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): June 28, 2021

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.)**

530 Seventh Avenue, Suite 2201
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 8.01. Other Events.

On June 28, 2021, Zentalis Pharmaceuticals, Inc. (the Company) announced clinical and regulatory updates across its pipeline of product candidates, including new interim clinical data from Phase 1 clinical trials of ZN-c3, a WEE1 inhibitor for advanced solid tumors, and ZN-c5, an oral selective estrogen receptor degrader (SERD).

Interim data results from the Phase 1 monotherapy trial of ZN-c3 as of a data cut-off date of May 15, 2021 are as follows:

- Two unconfirmed Partial Responses (PRs) previously reported at AACR were confirmed, bringing the total number of confirmed PRs from the ongoing Phase 1 monotherapy trial from three to five. Since reporting initial clinical data at AACR, an additional unconfirmed PR was reported in a patient with uterine serous carcinoma (USC), resulting in three out of seven USC patients enrolled having responded to treatment. Overall, the objective response rate (ORR) increased from 40% to 43% based on RECIST criteria. Clinical results were seen across four different tumor types, signaling potential for broad oncology application.

- Within the exceptional responder population of the ongoing Phase 1 monotherapy trial, in a patient with an ongoing treatment duration of more than eight months, the Company observed a deepening response of 65% to 69% tumor size decrease based on RECIST criteria.

In addition, as of a data cut-off date of May 14, 2021, ZN-c3 was observed to be well-tolerated, with a lower overall rate of severe hematological adverse events relative to that previously reported at AACR with respect to the previous data cut-off date of February 12, 2021. The rate of treatment related white blood cell count decrease / neutropenia decreased to 2.2% as of the May 14, 2021 data cut-off date from 3.6% as of the February 12, 2021 data cut-off date.

Additional regulatory and clinical updates announced with respect to ZN-c3 are as follows:

- Following an end-of-Phase 1 meeting, the U.S. Food and Drug Administration (FDA) concurred in principle with the proposal that ZN-c3 has the potential for an accelerated approval pathway based on the proposed global study design of ZN-c3-004, a Phase 2 monotherapy trial planned with registrational intent in women with recurrent or persistent USC. The trial has been initiated, with multiple sites open to date.

- The Company intends to launch a biomarker-driven Phase 2, study subject to FDA feedback. This Phase 2 tumor agnostic trial planned with registrational intent, which the Company expects to initiate by the end of 2021, would investigate ZN-c3 in patients with solid tumors that express the identified predictive biomarker.

- ZN-c3, in combination with chemotherapy, has received orphan drug designation, and rare pediatric disease designation from the FDA for pediatric osteosarcoma. The Company intends to initiate a Phase 1/2 clinical trial of ZN-c3 in combination with chemotherapy in pediatric patients with osteosarcoma in the third quarter of 2021. Additionally, if ZN-c3 were to obtain approval for the designated indication, the Company believes it may be eligible for a rare pediatric disease priority voucher upon approval.

- The Company will support two planned additional investigator-initiated trials: a trial with the Ivy Brain Center in glioblastoma multiforme that the Company expects to initiate in 2021, and a trial in combination with immunotherapy with Dana Farber in triple negative breast cancer that the Company expects to initiate in 2022.

- The Company's China joint venture, Zentera, is advancing corresponding clinical trial in China in ZN-c3.

The Company announced the following clinical updates with respect to its ongoing clinical trials evaluating ZN-c5 in combination and as monotherapy:

- In the ongoing Phase 1 monotherapy dose escalation and expansion studies evaluating a total of 56 patients with two median prior lines of treatment for safety and efficacy, the Company observed a clinical benefit rate (CBR) of 54% and an ORR of 13% at the 300 mg, once daily (QD), dose as of the May 11, 2021 data cut-off. Across all doses from 50 mg to 300 mg QD, the observed CBR was 33% and the ORR was 5%. ZN-c5 generated two PRs at the 150 mg and 300 mg doses. As of the May 11, 2021 data cut-off, treatment emergent adverse events (AEs) were found in less than 10% of the patients and there were no observed cases of bradycardia, visual disturbances, QTC or dizziness. Of note, treatment related diarrhea adverse event was 3.6%, with only Grade 1 or 2 events observed. The Phase 2 monotherapy trial has been initiated and the Company may evaluate ZN-c5 at multiple dose levels within the study. An oral dose of 50 mg QD (n=16) demonstrated a CBR of 40%, with many patients in this dose cohort remaining on study drug and in the trial. Final determination of the monotherapy recommended phase 2 dose (RP2D) will occur following completion of this 50 mg QD dose cohort.

- In the ongoing Phase 1/2 clinical trial evaluating ZN-c5 in combination with Pfizer's CDK4/6 palbociclib, and the Phase 1b clinical trial evaluating ZN-c5 in combination with Lilly's CDK4 and 6 abemaciclib, the safety and tolerability data suggested ZN-c5 has the potential to be a promising candidate for further evaluation in combinations. As of the May 11 cut-off, individual AEs related to ZN-c5 were found in less than 10% of the patients and no grade 3 or grade 4 AEs related to ZN-c5 were observed. The Company continues to enroll patients in the two separate combination trials and expects to report initial results in the first half of 2022 from one or more of these trials.

- In the ongoing Window of Opportunity Initial Biomarker study (n=35), estrogen receptor degradation was observed across all doses tested. One patient in the 300 mg dose cohort with Grade 3/4 LFT increases resolved without incident after study end. The Company continues to enroll patients in the Window of Opportunity study.

Additionally, the Company announced the following clinical updates with respect to its ZN-d5, a BCL-2 inhibitor for hematologic malignancies, and ZN-e4, an EGFR inhibitor for non-small cell lung cancer, product candidates:

- The Phase 1 monotherapy dose escalation trial for ZN-d5, initiated in the fourth quarter of 2020, has enrolled 14 patients with relapsed/refractory Non-Hodgkin's Lymphoma thus far in the fifth dose cohort. Additionally, no dose limiting toxicities have been identified. The Company expects patients with acute myeloid leukemia will begin enrollment in the third quarter of 2021. The Company intends to report initial results from this Phase 1 trial in the first half of 2022.

- The ongoing Phase 1/2 dose escalation trial for ZN-e4 in patients with advanced non-small cell lung cancer has enrolled 26 patients to date, both osimertinib-naïve and experienced. ZN-e4 has been well-tolerated at all doses as of the March 25, 2021 data cut-off, and clinical activity was identified at doses greater than 80 mg QD. The Company intends to report initial results from the Phase 1/2 trial in the fourth quarter of 2021.

Any statements in this Current Report that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding our expectations surrounding the development, potential, safety, efficacy, and regulatory and clinical progress of our product candidates in the Unites States and globally, and plans and timing for the initiation of and the release of data from our clinical trials and our ability to meet other key milestones. 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: the COVID-19 pandemic has adversely impacted and may continue to adversely impact our business, including our preclinical studies and clinical trials; 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 our lead product candidates; failure to identify additional product candidates and develop or commercialize marketable products; the early stage of our development efforts; 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 significant costs as a result of operating as a public company. These and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 filed with the U.S. Securities and Exchange Commission (SEC) and our other filings with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this Current Report. 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.

The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

The following exhibits relating to Item 8.01 shall be deemed to be furnished, and not filed:

Exhibit No.	Description
99.1	Press Release issued on June 28, 2021.
99.2	Corporate Update Presentation of Zentalis Pharmaceuticals, Inc., dated June 28, 2021.
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: June 28, 2021

By: /s/ Anthony Y. Sun, M.D.
Anthony Y. Sun, M.D.
President and Chief Executive Officer

Zentalis Pharmaceuticals Announces Updates Across its Pipeline Including Promising New Interim Clinical Data on ZN-c3 (WEE1) and ZN-c5 (SERD) and Two Potentially Registrational Trials for ZN-c3, with the First Trial Already Launched

Reports additional ZN-c3 Phase 1 interim monotherapy data demonstrating increased tumor reduction and durability in the exceptional responder population, as well as newly confirmed responses and an additional unconfirmed PR in USC

Potential accelerated approval path identified for monotherapy use of ZN-c3 in USC following End-of-Phase 1 FDA meeting, with registrational study recently initiated

Company will seek FDA guidance on a potentially registrational trial for a tumor-agnostic, novel predictive biomarker enabled ZN-c3 trial by year-end

Orphan drug and rare pediatric disease designations granted for ZN-c3 in combination with chemotherapy for osteosarcoma, trial expected to initiate in 3Q 2021

Interim data from ZN-c5 Phase 1 clinical trial supports its potential best-in-class safety and tolerability profiles in monotherapy and in combinations

Company to host webcast event today, June 28, 2021 at 8:30 a.m. EDT

NEW YORK and SAN DIEGO, June 28, 2021 – Zentalis Pharmaceuticals, Inc. (Nasdaq: ZNTL), a clinical-stage biopharmaceutical company focused on discovering and developing small molecule therapeutics targeting fundamental biological pathways of cancers, today announced key clinical and regulatory updates across its pipeline.

“We continue to build substantial value in Zentalis’ portfolio, driving toward approval of our differentiated cancer therapeutics to help patients worldwide,” commented Dr. Anthony Sun, Chairman and Chief Executive Officer of Zentalis. “Based on our clinical results reported to date, the emerging clinical profiles of our candidates support the potential for best-in-class positioning for a range of tumor types addressing large patient populations, is use as a monotherapy or in combinations. In particular, we are excited about the compelling profile of ZN-c3, our WEE1 inhibitor, as it demonstrated additional, deepening and durable tumor responses as a monotherapy in heavily pretreated solid tumors. These promising data set the stage for the many upcoming planned trials – two of which have the potential to be registrational monotherapy studies in indications with significant unmet medical needs. We look forward to a productive second half of 2021, as we focus on delivering on our milestones across our entire pipeline.”

ZN-c3: Oral WEE1 Inhibitor for Solid Tumors

Updates from our ongoing trials of ZN-c3 continue to support the potential for our WEE1 inhibitor, ZN-c3, to be both first-in-class and best-in-class. Since our last update at AACR in April 2021, and as of the data cut-off date of May 15, 2021:

- The 2 unconfirmed Partial Responses (PRs) reported at AACR were confirmed, bringing the total number of confirmed PRs from our monotherapy trial from 3 to 5. Since AACR, an additional unconfirmed PR was reported in a patient with uterine serous carcinoma (USC), resulting in 3 out of 7 USC patients enrolled having responded to treatment. Overall, the objective response rate (ORR) in the USC population increased from 40% to 43% based on RECIST criteria.
- Additionally, within the exceptional responder population in the Phase 1 monotherapy trial, we have observed a patient with an ongoing treatment duration of more than 8 months, with deepening response of 65% to 69% tumor size decrease based on RECIST criteria.
- Lower overall severe hematological adverse event rates – severe neutropenia adverse event rates decreased from 2.9% to 2.2% with an additional 11 patients enrolled since AACR 2021.
- Following an End-of-Phase 1 meeting, the U.S. Food and Drug Administration (FDA) concurred in principle with the proposal that ZN-c3 has the potential for an accelerated approval pathway based on the proposed global study design of a Phase 2 monotherapy trial in women with recurrent or persistent USC. The trial has initiated with multiple sites open.
- Zentalis is planning to launch a biomarker-driven Phase 2 study pending FDA feedback. The tumor-agnostic trial will investigate ZN-c3 in patients with solid tumors that express the identified predictive biomarker, and is expected to initiate by year-end.
- ZN-c3 has received orphan drug designation, and rare pediatric disease designation from the FDA for pediatric osteosarcoma. The Phase 1/2 trial of ZN-c3 in combination with chemotherapy in pediatric patients with osteosarcoma is expected to initiate in 3Q 2021. If ZN-c3 were to obtain approval for the designated indication, it could be eligible for a rare pediatric disease priority voucher upon approval.
- Zentalis will also support two planned additional investigator-initiated trials: a trial with the Ivy Brain Center in glioblastoma multiforme (GBM) and a trial with immunotherapy with Dana Farber in triple negative breast cancer.
- Zentalis' China JV Zentera is advancing corresponding clinical trials in China with ZN-c3.

ZN-c5: Oral SERD for ER+/HER2- Advanced or Metastatic Breast Cancer

Based on the interim results from multiple ongoing trials, ZN-c5 has demonstrated the potential to support best-in-class tolerability in both monotherapy and combination settings, with strong clinical results observed. As of May 11, 2021, the following data were collected:

Monotherapy Trials (Expansion and Dose Escalation)

- In total, 56 patients with 2 median prior lines of treatment were evaluated for safety and efficacy. Across all doses from 50 mg QD to 300 mg QD, the observed CBR was 33% and the ORR was 5%. ZN-c5 generated 2 PRs at the 150 mg and 300 mg doses. Adverse events (AEs) were found in less than 10% of the patients and there were no observed cases of bradycardia, visual disturbances, QTC or dizziness. Of note, treatment related diarrhea adverse event rate was 3.6%, with only grade 1 or 2 events observed. The Phase 2 monotherapy trial has been initiated and Zentalis may take multiple doses into this study.

- An oral dose of 50 mg QD (n=16) demonstrated a CBR of 40%, with many patients in this dose cohort remaining on study drug and in the trial. Final determination of the monotherapy RP2D will occur following completion of this 50 mg QD dose cohort.

Combination Dose Escalation Trials with Pfizer's CDK4/6 Palbociclib and Lilly's CDK4 and 6 Abemaciclib

- Tolerability data for ZN-c5 suggests it could be best-in-class in oral SERDS, making this candidate ideal for further evaluation in combination. The two separate trials will continue to enroll patients and the Company expects to report interim results in 1H 2022 from one or more of these trials.

Window of Opportunity Trial

- The Window of Opportunity trial (n=35) demonstrated ER degradation across all doses tested.

ZN-d5: Highly Selective Oral BCL-2 Inhibitor for Hematologic Tumors

- The Phase 1 monotherapy dose-escalation trial, initiated in 4Q 2020, has enrolled 14 patients with relapsed/refractory Non-Hodgkin's lymphoma (NHL) thus far in the fifth dose cohort. Additionally, no dose-limiting toxicities have been identified. Patients with acute myeloid leukemia will begin enrollment in 3Q 2021. Interim results from this Phase 1 trial are expected in 1H 2022.

ZN-e4: 3rd Generation Oral EGFR Inhibitor for Non-Small-Cell Lung Carcinoma

- The Phase 1/2 dose-escalation trial in patients with advanced non-small cell lung cancer is ongoing with 26 patients (both osimertinib-naïve and experienced) enrolled to date. ZN-e4 has been well-tolerated at all doses as of the March 25, 2021 data cut-off, and clinical activity was identified at doses greater than 80 mg QD. Interim results from the Phase 1/2 trial are expected in 4Q 2021.

Webcast Event:

Zentalis will host a webcast event today, June 28, 2021 at 8:30 a.m. EDT. To register and access the event, the webcast link is available on the Investors & Media section of the Zentalis website at www.zentalis.com.

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. The Company is developing a broad pipeline of potentially best-in-class oncology candidates, all internally discovered, which include ZN-c5, an oral selective estrogen receptor degrader (SERD) for ER+/HER2- breast cancer, ZN-c3, a WEE1 inhibitor for advanced solid tumors, ZN-d5, a BCL-2 inhibitor for hematologic malignancies, and ZN-e4, an EGFR inhibitor for non-small cell lung carcinoma (NSCLC). Zentalis has licensed ZN-c5, ZN-c3 and ZN-d5 to its majority-owned joint venture, Zentera Therapeutics, to develop and commercialize these candidates in China. 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 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 without limitation statements regarding our expectations surrounding the development, potential, safety, efficacy, and regulatory and clinical progress of our product candidates in the Unites States and globally, and plans and timing for the initiation of and the release of data from our clinical trials and our ability to meet other key milestones. 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: the COVID-19 pandemic has adversely impacted and may continue to adversely impact our business, including our preclinical studies and clinical trials; 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 our lead product candidates; failure to identify additional product candidates and develop or commercialize marketable products; the early stage of our development efforts; 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 significant costs as a result of operating as a public company. These and other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the quarter

ended March 31, 2021 filed with the U.S. Securities and Exchange Commission (SEC) and our other filings with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. 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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zentalis
Creating Differentiated Therapies to Improve
the Lives of Cancer Patients
Mid-Year Update
June 2021

Forward-Looking Statements and Disclaimer

Zentalis Pharmaceuticals, Inc. ("we," "us," "our," "Zentalis" or the "Company") cautions that this presentation (including oral commentary that accompanies this presentation) contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding our future financial or business performance, plans, prospects, trends or strategies, objectives of management, competition and other financial and business matters, the potential, safety, efficacy, and regulatory and clinical progress of our current and prospective product candidates, plans and timing for the initiation of and release of data from our clinical trials and our ability to meet other key milestones, planned preclinical activities, our current and prospective collaborations, the estimated size of the market for our product candidates, and the timing and success of our development and commercialization of our anticipated product candidates and the market acceptance thereof are forward-looking statements, as well as statements that include the words "expect," "intend," "plan," "believe," "project," "forecast," "estimate," "may," "should," "anticipate" and similar statements of a future or forward-looking nature. 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: the outbreak of the novel coronavirus disease, COVID-19, has adversely impacted and may continue to adversely impact our business, including our preclinical studies and clinical trials; 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 our lead product candidate; failure to identify additional product candidates and develop or commercialize marketable products; the early stage of our development efforts; 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; interim, initial, "topline", and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data; 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 significant costs as a result of operating as a public company. These and other important factors discussed under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 filed with the U.S. Securities and Exchange Commission (SEC) and our other filings with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management's estimates as of the date of this presentation. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. While we may elect to update these forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable law. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. Neither we nor our affiliates, advisors or representatives makes any representation as to the accuracy or completeness of that data or undertake to update such data after the date of this presentation.

Data of Fulvestrant, RAD1901, Abemaciclib, Alpelisib, AZD1775, Venetoclax and Osimertinib presented in this presentation is based on evaluation of comparable proxy chemical compounds purchased from commercial sources rather than the pharmaceutical company commercializing or developing, as applicable, the compound.

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Mid-Year Update: Executive Summary

- Since AACR 2021, ZN-c3 has generated new clinical responses, further depth of responses, increased durability and improved hematological tolerability; representing one of the most promising clinical advances in DNA Damage Response (DDR) and synthetic lethality to date
- With broad utility across multiple large indications in both monotherapy and in combination, ZN-c3 is potentially both a first-in-class and best-in-class WEE1 inhibitor
- Following a recent EOP1 meeting with FDA, Zentalis initiated a registrational trial for ZN-c3 in USC, and will also start a novel biomarker-enabled trial by EOY - both trials have potential accelerated approval pathways
- ZN-c5's favorable tolerability data suggests potential for superiority amongst the oral SERDs, rivaling leading competition
- Clinical development plans for ZN-d5 (BCL-2) and ZN-e4 (EGFR) on track, expanding clinical and commercial opportunities with potential combinations

Zentalis is accelerating shareholder value accretion with the start of a registrational study with intent of an additional such trial by year end; both have potential for accelerated approvals

ZN-c3

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ZN-c3 WEE1 Inhibitor - Executive Summary

Since AACR 2021, ZN-c3 has generated new clinical responses, further depth of responses, increased durability and improved hematological tolerability; representing one of the most promising clinical advances in DNA Damage Response (DDR) and synthetic lethality to date

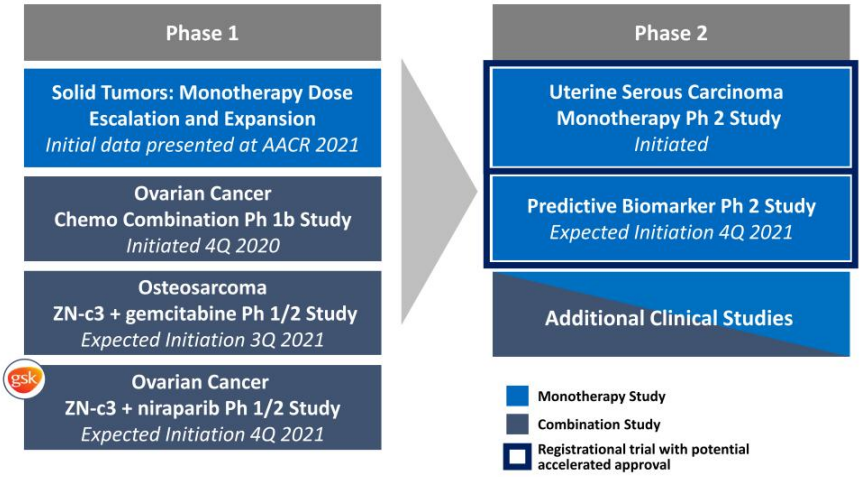
With broad utility across multiple large indications in both monotherapy and in combination, ZN-c3 is potentially both a first-in-class and best-in-class WEE1 inhibitor

Following a recent EOP1 meeting with FDA, Zentalis initiated a registrational trial for ZN-c3 in USC, and will also start a novel biomarker-enabled trial by EOY - both trials have potential accelerated approval pathways

- **Data presented at AACR 2021 continues to mature with both USC uPRs now confirmed PRs, and an additional uPR in a newly reported USC patient**
- **Further depth of tumor response and extended durability (8+ months) from exceptional responder observed**
- **Predictive biomarker may enable ZN-c3 to address tumor-agnostic indications**
- **Even lower overall severe hematological adverse event rates, with more patients enrolled on ZN-c3 since AACR 2021**
- **Two key designations (orphan drug and rare pediatric disease) received from FDA for ZN-c3 in combination with chemotherapy for osteosarcoma**
- **Two investigator-initiated trials (IIT) in GBM and TNBC with immunotherapy planned, in two very high unmet need indications**

ZN-c3: Clinical Development Plan

Ongoing and Planned Clinical Programs



Overview

- Initial Phase 1 monotherapy dose escalation and expansion data [1]
  - ZN-c3 was well-tolerated as a single agent
  - RP2D for ZN-c3 determined
  - ZN-c3 showed Exceptional Responses in heavily pre-treated subjects with advanced solid tumors
- Corresponding studies with Zentera in Greater China
- Two key designations now received from FDA for osteosarcoma for ZN-c3 combo with chemotherapy:
  - Orphan designation
  - Rare pediatric disease designation

(1) Reported at AACR 2021

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ZN-c3: Expanding Indications through Investigator Initiated Studies

- New IITs to start:

  – Glioblastoma Multiforme: Preclinical study completed. Clinical study to commence in 2021

  – Triple Negative Breast Cancer: Combination with anti-PDL1 and chemotherapy. Clinical study to commence in 2022.

ZN-c3 has the Potential to be Both First-in-Class and Best-in-Class

- **Key attributes to ZN-c3's Proof of Concept (POC) success:**
  1. Target biology known and validated
  2. Clinical results shown with monotherapy

- **ZN-c3's POC includes:**
  A. Determination of RP2D
  B. Evidence of relevant clinical activity in target populations
  C. Data on tolerability
  D. Strategy based on potential accelerated approvals in US

- **ZN-c3's POC has potential to lead to:**
  I. Multiple, large commercial opportunities as monotherapy and in combination

ZN-c3 has potential to be both first-in-class and best-in-class WEE1 inhibitor with broad market indications and path(s) to potential accelerated approval in US

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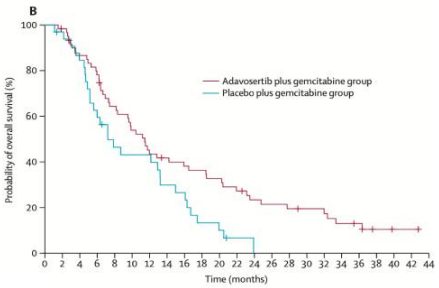
1. Target Biology Known and Validated

Adavosertib plus gemcitabine for platinum-resistant or platinum-refractory recurrent ovarian cancer: a double-blind, randomised, placebo-controlled, phase 2 trial

Stephanie Lheureux, Mihaela C Cristea, Jeffrey P Bruce, Swati Garg*, Michael Cabanero*, Gina Mantia-Smaldone, Alexander B Olawaiye, Susan L Ellard, Johanne I Weberpals, Andrea E Wahner Hendrickson, Gini F Fleming, Stephen Welch, Neesha C Dhani, Tracy Stockley, Prisni Rath, Katherine Karakasis, Gemma N Jones, Suzanne Jenkins, Jaime Rodriguez-Canales, Michael Tracy, Qian Tan, Valerie Bowering, Smitha Udagani, Lisa Wang, Charles A Kunos, Eric Chen, Trevor J Pugh, Amit M Oza*



similar results (p=0·007). Median overall survival at the time of data cutoff for the final analysis was 11·4 months (95% CI 8·2–16·5) in the adavosertib plus gemcitabine group versus 7·2 months (5·2–13·2) in the placebo plus gemcitabine group (HR 0·56 [95% CI 0·35–0·91]; log-rank p=0·017; figure 2). The proportion of

- **Publication in Lancet, Jan 23, 2021**
- **The inhibition of WEE1 has already been shown in a randomized double-blind, placebo-controlled study to exhibit a statistically significant overall survival advantage**
- **Rare for oncology drugs to show a survival advantage prior to approval**
- **Highly likely for a drug target to be approved if it shows a meaningful survival advantage (the "gold" standard)**

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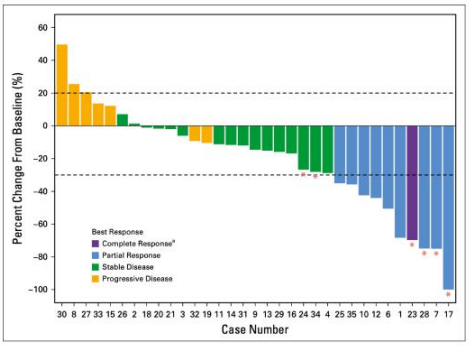
1. Target Biology Known and Validated

Phase II Study of the WEE1 Inhibitor Adavosert in Recurrent Uterine Serous Carcinoma

Joyce F. Liu, MD, MPH[1]; Niya Xiong, MS[2]; Susana M. Campos, MD[1]; Alexi A. Wright, MD, MPH[1]; Carolyn Krasner, MD[1]; Susan Schumer, MD[1]; Neil Horowitz, MD[1]; Jennifer Veneris, MD, PhD[1]; Nabihah Tayob, PhD[2]; Stephanie Morrissey, RN, BSN[1]; Gabriela West, BA[1]; Roxanne Quinn, BA[1]; Ursula A. Matulonis, MD[1]; and Panagiotis A. Konstantinopoulos, MD, PhD[1]



RESULTS In 34 evaluable patients, 10 total responses (one confirmed complete response, eight confirmed partial responses, and one unconfirmed partial response) were observed with adavosertib monotherapy, for an ORR of 29.4% (95% CI, 15.1 to 47.5). Sixteen patients were progression-free at 6 months, for a PFS6 rate of 47.1% (95% CI, 29.8 to 64.9). Median PFS was 6.1 months, and median duration of response was 9.0 months.

- **Publication in JCO March 12, 2021**
- **A third party WEE1 inhibitor exhibited a 29% ORR in a Phase 2 study in very sick endometrial cancer patients with USC subtype (most of these women die within 5 years upon diagnosis)**
- **AZ has just started a registrational P2 study in USC with monotherapy dosing**

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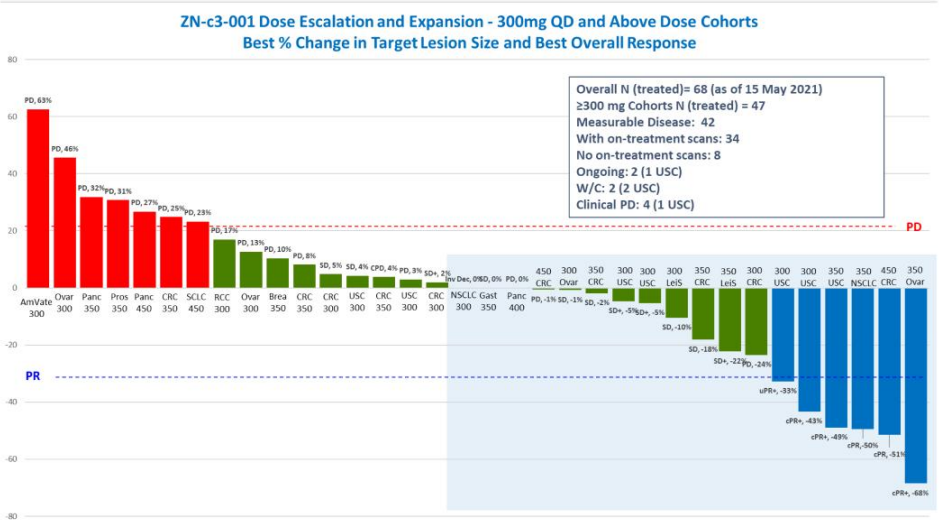
2. Evidence of Strong Clinical Activity Shown by ZN-c3



- **Clinically relevant responses seen in a refractory solid tumor untargeted all-comer population as monotherapy. Responses seen across four different tumor types signaling potential for broad oncology applicability**
- **We believe this is the first DDR drug (including ATM, ATR, CHK1/2, DNA-PK, or PARP) that has shown monotherapy responses in CRC and NSCLC pts (very difficult to treat)**
- **Currently 43% ORR (3/7) in USC pts[3]. AZD1775 observed a 29% ORR**
- **Exceptional responses seen were dramatic, unexpected and durable**

(1) 3 subjects with no treatment scans (CRC, USC, Pancreas), and experienced clinical progressive disease (CPD). + denotes treatment ongoing
(2) 3 confirmed Exceptional Responders PRs, including an additional confirmation of Exceptional Responder PR since AACR Presentation Press Release
(3) Waterfall as of 05/15/2021; both uPRs reported at AACR 2021 in USC are confirmed PRs. Newly reported uPR in USC is included. ORR based on radiographic responses.

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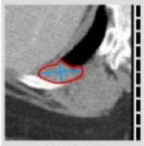
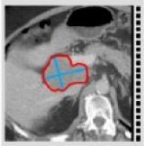
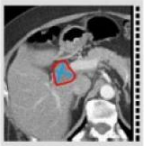
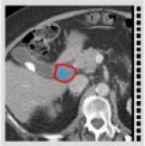
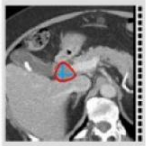
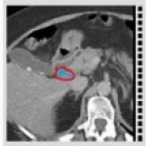
2. Exceptional Responder Clinical Update: Additional Scans Since AACR 2021 (Ovarian Cancer Exceptional Responder)

	Baseline (0 9/22/2020)	Follow-up 1 (11/24/2020)	Follow-up 2 (12/28/2020)	Follow-up 3 (03/01/2021)	Follow-up 4 (05/17/2021)
Target lesions					
T01 Pleura Pleura Size	 LA: 32.9 mm SA: 16.6 mm	Disappeared	Disappeared	Disappeared	Disappeared
T02 Peritoneum Peritoneum Size	 LA: 65.7 mm SA: 51.1 mm	 LA: 36.3 mm (-44.7% ΔP) SA: 34.0 mm (-33.5% ΔP)	 LA: 33.2 mm (-8.5% ΔP) SA: 27.2 mm (-20.0% ΔP)	 LA: 29.7 mm (-10.5% ΔP) SA: 27.6 mm (+1.5% ΔP)	 LA: 27.4 mm (-7.7% ΔP) SA: 18.9 mm (-31.5% ΔP)

All progress values are relative to their previous value (ΔP)

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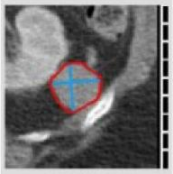
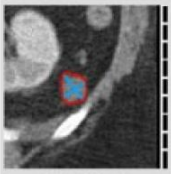
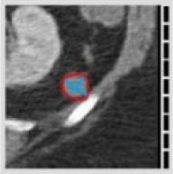
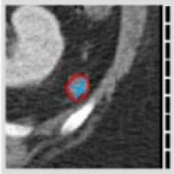
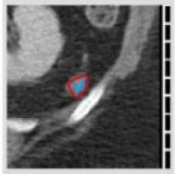
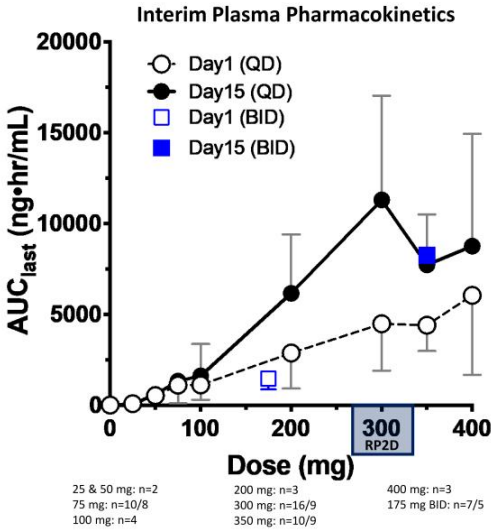
2. Exceptional Responder Clinical Update: Additional Scans Since AACR 2021 (Ovarian Cancer Exceptional Responder)

	Baseline (0 9/22/2020)	Follow-up 1 (11/24/2020)	Follow-up 2 (12/28/2020)	Follow-up 3 (03/01/2021)	Follow-up 4 (05/17/2021)
T03 Peritoneum Peritoneum Size					
	LA: 28,2 mm SA: 26,7 mm	LA: 17,8 mm (-36,9% ΔP) SA: 14,9 mm (-44,2% ΔP)	LA: 16,3 mm (-8,4% ΔP) SA: 13,9 mm (-6,7% ΔP)	LA: 13,9 mm (-14,7% ΔP) SA: 11,0 mm (-20,9% ΔP)	LA: 12,7 mm (-8,6% ΔP) SA: 9,1 mm (-17,3% ΔP)

All progress values are relative to their previous value (ΔP)

A. RP2D Selected



- Greater than dose proportional exposure up to 450 mg (not plotted)
- 1.87 to 2.50-fold accumulation at 200-350 mg dose
- No additional increase of exposure occurs beyond Day 15 (up to Cycle 6)
- 300 mg dose chosen as RP2D because it exhibited the highest mean AUC between 25-400 mg
- 300 mg dose was well-tolerated without dose reductions in majority of patients

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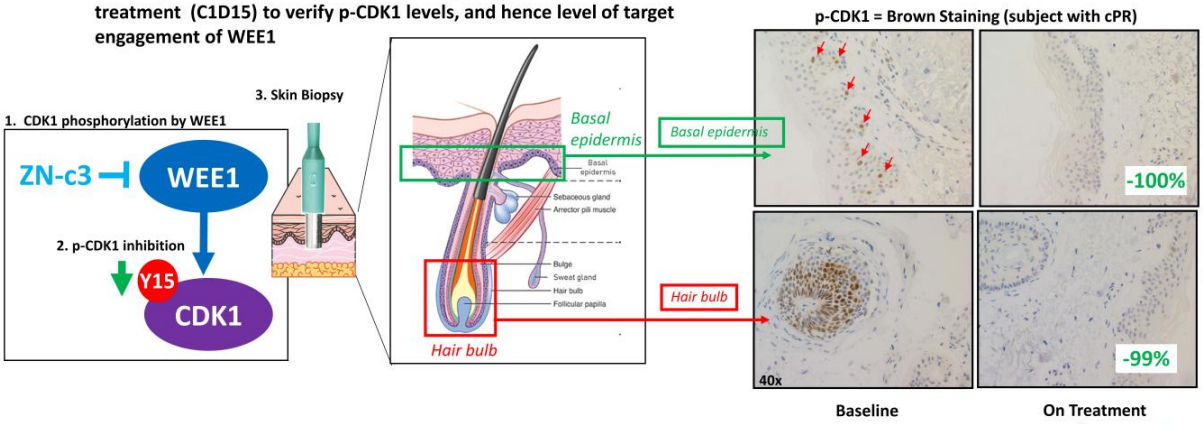
A. RP2D Selected (Cont.)

Confirmation of WEE1i Target Engagement in Surrogate Tissue

1. CDK1 phosphorylation (p-CDK1) is mediated by WEE1
2. Inhibition of WEE1 therefore will lead to inhibition of p-CDK1
3. Skin biopsies were performed at baseline (C1D1) and on-treatment (C1D15) to verify p-CDK1 levels, and hence level of target engagement of WEE1



Source: Drawing adapted from Servier Medical Art

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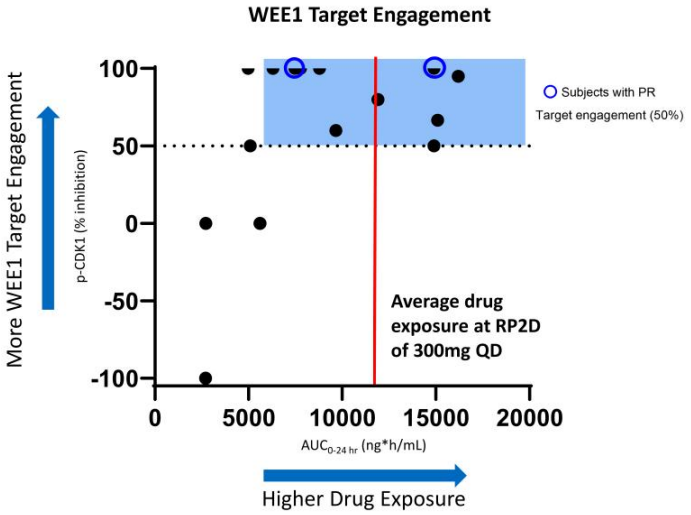
A. RP2D Selected (Cont.)



- **Inhibition of p-CDK1 demonstrated WEE1 target engagement**

  Increase in dose / drug exposure directly related to WEE1 target engagement

- **RP2D showed an AUC with excellent target engagement with p-CDK1 levels decreased at least by 50%**
- **In short, RP2D showed highest AUC with excellent Pharmacodynamic data directly supportive of 300 mg QD**

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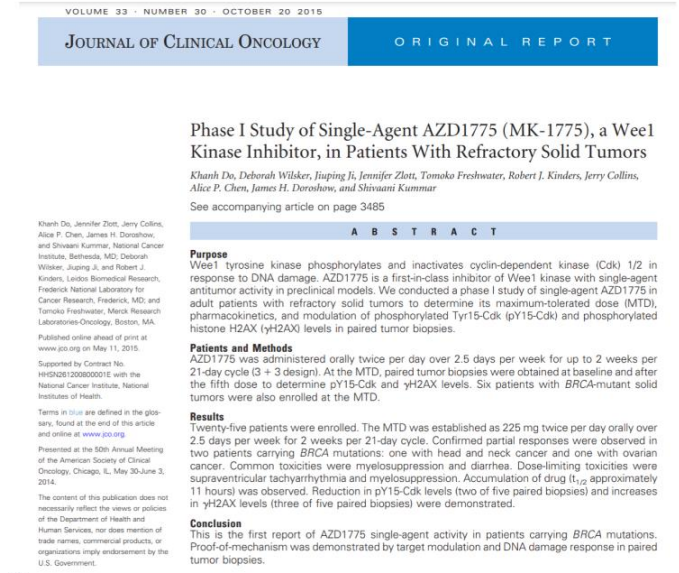
B. Strong Comparative Efficacy Data of ZN-c3 vs AZD1775



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JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Phase I Study of Single-Agent AZD1775 (MK-1775), a Wee1 Kinase Inhibitor, in Patients With Refractory Solid Tumors

Khanh Do, Deborah Wilsker, Jiuping Ji, Jennifer Zlott, Tomoko Freshwater, Robert J. Kinders, Jerry Collins, Alice P. Chen, James H. Doroshow, and Shivaani Kumnar

See accompanying article on page 3485

Khanh Do, Jennifer Zlott, Jerry Collins, Alice P. Chen, James H. Doroshow, and Shivaani Kumnar, National Cancer Institute, Bethesda, MD; Deborah Wilsker, Jiuping Ji, and Robert J. Kinders, Leidos Biomedical Research, Frederick National Laboratory for Cancer Research, Frederick, MD; and Tomoko Freshwater, Merck Research Laboratories-Oncology, Boston, MA.

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Terms in blue are defined in the glossary, found at the end of this article and online at www.jco.org.

Presented at the 50th Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, May 30-June 3, 2014.

A B S T R A C T

Purpose
Wee1 tyrosine kinase phosphorylates and inactivates cyclin-dependent kinase (Cdk) 1/2 in response to DNA damage. AZD1775 is a first-in-class inhibitor of Wee1 kinase with single-agent antitumor activity in preclinical models. We conducted a phase I study of single-agent AZD1775 in adult patients with refractory solid tumors to determine its maximum-tolerated dose (MTD), pharmacokinetics, and modulation of phosphorylated Tyr15-Cdk (pY15-Cdk) and phosphorylated histone H2AX (γH2AX) levels in paired tumor biopsies.

Patients and Methods
AZD1775 was administered orally twice per day over 2.5 days per week for up to 2 weeks per 21-day cycle (3 + 3 design). At the MTD, paired tumor biopsies were obtained at baseline and after the fifth dose to determine pY15-Cdk and γH2AX levels. Six patients with *BRCA*-mutant solid tumors were also enrolled at the MTD.

Results
Twenty-five patients were enrolled. The MTD was established as 225 mg twice per day orally over 2.5 days per week for 2 weeks per 21-day cycle. Confirmed partial responses were observed in two patients carrying *BRCA* mutations: one with head and neck cancer and one with ovarian cancer. Common toxicities were myelosuppression and diarrhea. Dose-limiting toxicities were supraventricular tachyarrhythmia and myelosuppression. Accumulation of drug ($t_{1/2}$ approximately 11 hours) was observed. Reduction in pY15-Cdk levels (two of five paired biopsies) and increases in γH2AX levels (three of five paired biopsies) were demonstrated.

Conclusion
This is the first report of AZD1775 single-agent activity in patients carrying *BRCA* mutations. Proof-of-mechanism was demonstrated by target modulation and DNA damage response in paired tumor biopsies.

- **Early study published in JCO Oct 20, 2015, enabling comparison head-to-head with ZN-c3's monotherapy refractory solid tumor study**
- **Due to tolerability issues for AZD1775 as monotherapy, MTD was established as 225 mg BID for 5 days per 21-day cycle vs ZN-c3's 300 mg QD continuous dosing**
- **ZN-c3 delivered 6.3 grams vs 2.25 grams per 21 days cycle for AZD1775 with better tolerability (~3x more drug with ZN-c3 at its RP2D)**
- **Zentalis has seen responses in four different tumor types including NSCLC, CRC, ovarian, and endometrial to date. AZ has not observed responses in CRC or NSCLC**
- **AZD1775's two PRs in USC were seen in BRCA mutant patients; ZN-c3 responses were seen in BRCA wildtype patients**

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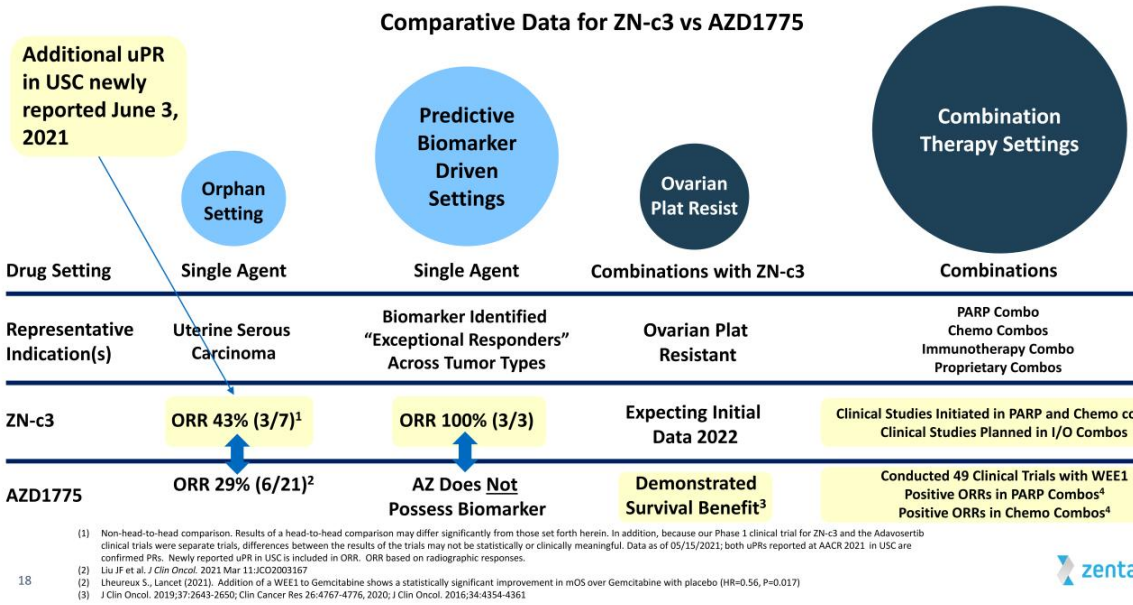
B. Compelling Data for ZN-c3 vs AZD1775 (Cont.)



(1) Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the Adavosertib clinical trials were separate trials, differences between the results of the trials may not be statistically or clinically meaningful. Data as of 05/15/2021; both uPRs reported at AACR 2021 in USC are confirmed PRs. Newly reported uPR in USC is included in ORR. ORR based on radiographic responses.

(2) Liu JF et al. *J Clin Oncol.* 2021 Mar 11:JCO2003167

(2) Lheureux S., Lancet (2021). Addition of a WEE1 to Gemcitabine shows a statistically significant improvement in mOS over Gemcitabine with placebo (HR=0.56, P=0.017)

(3) J Clin Oncol. 2019;37:2643-2650; Clin Cancer Res 26:4767-4776, 2020; J Clin Oncol. 2016;34:4354-4361

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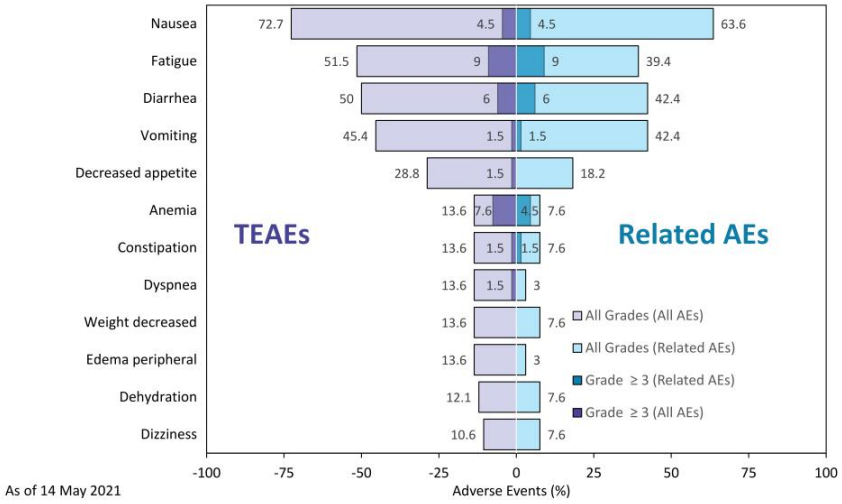
C. Tolerability Profile of ZN-c3



As of 14 May 2021

- **AEs (≥10%) for all dose levels (25 mg QD to 450 mg QD)**
- **In N=66, most AEs were of Grade 1/2 nature with GI symptoms**
- **Grade 1/2 GI symptoms particularly nausea managed well with antiemetic use; GI symptoms abated after first cycle**
- **Majority of patients tolerated RP2D without dosing change**
- **Grade 3/4 AEs were of single percentage point nature**

Promising tolerability data suggest the potential for a wide therapeutic window

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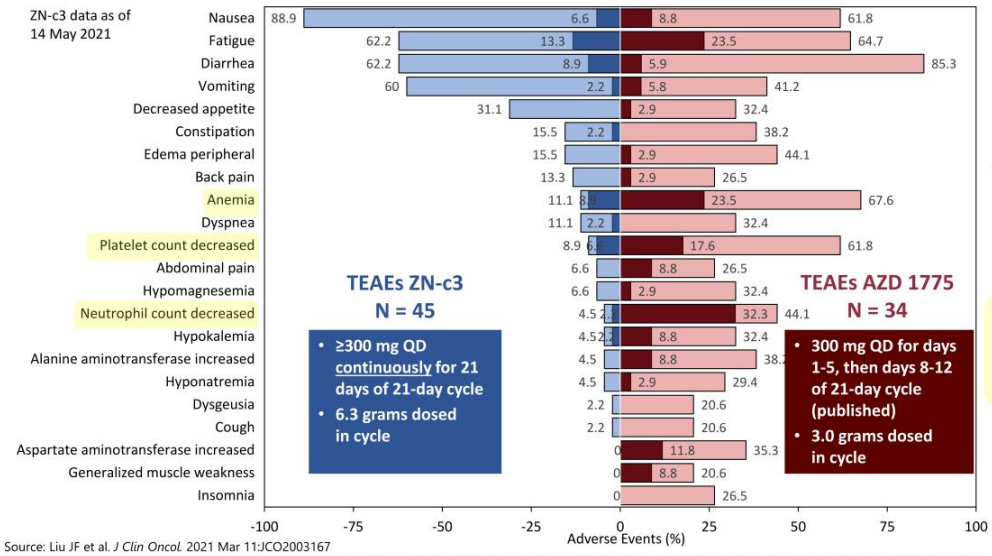
C. Safety/Tolerability vs AZD1775 (1)



- **Due to the tolerability issues of AZD1775 the drug was dosed intermittently while ZN-c3 was dosed continuously**
- **Despite having a 2x higher dose intensity (6.3g vs 3g), ZN-c3 safety and tolerability were favorable**

Source: Liu JF et al. *J Clin Oncol.* 2021 Mar 11:JCO2003167

(1) Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the Adavosertib clinical trials were separate trials, differences between the results of the trials may not be statistically or clinically meaningful

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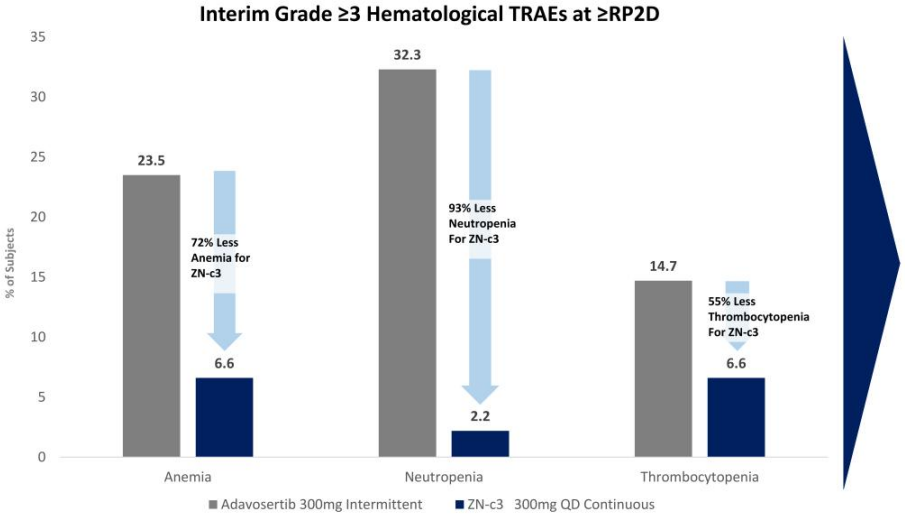
C. Safety/Tolerability vs AZD1775 (Cont.)



- **Even lower overall severe hematological AE rate over AZD1775 even with 11 more ZN-c3 patients enrolled since AACR 2021**
- **Despite continuous dosing delivering twice the drug load, ZN-c3 induced markedly less hematological toxicity than AZD1775 did in its clinical trials**
- **Better tolerability also unlocks the potential for wide ranging drug combinations providing potential for both increased efficacy and commercial potential**

Source: Liu JF et al. J Clin Oncol. 2021 Mar 11:JCO2003167

(1) Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the Adavosertib clinical trials were separate trials, differences between the results of the trials may not be statistically or clinically meaningful

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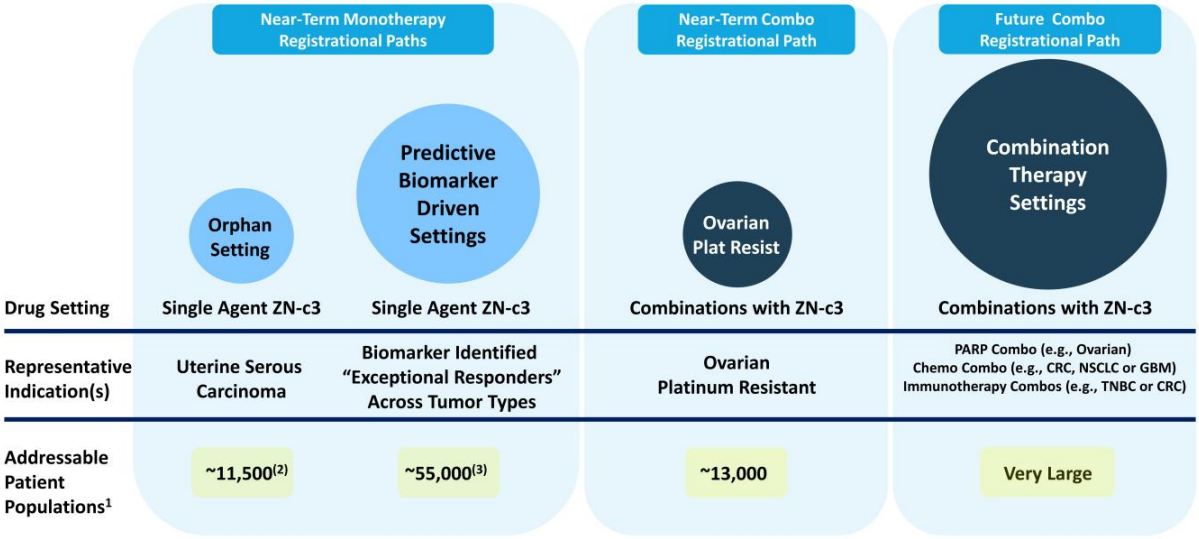
D. Path to Potential Accelerated Approvals

- Conducted EOP1 Mtg with FDA re: study ZN-c3-004, a monotherapy trial planned with registrational intent in women with recurrent or persistent USC
  - **Proposed study for ZN-c3-004 designed with registrational intent for potential accelerated approval**
- In 2H 2021, Zentalis expects to approach FDA with a biomarker-driven, tumor-agnostic monotherapy clinical trial design with registrational intent
- FDA has now granted two key designations for ZN-c3's use in combination with chemotherapy in osteosarcoma
  - **Orphan Drug Designation**
  - **Rare Pediatric Disease Designation**

I. Commercial Opportunity



Drug Setting	**Single Agent ZN-c3**	**Single Agent ZN-c3**	**Combinations with ZN-c3**	**Combinations with ZN-c3**
Representative Indication(s)	**Uterine Serous Carcinoma**	**Biomarker Identified "Exceptional Responders" Across Tumor Types**	**Ovarian Platinum Resistant**	**PARP Combo (e.g., Ovarian) Chemo Combo (e.g., CRC, NSCLC or GBM) Immunotherapy Combos (e.g., TNBC or CRC)**
Addressable Patient Populations[1]	**~11,500[(2)]**	**~55,000[(3)]**	**~13,000**	**Very Large**

(1) North America, Western Europe and Japan
(2) Gynecologic Oncology 115 (2009) 142-153, David Boruta et al.; National Cancer Institute, SEER 2020 Data
(3) Observed predictive biomarker frequency data across solid tumor types; predictive biomarker not disclosed

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ZN-c5

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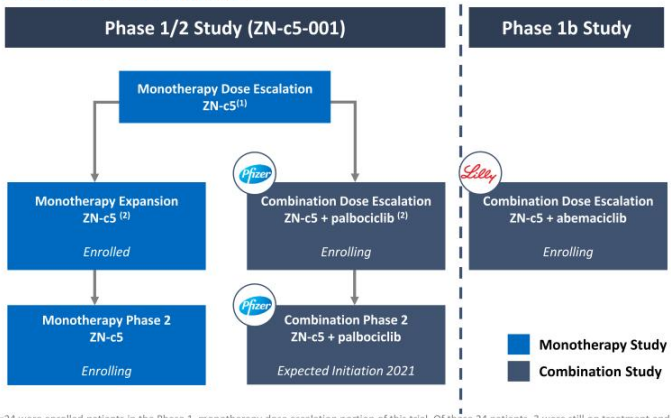
ZN-c5 Executive Summary

- New interim clinical data from Phase 1/2 monotherapy studies suggest ZN-c5 has the potential to be best-in-class with favorable safety/tolerability data in mono and combo settings
- New interim clinical data rival other oral SERD efficacy data; awaiting completion of study before final selection of RP2D (likely to be 50 mg QD)
- Combination studies with palbociclib and abemaciclib continue on track

ZN-c5: Clinical Development Plan

Ongoing Clinical Programs



Other studies

- Window of Opportunity study initiated in 2020 to analyze tumor ER degradation (enrollment completed, 35 patients)
- Food effect study (18 subjects) completed, CSR in preparation
  - Results showed ZN-c5 could be administered with or without food
- Multiple dose cohorts may be chosen in monotherapy Phase 2 study

(1) As of May 11, 2021, n=24 were enrolled patients in the Phase 1, monotherapy dose escalation portion of this trial. Of these 24 patients, 3 were still on treatment and 21 discontinued due to disease progression (n = 20), and physician decision (n = 1).

(2) As of May 11, 2021, 32 patients were enrolled in the Phase 1, monotherapy expansion portion of this trial. Of these 32 patients, 12 were still on treatment and 20 discontinued due to disease progression (n = 18), adverse event (n = 1, hypersensitivity) and physician decision (n = 1). As of May 11, 2021, we have enrolled 41 patients in the Phase 1, combination dose escalation portion of this trial. Of these 41 patients, 23 were still on treatment and 18 discontinued due to disease progression (n = 14), patient decision (n = 2), intercurrent illness (n = 1, endometrial cancer) and physician decision (n = 1).

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ZN-c5-001: First-in-Human Study - Design & Endpoints

Design		Primary Endpoint
• Monotherapy Dose escalation (3+3 design)	→	Maximum tolerated dose/Recommended Phase 2 Dose
• Monotherapy Expansion	→	Safety and tolerability
• Monotherapy Phase 2	→	Clinical Benefit Rate (CBR)
• Combination with Palbociclib Dose escalation (3+3)	→	Maximum tolerated dose/Recommended Phase 2 Dose
• Combination with Palbociclib Phase 2	→	Clinical Benefit Rate (CBR)

Key Secondary Endpoints

- Safety and tolerability
- Pharmacokinetics
- Anti-tumor activity (RECIST): objective response rate, CBR, duration of response, progression-free survival, overall survival
- Pharmacodynamic and prognostic biomarkers

Dosing

- Administered orally, doses from 25 to 300 mg/day, dose once (QD) or twice (BID) a day

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ZN-c5-001: Key Inclusion Criteria

- ER+/HER2-negative advanced breast cancer
- ECOG PS 0 – 2
- Females postmenopausal or pre/peri-menopausal
- Evaluable or measurable disease by RECIST v1.1

Protocol Portion	N Prior therapies allowed for advanced/met disease	
	Endocrine-based therapies	Chemotherapies
Phase 1 Monotherapy Dose Escalation	unlimited	0 – 2
Phase 1 Combination Dose Escalation	unlimited	0 – 1
Phase 1 Monotherapy Expansion	0 – 2	0 – 1
Phase 2 Monotherapy	1 – 2	0
Phase 2 Combination	0 – 1	0 – 1

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ZN-c5-001: Baseline Demographics - ZN-c5 Monotherapy

Patient Characteristics	ZN-c5 Monotherapy N = 56
Median age, years (range)	58.5 (38 – 89)
ECOG status, n (%) 0 1 2	 30 (55%) 25 (45%) 0
N (range) prior lines of therapy (adv/mt) N (range) endocrine-based N (range) chemotherapy N prior CDK4/6i N prior fulvestrant N Prior PI3Ki	2 (0 – 9) 2 (0 – 6) 0 (0 – 3) 38 (68%) 26 (46%) 4 (7%)
Measurable disease, n (%) N Visceral disease	40 (71%) 28 (50%)

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New Clinical Data: ZN-c5-001 Monotherapy Efficacy Summary by Dose

Interim Monotherapy Efficacy Results

Data cut-off 11 May 2021

Dose (mg)	50 (Likely RP2D)	75	100	150	300	Overall
N (enrolled)	16	3	3	21	13	56
CBR	2/5 (40%)	0/3 (0%)	1/3 (33%)	4/21 (19%)	7/13 (54%)	14/42 (33%)
ORR*	0/14	0/2	0/3	1/13 (8%)	1/8 (13%)	2/40 (5%)

* Patients with measurable disease

- **Interim clinical data for ZN-c5 consistent with data from third party studies of other oral SERD competitors suggest that lower dose SERD may drive better efficacy (see next slides)**
- **Last cohort in ZN-c5's monotherapy studies is the 50 mg dose, with a large number of patients on study**
- **RP2D selection to finalize after completion of study, with the 50 mg QD dose as likely RP2D**

Awaiting Large Number of Patients on 50 mg to Complete Study

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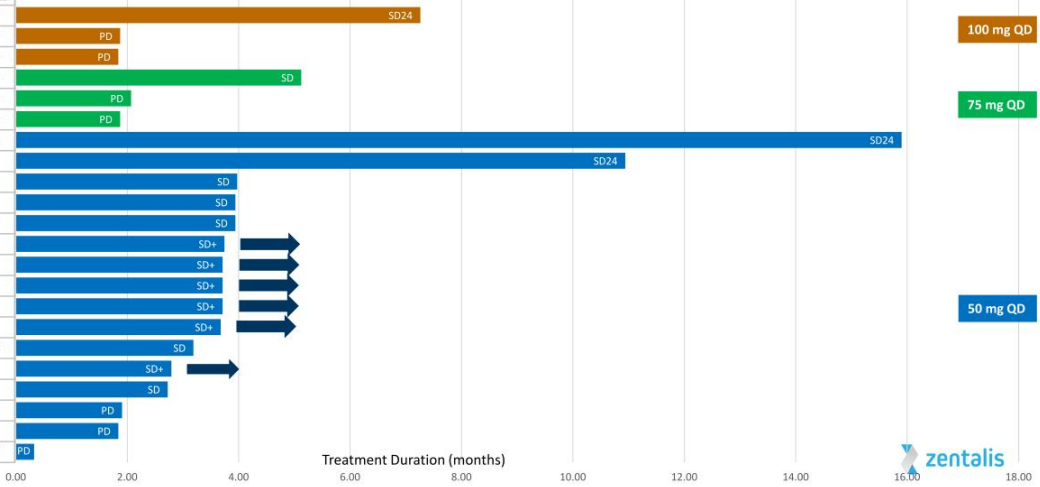
New Interim Clinical Data: ZN-c5-001 Monotherapy 50-100 mg

Treatment Duration (months) and Response by Dose as of 11 May 2021

ESR1 Mutation	Prior Hormonal based (1)	Prior Chemo (1)	Prior CDK4/6 (2)	Prior Fulvestrant
+	3	1	P	Y
+	4	1	P	Y
-	3	1	P, R	Y
U	6	2	-	Y
+	3	0	P	Y
U	3	1	P	Y
U	2	2	P	Y
-	2	0	-	-
-	0	1	-	-
+	1	0	P	-
+	1	1	-	-
+	2	1	-	-
+	0	0	-	-
U	1	1	-	-
+	0	0	R	-
-	2	0	-	-
-	3	1	P, A	Y
Y	0	0	P	-
-	0	0	P	-
+	1	1	-	-
Y	0	0	P	-
+	0	0	-	Y

(1) Number of treatments reflect advanced or metastatic setting, not neo/adjuvant; also reflects combinations with targeted therapies CDK4/6, mTOR, PI3Ki
(2) P-palbociclib, A- abemaciclib, R-ribociclib, E-experimental treatment, could be placebo



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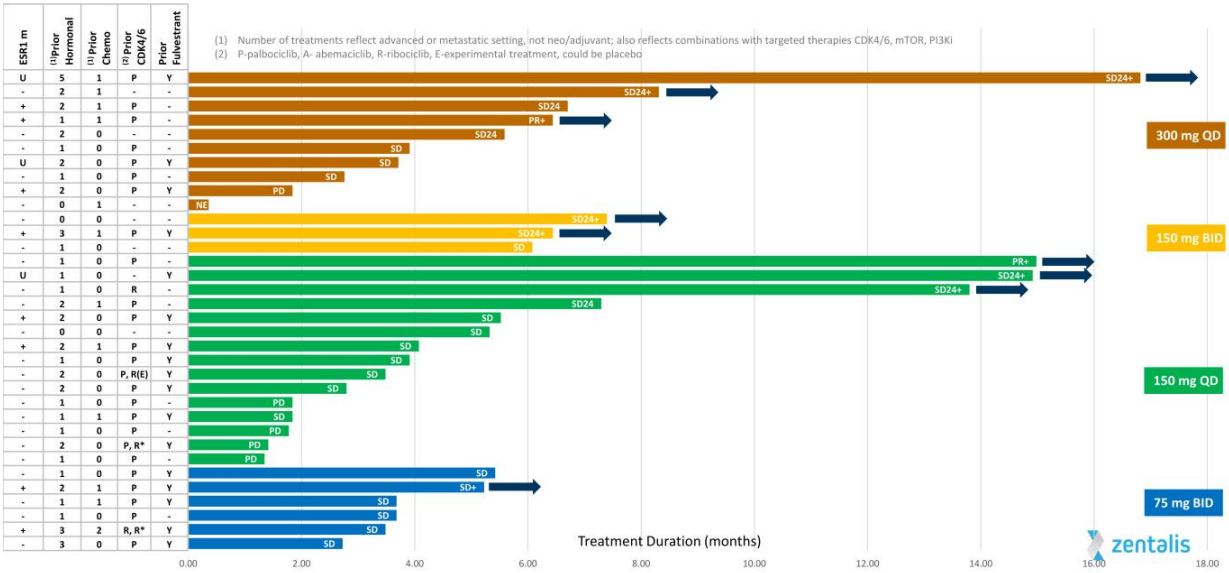
New Interim Clinical Data: ZN-c5-001 Monotherapy 150-300 mg

Treatment Duration (months) and Response by Dose as of 11 May 2021

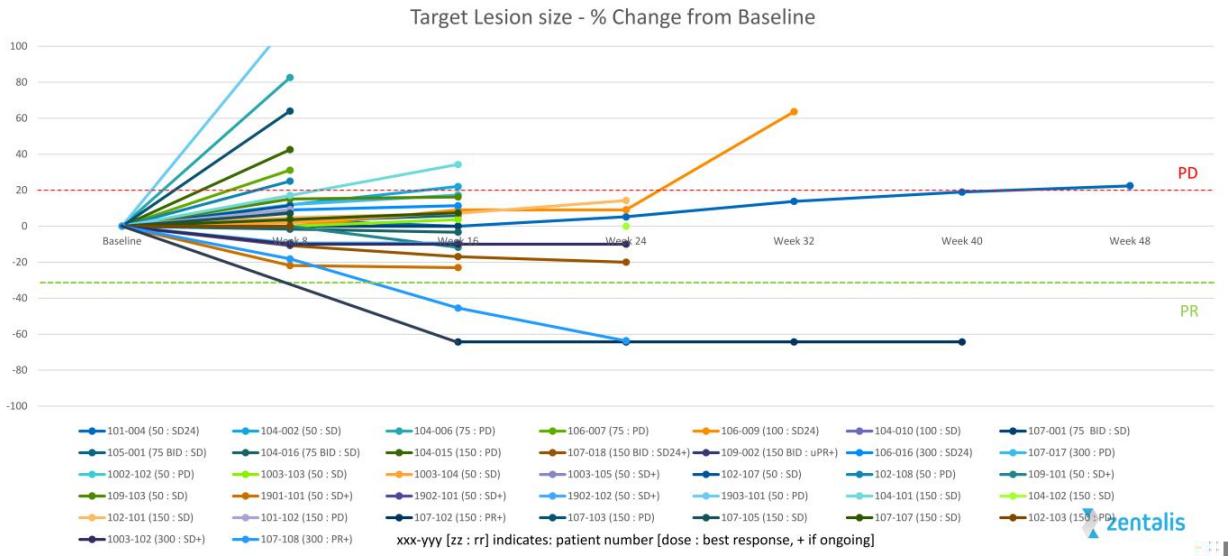
ESR1 m	[1]Prior Hormonal	[1] Prior Chemo	[2] Prior CDK4/6	Prior Fulvestrant
U	5	1	P	Y
-	2	1	-	-
+	2	1	P	-
+	1	1	P	-
-	2	0	-	-
-	1	0	P	-
U	2	0	P	Y
-	1	0	P	-
+	2	0	P	Y
-	0	1	-	-
-	0	0	-	-
+	3	1	P	Y
-	1	0	-	-
-	1	0	P	-
U	1	0	-	Y
-	1	0	R	-
-	2	1	P	-
+	2	0	P	Y
-	0	0	-	-
+	2	1	P	Y
-	1	0	P	Y
-	2	0	P, R(E)	Y
-	2	0	P	Y
-	1	0	P	-
-	1	1	P	Y
-	1	0	P	-
-	2	0	P, R*	Y
-	1	0	P	-
-	1	0	P	Y
+	2	1	P	Y
-	1	1	P	Y
-	1	0	P	-
+	3	2	R, R*	Y
-	3	0	P	Y

(1) Number of treatments reflect advanced or metastatic setting, not neo/adjuvant; also reflects combinations with targeted therapies CDK4/6, mTOR, PI3Ki
(2) P-palbociclib, A- abemaciclib, R-ribociclib, E-experimental treatment, could be placebo



New Interim Clinical Data: ZN-c5-001 Monotherapy

Subjects with Measurable Disease as of 11 May 2021



101-004 (50 : SD24) 104-002 (50 : SD) 104-006 (75 : PD) 106-007 (75 : PD) 106-009 (100 : SD24) 104-010 (100 : SD) 107-001 (75 BID : SD)
105-001 (75 BID : SD) 104-016 (75 BID : SD) 104-015 (150 : PD) 107-018 (150 BID : SD24+) 109-002 (150 BID : uPR+) 106-016 (300 : SD24) 107-017 (300 : PD)
1002-102 (50 : PD) 1003-103 (50 : SD) 1003-104 (50 : SD) 1003-105 (50 : SD+) 102-107 (50 : SD) 102-108 (50 : PD) 109-101 (50 : SD+)
109-103 (50 : SD) 1901-101 (50 : SD+) 1902-101 (50 : SD+) 1902-102 (50 : SD+) 1903-101 (50 : PD) 104-101 (150 : SD) 104-102 (150 : SD)
102-101 (150 : SD) 101-102 (150 : PD) 107-102 (150 : PR+) 107-103 (150 : PD) 107-105 (150 : SD) 107-107 (150 : SD) 102-103 (150 : PD)
1003-102 (300 : SD+) 107-108 (300 : PR+)

xxx-yyy [zz : rr] indicates: patient number [dose : best response, + if ongoing]

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New Interim Clinical Data: ZN-c5 Plasma PK Parameters in Combo Arms

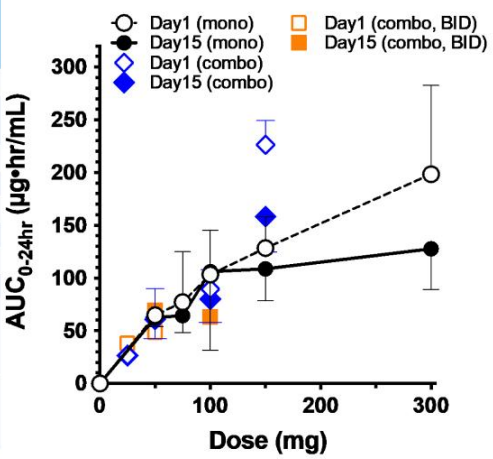
25 – 150 mg ZN-c5 + 125 mg Palbociclib (*preliminary*) as of 1 May 2021

ZN-c5 Dose (mg)		ZN-c5 on Day 1			ZN-c5 on Day 15			ZN-c5 Accum by AUC
		C_{max} (ng/mL)	T_{max} (hr)	$AUC_{0\text{-}24hr}$ (ng*h/mL)	C_{max} (ng/mL)	T_{max} (hr)	$AUC_{0\text{-}24hr}$ (ng*h/mL	
25 (n=3/2)	Mean	2,230	2	26,800	2,360	2	26,500	1.2
	SD	*447*	*2-2*	*7,040*	*(2,230, 2,490)*	2,2	*28,000, 25,100)*	*(1.2, 1.2)*
50 (n=6)	Mean	5,140	1.5	62,700	5,390	1.5	60,800	1.1
	SD	*1,080*	*1-24*	*27,100*	*1,380*	*1-4*	*18,400*	*0.36*
100 (n=8)	Mean	6,960	2	89,600	6,640	2	80,000	0.90
	SD	*1,290*	*1-8*	*18,500*	*1,050*	*2-8*	*22,000*	*0.19*
150 (n=3)	Mean	18,500	2	226,000	13,300	2	158,000	0.71
	SD	*4,370*	*1-8*	*22,700*	*3,370*	*1-2*	*33,800*	*0.23*
25BID (n=3)	Mean	3,280	2	$AUC_{0\text{-}inf}$ 38,200	4,730	1	69,500*	1.0**
	SD	*121*	*1-2*	*5,930*	*2,300*	*1-2*	*37,100*	
50BID (n=2)	Mean	5,030 *(3990, 6070)*	2 *(2, 2)*	$AUC_{0\text{-}inf}$ 48,900	4,430 *(3,900, 4,950)*	1.5 *(1, 2)*	63,400* *(48,400, 78,200)*	0.94**

*For BID, $AUC_{0\text{-}24hr}$ on Day 15 is calculated as 2 x $AUC_{0\text{-}12hr}$

**For BID, accumulation is calculated based in $AUC_{0\text{-}12hr}$

- **ZN-c5 exposure on Day 15 was approximately dose proportional between 25 and 150 mg QD (with somewhat lower exposure at 100 mg)**



- ZN-c5 PK at 50 & 100 mg is consistent with mono, at 150 mg – higher than in mono

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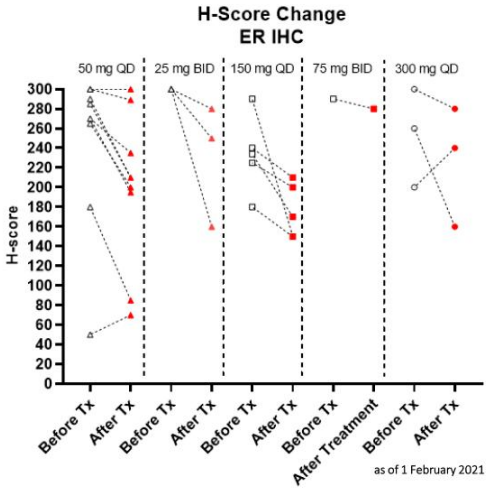
New Interim Clinical Data: ZN-c5 Window of Opportunity Initial Biomarker Study



	N	Mean	STD
All doses	**21**	**-17%**	**22%**
25 BID	3	-23%	21%
50 QD	9	-15%	26%
50 mg*	12	-17%	24%
150 mg*	6	-20%	16%
300 QD	3	-8%	29%

*total daily dose

Linear Regression %H-score change from baseline = intercept + slope*total daily dose

R-squared=0.013
intercept= 20% 95% CI (-37%, -3%) p-value=0.022
slope= 0 95% CI (-.1, .1) p-value=0.623

Initial Impressions of Interim Data:

- No dose correlation with ER degradation status
- High variability with assay and difficulty in cross comparing with other studies
- One pt at 300 mg dose with Grade 3/4 LFT increases resolved without incident after study end: patient with concomitant issues of fever, infection, acetaminophen use and steatosis
- Study continues to enroll; full study results to be published in future

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New Interim Clinical Data: ZN-c5 Monotherapy – Related AEs in ≥ 10%

TEAE's Related to ZN-c5

Data cut-off 11 MAY 2021

AEs in N	50 mg QD N = 16			75 mg QD N = 3			100 mg QD N = 3			75 mg BID N = 6			150 mg QD N = 15			150 mg BID N = 3			300 mg QD N = 10			Total N = 56			
Grade	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**All N (%)**
Any AE	6	2	0	1	0	0	0	0	0	2	2	0	5	4	0	1	1	1	5	2	1	20	11	2	33 (59%)
Hot Flushes										2			3						1	2		6	2	0	8 (14%)
Nausea	1									1			1	1			1		1	2		4	4	0	8 (14%)
Fatigue	1									1			2			1			1	1		6	1	0	7 (13%)

Diarrhea events: 2 out of 56 subjects (3.6%), only grade 1 or 2 events observed
Grade 3 events: n=1 hypersensitivity (300 mg qd); n=1 γGT increase (150 mg bid)

No observed bradycardia, no visual disturbances, no QTC, no dizziness

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New Interim Clinical Data: ZN-c5 Combination with Palbociclib – Related TEAEs ≥ 10%

Data cut-off 11 MAY 2021

TEAE's Related to ZN-c5

	25 mg QD N = 6				25 mg BID N = 5				50 mg QD N = 13				50 mg BID N = 2				100 mg QD N = 12				150 mg QD N = 3				Total N = 41			
Grade	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Any AE	1	1			2				4	3			1	1			3	1			2	1			13	7		
Hot Flush		1			1				1	1			1								1				4	2		
Arthralgia					1				2	1															3	1		

TEAE's Related to Palbociclib

	25 mg QD N = 6				25 mg BID N = 5				50 mg QD N = 13				50 mg BID N = 2				100 mg QD N = 12				150 mg QD N = 3				Total N = 41			
Grade	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Any AE		4	1	1	2	2			1	7	5		1	1			5	2	5				3		9	16	14	1
Neutrophil count decreased		4	1		1	1				7	3		1					2	5				3		2	14	12	
WBC count decreased	1	2	1		2	1			2	4	2		1				5	2	2			1	1		11	10	6	
Anemia	1	1			1				4	1							4				1	1			11	3		
Lymphocyte count decreased		1	1	1		1				2	2			1			2				1				3	5	3	1
Fatigue	1								3	2							3				1				8	2		
Platelet count decreased		2			1				2								3				1				7	2		
Nausea									2								2				1				5			
Hot Flush		1			1				1												1				3	1		
Arthralgia					1				2	1															3	1		

Grade 3 events: n=1 hypersensitivity (300 mg qd); n=1 γGT increase (150 mg bid)

ZN-c5 tolerability data suggest best-in-class of oral SERDs and ideal for combos

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ZN-d5

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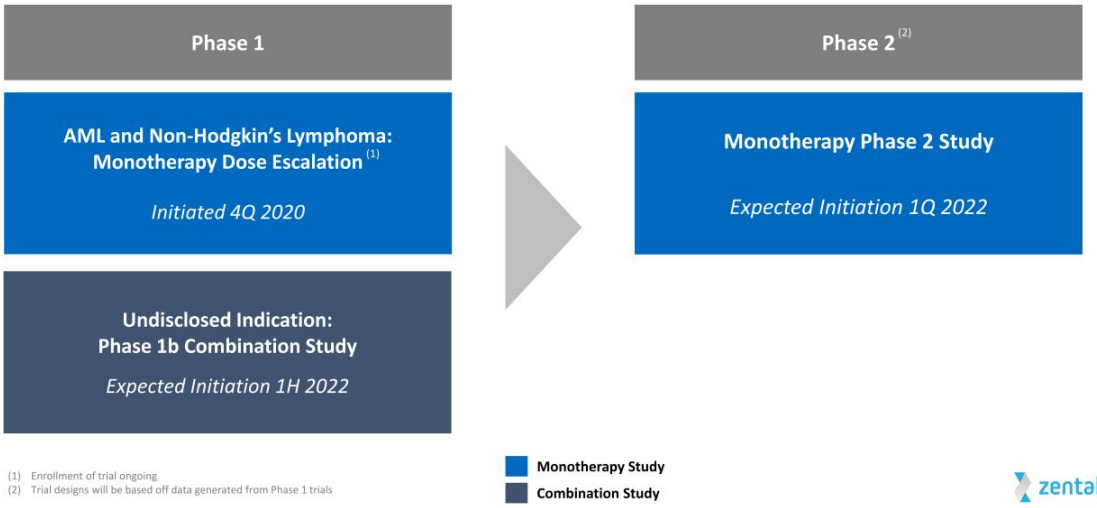
ZN-d5: Clinical Development Plan

Ongoing and Planned Clinical Programs



(1) Enrollment of trial ongoing
(2) Trial designs will be based off data generated from Phase 1 trials

Monotherapy Study
Combination Study

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ZN-d5 Update

- ZN-d5 is a highly selective, oral BCL-2 inhibitor
  - In internal preclinical studies, ZN-d5 is 14x more selective for BCL-2 over BCL-xL than venetoclax, potentially yielding less thrombocytopenia
- Entered the clinic in October 2020 in a dose-escalation study in relapsed/ refractory non-Hodgkin's lymphoma (NHL) and acute myeloid leukemia (AML)
  - 14 subjects with NHL enrolled (diffuse large B cell, mantle cell, follicular and marginal zone lymphomas all represented)
  - Completed first 4 dosing cohorts without dose-limiting toxicities; 5th cohort ongoing
  - No unexpected safety findings; evidence of biological activity
  - Plan to open the study to AML this summer

ZN-e4

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ZN-e4 Update

- ZN-e4 is a potent, third generation EGFR inhibitor
  - Lack of active metabolite binding to wild type EGFR provides potential for better tolerability than osimertinib
- First-in-human dose escalation study in EGFR-mutant non-small cell lung cancer is ongoing
  - Enrolled 26 subjects, both osimertinib-naïve and -experienced
  - Escalated from 20 mg through 480 mg, with clinical activity at doses >80 mg QD
  - Well-tolerated at all doses; rash AE observed in one subject and only grade 1 (1/26 subjects, 4%) as of March 25, 2021 data cutoff
  - Currently back-filling several dose cohorts to have robust PK and exposure-toxicity data to support Phase 2 dose selection

Milestones

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Updated Key Milestones

Event	Expected Timing
ZN-c3 (WEE1 Inhibitor)	
Initiate Phase 2 monotherapy in uterine serous carcinoma	Completed
Initiate Phase 1/2 chemotherapy combo in osteosarcoma	3Q 2021
Initiate Phase 1/2 niraparib combo in ovarian cancer	4Q 2021
Initiate Phase 1/2 tumor agnostic, predictive biomarker study	4Q 2021
Initial readouts on Phase 1 USC expansion cohort and Phase 1b ovarian chemo combo	1H 2022
Initial readouts on Phase 2 USC trial and Phase 1/2 chemotherapy combo in osteosarcoma	2H 2022
ZN-c5 (Oral SERD)	
Phase 1 interim results from monotherapy dose expansion and escalation studies, Window of Opportunity study, palbo combo safety	Completed
Initiate Phase 2 monotherapy study	Completed
Phase 1b combination study topline results with palbociclib; Phase 1b combination study topline results with abemaciclib	1H 2022
ZN-d5 (BCL-2 Inhibitor)	
Initiate monotherapy Phase 2 trial	1Q 2022
Phase 1 initial results from dose escalation study in AML and Non-Hodgkin's Lymphoma	1H 2022
Initiate combination Phase 1b trial in undisclosed indication	1H 2022
ZN-e4 (EGFR Inhibitor)	
Phase 1 initial results from dose escalation study	4Q 2021
Evaluate potential for use in combinations for treatment of lung cancer	2021+
Integrated Discovery Engine	
R&D Day	4Q 2021
Zentera	
Submit ZN-c5, ZN-c3, ZN-d5 CTAs in China	Completed
Potential HK listing	2022

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