candidates may cause serious adverse side effects; the interim, initial, "topline," and preliminary data from our clinical trials may change as more patient data becomes available, and are subject to audit and verification procedures that could result in material changes in the final data; 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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