UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of report (Date of earliest event reported): May 25, 2023

ZENTALIS PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-39263**	**82-3607803**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

1359 Broadway, Suite 801
New York, New York 10018
(Address of principal executive offices) (Zip Code)

(212) 433-3791
(Registrant's telephone number, include area code)

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	ZNTL	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On May 25, 2023, Zentalis Pharmaceuticals, Inc. (the "Company") issued the press release furnished as Exhibit 99.1 to this Current Report on Form 8-K (this "Current Report") and incorporated herein by reference.

The information contained in Item 7.01 of this Current Report (including Exhibit 99.1 attached hereto) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, except as expressly provided by specific reference in such a filing.

Item 8.01 Other Events.

On May 25, 2023, the Company announced positive data from the Phase 1b trial of azenosertib, the Company's potentially first-in-class WEE1 inhibitor, in combination with chemotherapy in patients with platinum-resistant ovarian cancer. Azenosertib was well tolerated in combination with multiple types of chemotherapy and demonstrated encouraging clinical activity, with noteworthy improvements in objective response rates ("ORRs") and median progression free survival ("mPFS") in all patients, especially those with Cyclin E1+ tumors, a subgroup recognized to have a poor prognosis and be refractory to chemotherapy. Results will be presented in a poster discussion session at the 2023 American Society of Clinical Oncology Annual Meeting on June 5th.

Efficacy and Safety Results:

A total of 115 patients were enrolled in the study across all chemotherapy combination groups. At the data cut-off of April 10, 2023, 94 were response evaluable. Across all dosing schedules, azenosertib plus paclitaxel demonstrated the highest ORR of 50.0% (mPFS of 7.4m; mDOR of 5.6m), followed by an ORR of 38.5% (mPFS of 8.3m; mDOR of 6.2m) for azenosertib plus gemcitabine. Azenosertib plus carboplatin demonstrated an ORR of 35.7% (mPFS of 10.4m; mDOR of 11.4m), and azenosertib plus PLD demonstrated an ORR of 19.4% (mPFS of 6.3m; mDOR of 8.3m).

Of patients who had available tissue for immunohistochemistry ("IHC"), 87% were Cyclin E1+ (H-score >50). Cyclin E1+ status was associated with a superior ORR and a longer mPFS across the response-evaluable patient population with IHC data (ORR of 40.0% vs 8.3%; mPFS of 9.86 vs 3.25 months; HR = 0.37; P = 0.0078), showcasing the potential synergy of WEE1 inhibition with chemotherapy in this patient population.

Frequent Grade ≥3 treatment-related adverse events (%) across all azenosertib intermittent dosing groups were thrombocytopenia (27.5%), neutropenia (25.5%), anemia (15.7%), and fatigue (9.8%). A recommended Phase 2 dose was determined for each of the azenosertib combinations with paclitaxel, carboplatin, and PLD.

Based on these results, the Company is planning to initiate a Phase 3 study comparing azenosertib dosed intermittently in combination with either carboplatin or paclitaxel in patients with Cyclin E1+ platinum-sensitive ovarian cancer. The Company expects to initiate the Phase 3 study in the first quarter of 2024.

Cautionary Note Regarding Forward-Looking Statements

Statements in this Current Report regarding the Company's strategy, plans, prospects, expectations, beliefs, intentions and goals are forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements regarding the potential benefits of azenosertib in combination with chemotherapy; the potential for azenosertib to be first-in-class; the Company's plans to present information regarding azenosertib, and the timing and content thereof; future initiation of clinical studies and the expected timing thereof; and the potential for synergy of WEE1 inhibition with chemotherapy in patients with Cyclin E1+ tumors. The terms "plan," "potential," "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 the Company's 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: the Company's limited operating history, which may make it

difficult to evaluate the Company's current business and predict the Company's future success and viability; the Company has and expects to continue to incur significant losses; the Company's need for additional funding, which may not be available; the Company's plans, including the costs thereof, of development of any companion diagnostics; the Company's substantial dependence on the success of its 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; the Company's product candidates may cause serious adverse side effects; inability to maintain collaborations, or the failure of these collaborations; the Company's reliance on third parties; effects of significant competition; the possibility of system failures or security breaches; risks relating to intellectual property; the Company's 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 the Company's 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 the Company's other filings with the SEC. These forward-looking statements (except as otherwise noted) speak only as of the date of this Current Report, and the Company does not undertake, and specifically disclaims, any obligation to update any forward-looking statements contained in this Current Report.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

The following Exhibit 99.1 relating to Item 7.01 shall be deemed to be furnished, and not filed:

ExhibitNo.	Description
99.1	Press Release issued on May 25, 2023.
104	Cover Page Interactive Data File (embedded within the inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

ZENTALIS PHARMACEUTICALS, INC.

Date: May 26, 2023

By: /s/ Melissa Epperly
Melissa Epperly
Chief Financial Officer

Exhibit 99.1

Zentalis Announces Presentation of Positive Phase 1b Data Demonstrating Durable Responses and Favorable Safety Profile of Azenosertib in Combination with Chemotherapy at the 2023 ASCO Annual Meeting

Strong anti-tumor activity shown in a platinum-resistant ovarian cancer population, with a confirmed ORR of 50.0% and mPFS of 7.4 months in combination with paclitaxel, and a confirmed ORR of 35.7% and mPFS of 10.4 months in combination with carboplatin

Patients with Cyclin E1+ tumors benefited most in chemotherapy combination arms, illustrating potential synergy between azenosertib and chemotherapy in this patient population

Intermittent dosing of azenosertib in combination with either paclitaxel or carboplatin compares favorably to historic tolerability data from chemotherapy doublets or other WEE1 inhibitor-chemotherapy combinations

Company plans to initiate Phase 3 trial of azenosertib using intermittent dosing in combination with chemotherapy in Cyclin E1+ platinum-sensitive ovarian cancer in the first quarter 2024

Live webcast to be held on Tuesday, June 6th at 8:00 a.m. ET

NEW YORK & SAN DIEGO, May 25, 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 positive data from the Phase 1b trial of azenosertib, the Company's potentially first-in-class WEE1 inhibitor, in combination with chemotherapy in patients with platinum-resistant ovarian cancer. Azenosertib was well tolerated in combination with multiple types of chemotherapy and demonstrated encouraging clinical activity, with noteworthy improvements in objective response rates (ORRs) and median progression free survival (mPFS) in all patients, especially those with Cyclin E1+ tumors, a subgroup recognized to have a poor prognosis and be refractory to chemotherapy. Results will be presented in a poster discussion session at the 2023 ASCO Annual Meeting on June 5th (Abstract #5513).

"Azenosertib is emerging as a very promising clinical candidate, with demonstrated anti-tumor activity in difficult-to-treat tumor types when used in combination with standard chemotherapy regimens," said Kimberly Blackwell, M.D., Chief Executive Officer of Zentalis. "The addition of azenosertib increased ORRs and mPFS over those observed historically with chemotherapy alone, or compared to adavosertib in combination with chemotherapy. We are very encouraged by our robust chemotherapy combination data, particularly the strong efficacy and tolerability results when dosing azenosertib intermittently. These data provide a compelling rationale to advance azenosertib into a registrational study in combination with either carboplatin or paclitaxel in Cyclin E1+ ovarian cancer. We look forward to providing additional insights into our azenosertib clinical programs and the franchise potential we see for this product candidate during our June 6 investor webcast."

Efficacy and Safety Results:

A total of 115 patients were enrolled in the study across all chemotherapy combination groups. At the data cut-off of April 10, 2023, 94 were efficacy evaluable. Across all dosing schedules, azenosertib plus paclitaxel demonstrated the highest ORR of 50.0% (mPFS of 7.4m), followed by an ORR of 38.5% (mPFS

of 8.3m) for azenosertib plus gemcitabine. Azenosertib plus carboplatin demonstrated an ORR of 35.7% (mPFS of 10.4m), and azenosertib plus PLD demonstrated an ORR of 19.4% (mPFS of 6.3m).

A total of 82 response-evaluable patients had available Cyclin E1 expression data by immunohistochemistry (IHC). Cyclin E1+ status (H-score >50) was associated with a superior ORR and a longer mPFS across the total patient population (ORR of 40.0% vs 8.3%; mPFS of 9.86 vs 3.25 months, HR = 0.37; P = 0.0078), showcasing the potential synergy of WEE1 inhibition with chemotherapy in this patient population.

Overall, the tolerability of azenosertib dosed intermittently in combination with either paclitaxel or carboplatin compares favorably to historical data from standard of care chemotherapy doublets of either paclitaxel-carboplatin or PLD-carboplatin. Frequent Grade ≥3 treatment-related adverse events (%) across all azenosertib intermittent dosing groups were thrombocytopenia (27.5%), neutropenia (25.5%), anemia (15.7%), and fatigue (9.8%). A recommended Phase 2 dose was determined for each of the azenosertib combinations with paclitaxel, carboplatin, and PLD.

Based on these results, the Company is planning to initiate a Phase 3 study comparing azenosertib dosed intermittently in combination with either carboplatin or paclitaxel in patients with Cyclin E1+ platinum-sensitive ovarian cancer. The Company expects to initiate the Phase 3 study in the first quarter of 2024.

“The results thus far for azenosertib in combination with chemotherapy are very promising, as there remains high unmet need in this patient population, particularly patients with Cyclin E1+ tumors who historically have not responded well to chemotherapy,” said Joyce Liu, M.D., M.P.H., Associate Chief and Director of Clinical Research for the Division of Gynecologic Oncology at the Dana-Farber Cancer Institute. “I look forward to continuing to work with the Zentalis team to advance azenosertib in the clinic and, if approved, ultimately into medical practice as an important and novel treatment option for platinum-sensitive ovarian cancer patients.”

Premal H. Thaker, M.D., Professor of Obstetrics and Gynecology, Director of Gynecological Oncology Clinical Research, Division of Gynecologic Oncology, Washington University School of Medicine, and an investigator on the study added, “The data for azenosertib in combination with chemotherapy are increasingly robust and encouraging. Moreover, the enrichment of patients by Cyclin E1+ status provides a compelling strategy for future clinical trials. I look forward to the initiation of a study examining the role of azenosertib in combination with chemotherapy in earlier lines of therapy.”

The Company will host a webcast on Tuesday, June 6, 2023 at 8:00 a.m. ET to provide a clinical update, including an overview of the ASCO data, as well as safety, pharmacology and efficacy results for azenosertib as a monotherapy, and plans for future development of azenosertib as a monotherapy and in combination with chemotherapy. The corporate 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.

ASCO Presentation Details:

Poster Title: Correlation of Cyclin E1 expression and clinical outcomes in a Phase 1b dose-escalation study of Azenosertib (ZN-c3), a WEE1 inhibitor, in combination with chemotherapy in patients with platinum-resistant or refractory (R/R) epithelial ovarian, peritoneal, or fallopian tube cancer
Presenter: Dr. Liu, M.D., M.P.H., Associate Chief and Director of Clinical Research for the Division of Gynecologic Oncology at the Dana-Farber Cancer Institute.
Session Title: Gynecologic Cancer

Session Date and Time: Monday, June 5, 2023, 1:15 – 4:15 p.m. CT
Location: Hall A
Poster Board Number: 208
Poster Discussion Session Date and Time: Monday, June 5, 2023, 4:30 – 6:00 p.m. CT
Location: S100bc
Abstract Presentation Number: 5513

A video summary of the poster by Dr. Liu will be available on the ASCO virtual platform.

Once presented, the poster can be found on the Company's website using this link.

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 focused on 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 the potential benefits of azenosertib in combination with chemotherapy; the potential for azenosertib to be first-in-class and best-in-class; the potential benefits of azenosertib and its promise as a clinical candidate and, if approved, a treatment used in medical practice; our plans to provide additional insights into and information with respect to our azenosertib clinical program and the franchise potential for azenosertib, and the timing and content thereof; future initiation of clinical studies and the expected timing thereof; the potential for synergy of WEE1 inhibition with chemotherapy in patients with Cyclin E1+ tumors; plans to advance azenosertib in the clinic; and the potential benefits of the design of azenosertib. The terms "continuing," "design," "encouraging," "expects," "look forward," "plan," "potential," "promising," "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