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): April 8, 2022

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 1710
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 April 8, 2022, Zentalis Pharmaceuticals, Inc. (the "Company") issued a press release announcing initial efficacy and safety data from the ongoing Phase 1b trial of ZN-c3 in combination with chemotherapy in patients with platinum-resistant or -refractory ovarian cancer, and certain other clinical and preclinical developments. A copy of the press release is furnished as Exhibit 99.1 hereto.

The information contained in Item 7.01 of this Current Report on Form 8-K (the "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, except as expressly provided by specific reference in such a filing.

Item 8.01. Other Events.

On April 8, 2022, the Company announced initial efficacy and safety data from the ongoing Phase 1b trial of ZN-c3 in combination with chemotherapy in patients with platinum-resistant or -refractory ovarian cancer. These data were reviewed during the American Association of Cancer Research (AACR) Annual Meeting, being held in New Orleans, Louisiana on April 8-13, 2022.

Initial Efficacy and Safety Data of ZN-c3 in Combination with Chemotherapy

The ongoing Phase 1b dose-escalation trial is evaluating the safety, tolerability, preliminary clinical activity, pharmacokinetics and pharmacodynamics of ZN-c3 in combination with standard chemotherapies in platinum-resistant or -refractory ovarian cancer. The study consists of four combination dose cohorts: ZN-c3 + PLD, ZN-c3 + carboplatin, ZN-c3 + paclitaxel, and ZN-c3 + gemcitabine, and is enrolling a more advanced patient population, with the inclusion of platinum-refractory patients and higher prior rates of bevacizumab treatment, than similar trials that included a Wee1 inhibitor.

At the time of the data cutoff on January 28, 2022, 56 patients – which were enrolled across three of the cohorts – were evaluated for safety, the primary endpoint, and 43 were response-evaluable. The fourth cohort, ZN-c3 + gemcitabine, had not begun enrollment at the time of the data cutoff. The evaluation of the recommended Phase 2 dose remains ongoing, with the key efficacy data presented at AACR included in the table below.

Summary of Clinical Activity

Cohort	N	Evaluable* (n)	PR/uPR+ (n)	SD/SD+ (n)	PD (n)	DCR (%)	ORR (%)
Total	56	43	13	24	6	86.0	30.2
ZN-c3 + PLD	30	24	3	17	4	83.3	12.5
ZN-c3 + carboplatin	17	11	5	4	2	81.8	45.5
ZN-c3 + paclitaxel	9	8	5	3	-	100	62.5

ZN-c3 was generally well-tolerated in combination with chemotherapy. As of the cutoff date, the most common treatment-related adverse events at all grades included nausea (48.2% of patients), neutropenia (41.1% of patients), thrombocytopenia (37.5% of patients), vomiting (30.4% of patients) and anemia (26.8% of patients).

Interim Data on ZN-c3 in Uterine Serous Carcinoma

On April 8, 2022, the Company disclosed interim data from the ongoing Phase 1 clinical trial evaluating ZN-c3 as a monotherapy for the treatment of advanced solid tumors, in the uterine serous carcinoma dose expansion cohort of patients receiving a dose of ≥300 mg once daily. As of the October 28, 2021 data cutoff date (n=12 evaluable), ZN-c3 demonstrated a disease control rate (DCR) of 88.9%. The cohort included one subject who achieved an unconfirmed complete response.

Preclinical Poster Updates

Three posters were presented at AACR that demonstrated the broad potential of ZN-c3 in multiple settings including AML, PARP-resistant ovarian cancer, and in novel biology when combined with the Company's BCL-2 inhibitor, ZN-d5.

Initial Clinical Data and Updates on ZN-c5

The Company also reported in its press release that initial clinical data from its ongoing Phase 1/2 clinical trial evaluating ZN-c5 in combination with Pfizer's CDK4/6 palbociclib and Lilly's CDK4/6 abemaciclib demonstrated a favorable tolerability profile. As of a January 31, 2022 data cutoff, the combination of ZNc-5 and palbociclib, at selected doses, had a clinical benefit rate ("CBR") of 34% in ER+/HER2- breast cancer patients (n=50), and drug-drug interactions ("DDIs") were seen at 50 mg of ZN-c5 with a 35% decrease in palbociclib exposure relative to historical patient data. As of a January 11, 2022 data cutoff, a 20% CBR was observed in a cohort of ER+/HER2- breast cancer patients (n=10) receiving ZN-c5 in combination with abemaciclib, and DDI was seen at 50 mg of ZN-c5 with a 67% decrease in abemaciclib exposure at steady state. However, ZN-c5 is not expected to have DDIs with commonly used medicines or ZN-c3 at relevant doses.

ZN-c5 demonstrated meaningful bone protectant activity in ovariectomized mice, highlighting a further point of differentiation within the oral SERD class, along with favorable tolerability. The Company believes this profile positions ZN-c5 well for an adjuvant setting.

The Company plans to initiate a combination study of ZN-c5 + ZN-c3 in $ER^{+}/HER2^{-}$ CDK 4/6i-resistant breast cancer patients in 2022.

Forward-Looking Statements

This Current Report contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. 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 United States and globally, 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; our need for additional funding, which may not be available; our substantial dependence on the success of our lead product candidates; 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; risks relating to intellectual property; our ability to attract, retain and motivate qualified personnel; and the other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2021 filed 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 Current Report. 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.

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:

Exhibit No.	Description
99.1	Press Release issued on April 8, 2022.
99.2	Corporate Update Presentation of Zentalis Pharmaceuticals, Inc. dated April 8, 2022.
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: April 8, 2022

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

Exhibit 99.1

Zentalis Pharmaceuticals Announces Positive Initial Clinical Data on ZN-c3, its Wee1 Inhibitor, in Patients with Advanced Ovarian Cancer at AACR

ZN-c3 in combination with chemotherapy demonstrated strong anti-tumor activity in a heavily pretreated population, with an ORR of 30.2% across all evaluable chemotherapy cohorts

ZN-c3 in combination with chemotherapy was well-tolerated, exhibiting a better hematologic and gastrointestinal tolerability profile within the Wee1 inhibitor class

Mini symposium on the ZN-c3 uterine serous carcinoma (USC) expansion cohort to be presented on April 11, 2022 at 2:50 p.m. CT

Updates on clinical and preclinical studies with ZN-c5 and ZN-d5

Company to host webcast event with key opinion leader, Kathleen Moore, MD, today, Friday, April 8 at 4:00 p.m. EDT

NEW YORK and SAN DIEGO, April 8, 2022 – 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 initial efficacy and safety data from the ongoing Phase 1b trial of ZN-c3 in combination with chemotherapy in patients with platinum-resistant or -refractory ovarian cancer. Data were reviewed as a clinical poster during the American Association of Cancer Research (AACR) Annual Meeting, being held in New Orleans, Louisiana on April 8-13, 2022.

"The initial combination clinical activity reported from our ongoing trial supports ZN-c3's potential best-in-class efficacy and safety profile and for the first time, showcases its synergistic combinability with various chemotherapies," commented Dr. Anthony Sun, Chairman and Chief Executive Officer of Zentalis. "Utilizing a continuous dosing regimen in patients with advanced disease, ZN-c3 demonstrated an Objective Response Rate of 30.2% across all cohorts – achieving up to 62.5% with one cohort – and a markedly better tolerability profile within the Wee1 inhibitor class. Based on these promising initial results, we believe the data support the development of a Phase 3 trial to further investigate this combination's effect in ovarian cancer patients. We look forward to announcing our future development plans for this program before year-end and are motivated by the opportunity to potentially deliver an improved and best-in-class treatment option to patients."

Initial Efficacy and Safety Data

The ongoing Phase 1b dose-escalation trial is evaluating the safety, tolerability, preliminary clinical activity, pharmacokinetics and pharmacodynamics of ZN-c3 in combination with standard chemotherapies in platinum-resistant or -refractory ovarian cancer. The study consists of four combination dose cohorts: ZN-c3 + PLD, ZN-c3 + carboplatin, ZN-c3 + paclitaxel, and ZN-c3 + gemcitabine, and is enrolling a more advanced patient population, with the inclusion of platinum-refractory patients and higher prior rates of bevacizumab treatment, than similar trials that included a Wee1 inhibitor.

*Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1; Patients with measurable disease and at least one post-baseline scan
Of evaluable subjects, ORR is percentage with PR/uPR; and DCR is percentage with ORR + SD/SD+
+ Indicates treatment is ongoing for this subject
PR = partial response; uPR = unconfirmed partial response; ORR = objective response rate; DCR = disease control rate; SD = stable disease; PD = progressive disease
Data cutoff January 28, 2022

At the time of the data cutoff on January 28, 2022, 56 patients – which were enrolled across three of the cohorts – were evaluated for safety, the primary endpoint, and 43 were response-evaluable. The fourth cohort, ZN-c3 + gemcitabine, had not begun enrollment at the time of the data cutoff. The evaluation of the recommended Phase 2 dose remains ongoing, with the key efficacy data presented at AACR included in the table below.

Summary of Clinical Activity

Cohort	N	Evaluable* (n)	PR/uPR+ (n)	SD/SD+ (n)	PD (n)	DCR (%)	ORR (%)
Total	56	43	13	24	6	86.0	30.2
ZN-c3 + PLD	30	24	3	17	4	83.3	12.5
ZN-c3 + carboplatin	17	11	5	4	2	81.8	45.5
ZN-c3 + paclitaxel	9	8	5	3	-	100	62.5

ZN-c3 was generally well-tolerated in combination with chemotherapy and exhibited lower hematologic toxicity and a better gastrointestinal tolerability profile in comparison to the Wee1 inhibitor class. As of the cutoff date, the most common treatment-related adverse events at all grades included nausea (48.2% of patients), neutropenia (41.1% of patients), thrombocytopenia (37.5% of patients), vomiting (30.4% of patients) and anemia (26.8% of patients).

“Platinum-resistant and -refractory ovarian cancer are associated with poor prognoses and limited treatment options, with standard of care having an Overall Response Rate of less than 12%,” commented Kathleen Moore, MD, Director of the Oklahoma TSET Phase I Program for the Stephenson Cancer Center at the University of Oklahoma College of Medicine. “A treatment option that could elicit a clinically meaningful improvement in efficacy, while being well-tolerated, would make a meaningful difference for patients. In this initial cut of data, ZN-c3 in combination with standard chemotherapies has surpassed this goal, achieving an improved efficacy and tolerability profile in a sicker patient population within the Wee1 inhibitor class. Wee1 inhibition remains a promising therapeutic approach to treating an array of solid tumors, including advanced ovarian cancer, and these results further support the class’ potential in changing the treatment paradigm.”

Update on Additional AACR Presentations

Interim data from the Phase 1 monotherapy USC expansion cohort receiving ZN-c3 ≥300mg QD were also released today. ZN-c3 is potentially a best-in-class Wee1 inhibitor and is in an ongoing potentially registrational Phase 2 trial for USC patients (NCT04814108). Updated data from the USC expansion cohort of the Phase 1 monotherapy trial will be presented at the mini symposium on April 11, 2022 at 2:50 p.m. CT.

In addition, Zentalis has three preclinical posters demonstrating the broad potential of ZN-c3 in multiple settings including AML (Abstract #2591), overcoming PARP resistance (Abstract #2606), and in novel biology when combined with our BCL-2 inhibitor, ZN-d5 (Abstract #2605). These findings further support ZN-c3 as a potential cornerstone treatment, creating a significant market opportunity across a broad range of solid and liquid tumors.

The clinical poster, two clinical abstracts and three preclinical posters are currently available on the AACR Annual Meeting 2022 website at https://www.aacr.org/meeting/aacr-annual-meeting-2022.

*Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1; Patients with measurable disease and at least one post-baseline scan
Of evaluable subjects, ORR is percentage with PR/uPR; and DCR is percentage with ORR + SD/SD+
+ Indicates treatment is ongoing for this subject
PR = partial response; uPR = unconfirmed partial response; ORR = objective response rate; DCR = disease control rate; SD = stable disease; PD = progressive disease
Data cutoff January 28, 2022

Exhibit 99.1

Updates on ZN-c5

Initial clinical data of ZN-c5 in combination with CDK 4/6 inhibitors demonstrated excellent safety and tolerability. Drug-drug interactions were seen with ZN-c5 doses; however, ZN-c5 is not expected to have DDIs with commonly used medicines or ZN-c3 at relevant doses.

Uniquely among the leading oral SERDs, ZN-c5 demonstrated meaningful bone protectant activity in ovariectomized mice, highlighting a further point of differentiation within the oral SERD class, along with excellent tolerability. Zentalis believes this profile positions ZN-c5 well for an adjuvant setting.

Zentalis plans to initiate a combination study of ZN-c5 + ZN-c3 in $ER^{+}/HER2^{-}$ CDK 4/6i-resistant breast cancer patients in 2022.

KOL Webcast Event:

Zentalis will host a webcast event with key opinion leader, Kathleen Moore, MD, today, Friday, April 8, 2022 at 4:00 p.m. EDT. Dr. Moore is the Associate Professor in the Section of Gynecologic Oncology; the Jim and Christy Everest Endowed Chair in Cancer Research; and the Director of the Oklahoma TSET Phase I Program for the Stephenson Cancer Center at the University of Oklahoma College of Medicine. She has a clinical research interest in drug development and Phase I trials and is a leading expert in gynecological oncology.

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 ZN-c3

ZN-c3 is a potentially first-in-class and best-in-class oral inhibitor of Wee1 in development for the treatment of advanced solid tumors. The inhibition of Wee1, a DNA damage response protein, aims to generate sufficient DNA damage in cancer cells, causing cell death, thereby preventing tumor growth and potentially causing tumor regression. ZN-c3 has broad potential as a monotherapy and in combination. We are currently evaluating this candidate in several ongoing and planned studies, including two potentially registrational monotherapy trials in USC and a biomarker-driven setting, as well as combination studies, including in combination with chemotherapy in patients with advanced ovarian cancer. We also received orphan drug and rare pediatric disease designations from the FDA for pediatric osteosarcoma and have initiated a Phase 1/2 trial in combination with chemotherapy.

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-c3, a Wee1 inhibitor for advanced solid tumors, ZN-c5, an oral selective estrogen receptor degrader (SERD) for ER+/HER2- breast cancer, ZN-d5, a BCL-2 inhibitor for hematologic malignancies and related disorders, ZN-e4, an EGFR inhibitor for non-small cell lung carcinoma (NSCLC) and a heterobifunctional degrader of BCL-xL for solid and hematological malignancies. The Company has licensed ZN-c3, ZN-c5 and ZN-d5 to its 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.

*Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1; Patients with measurable disease and at least one post-baseline scan
Of evaluable subjects, ORR is percentage with PR/uPR; and DCR is percentage with ORR + SD/SD+
+ Indicates treatment is ongoing for this subject
PR = partial response; uPR = unconfirmed partial response; ORR = objective response rate; DCR = disease control rate; SD = stable disease; PD = progressive disease
Data cutoff January 28, 2022

Exhibit 99.1

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 United States and globally, plans and timing for the initiation of and the release of data from our clinical trials and our ability to meet other key milestones and our participation in upcoming events and presentations. 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; and the other important factors discussed under the caption “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2021 filed 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 Contact:
Alexandra Roy
Solebury Trout
aroy@soleburytrout.com

Media Contact:
Julia Deutsch
Solebury Trout
jdeutsch@soleburytrout.com

*Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1; Patients with measurable disease and at least one post-baseline scan
Of evaluable subjects, ORR is percentage with PR/uPR; and DCR is percentage with ORR + SD/SD+
+ Indicates treatment is ongoing for this subject
PR = partial response; uPR = unconfirmed partial response; ORR = objective response rate; DCR = disease control rate; SD = stable disease; PD = progressive disease
Data cutoff January 28, 2022

zentalis

AACR 2022 Investor Event

April 8, 2022

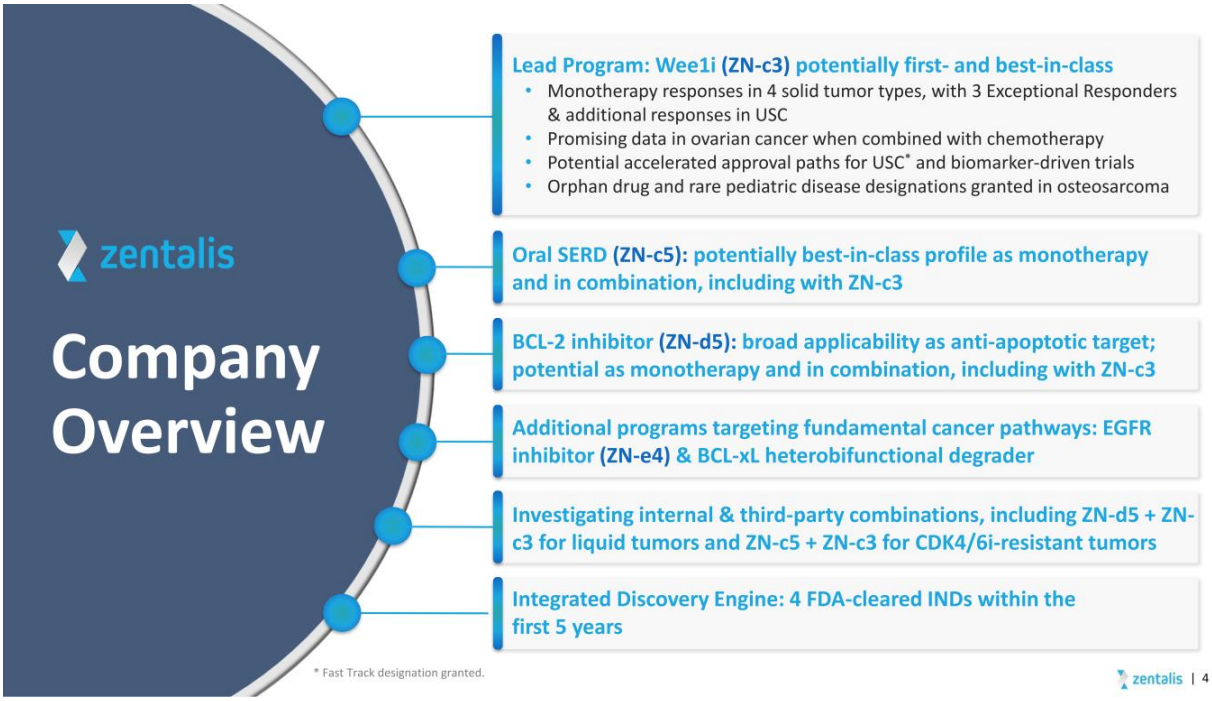
Forward-Looking Statements and Disclaimer

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, including ZN-c3, ZN-c5, ZN-d5 and ZN-e4, 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 Annual Report on Form 10-K for the year ended December 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.

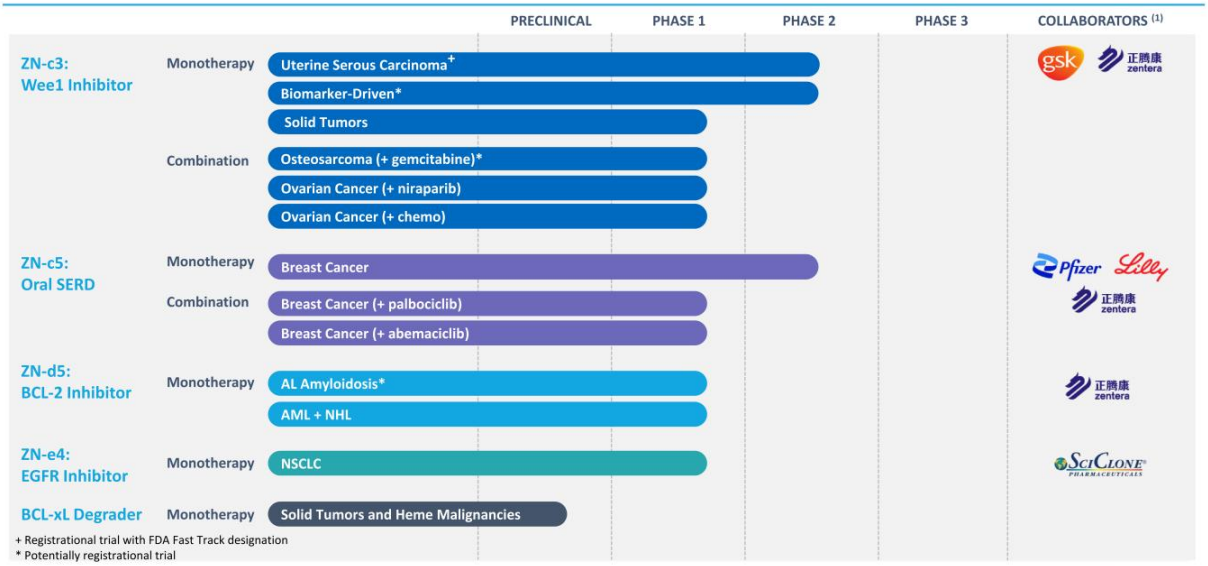
This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data and estimates. 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.

Today's Agenda

1. **ZN-c3 (Wee1 inhibitor) Updates**
   - Phase 1 monotherapy update from USC cohort
   - Phase 1b chemotherapy combination data in ovarian cancer
2. **ZN-c5 (oral SERD) Updates**
3. **ZN-d5 (Bcl-2 inhibitor) Updates**
4. **Summary and Catalysts**


zentalis
Company Overview
Lead Program: Wee1i (ZN-c3) potentially first- and best-in-class
• Monotherapy responses in 4 solid tumor types, with 3 Exceptional Responders & additional responses in USC
• Promising data in ovarian cancer when combined with chemotherapy
• Potential accelerated approval paths for USC* and biomarker-driven trials
• Orphan drug and rare pediatric disease designations granted in osteosarcoma
Oral SERD (ZN-c5): potentially best-in-class profile as monotherapy and in combination, including with ZN-c3
BCL-2 inhibitor (ZN-d5): broad applicability as anti-apoptotic target; potential as monotherapy and in combination, including with ZN-c3
Additional programs targeting fundamental cancer pathways: EGFR inhibitor (ZN-e4) & BCL-xL heterobifunctional degrader
Investigating internal & third-party combinations, including ZN-d5 + ZN-c3 for liquid tumors and ZN-c5 + ZN-c3 for CDK4/6i-resistant tumors
Integrated Discovery Engine: 4 FDA-cleared INDs within the first 5 years
* Fast Track designation granted.
zentalis | 4

Broad Oncology Pipeline Designed to Improve Patient Outcomes

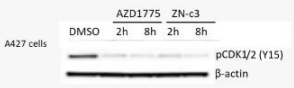


(1) Zentalis is currently evaluating ZN-c5 in combination with palbociclib (Ibrance®), as part of a clinical research collaboration with Pfizer, evaluating ZN-c5 in combination with abemaciclib (Verzenio®), as part of a clinical research collaboration with Lilly. Zentalis intends to evaluate ZN-c3 in combination with niraparib (ZEJULA®), as part of a clinical research collaboration with GlaxoSmithKline. Zentalis maintains full ownership of ZN-c5 and ZN-c3 in each such collaboration. SciClone has development and commercial rights to ZN-e4 in Greater China (including Macau and Hong Kong), South Korea, Taiwan and Vietnam. Zentera, our joint venture, has development and commercial rights to ZN-c5, ZN-c3 and ZN-d5 in select Asian countries (including China). Zentera received CTA acceptances in China for ZN-c3, ZN-c3 in combination, ZN-c5 and ZN-d5 and four clinical trials are ongoing.

zentalis

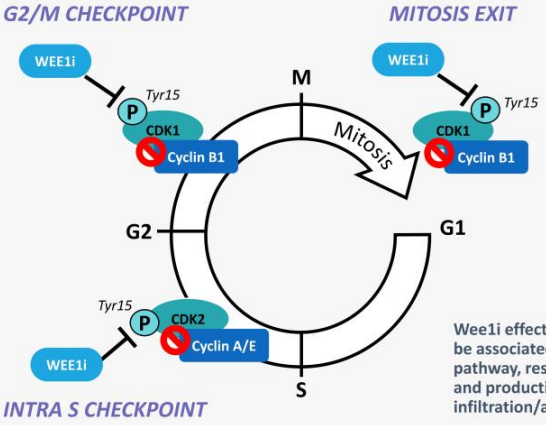
ZN-c3: Wee1 Inhibitor Background

Wee1 Inhibition: Clinically Proven DDR Target for Cancer



ZN-c3 inhibits CDK1/2 phosphorylation

Wee1 inhibition causes cancer cells to proceed to mitosis without repairing DNA damage, resulting in premature mitotic entry and apoptosis



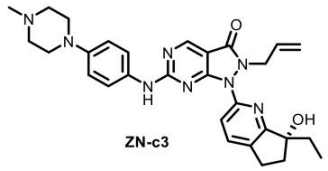
Inhibition of Wee1 may cause tumor cell death by:

- Aberrant origin firing causing exhaustion of the replication protein A1 (RPA1)[1]
- Degradation of ribonucleotide reductase subunit leading to exhaustion of dNTP pools[2]

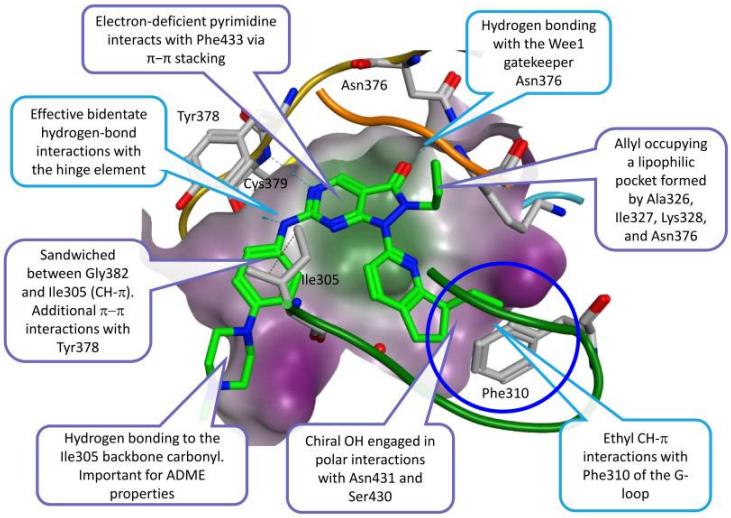
Wee1i effects on cell cycle and DNA damage may be associated with activation of cGAS/STING pathway, resulting in Type I interferon response and production of cytokines driving immune cell infiltration/activation into tumor[3-5]

(1) Di Rora AGL et al. J Hematol Oncol. 2020 Sep 21;13(1):126
(2) Pfister SX et al. Cancer Cell. 2015 Nov 9; 28(5): 557–568
(3) Keenan et al. Clin Canc Res. (2021)
(4) Hai J et al. Clin Cancer Res. 2020 Jul 1;26(13):3431-3442
(5) Guo e et al. J. Exp. Med. 2021 Vol. 219 No. 1

Structure-Based Drug Design (SBDD) Led to the Discovery of a Highly Potent and Selective Wee1 Inhibitor ZN-c3 with Improved ADME Properties(1)

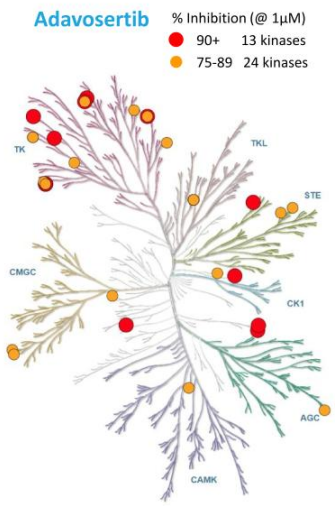


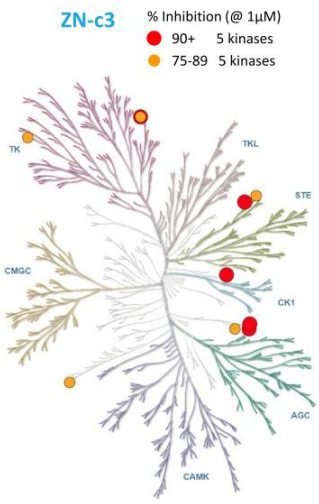
ZN-c3 potency and ADME	
Wee1 IC_{50}	3.8 nM
H23 IC_{50}	103 nM
A427 IC_{50}	75 nM
Log *D*	2.4
*h*PPB	66%
*h*Hep	<18 mL/min/kg
solubility	> 2000 µM
CYP3A4	7 µM
hERG	> 30 µM



(1) Huang, PQ; *et al.* J. Med. Chem. **2021**, *64*, 13004-13024

ZN-c3: Differentiated Selectivity Profile(1)





(1) Illustrations reproduced courtesy of Cell Signaling Technology, Inc. (www.cellsignal.com)

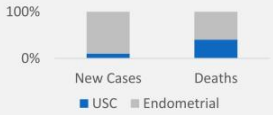
zentalis

ZN-c3: Phase 1 USC Monotherapy Update

The Unmet Need in Uterine Serous Carcinoma is Significant

UNMET NEED

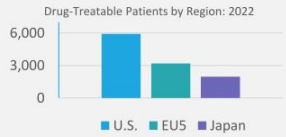
- USC results in **~40% of endometrial cancer deaths** despite comprising only 10% of cases



  - **Prior to pembro+len approval, ORR of 9.5% with PLD was chemo SOC for third-line USC**[1]
  - The 5-year survival rate for late-stage USC is 33% [2]
- >90% of USC patients have TP53 mutations[3]

PATIENT POPULATION

- In 2022, the total number of drug treatable **third line** advanced or recurrent endometrial cancer patients is approximately **10,000 in the United States, EU5 and Japan**[4]



- **Improvement in efficacy while limiting toxicities** would make a meaningful difference for patients

COMPETITIVE LANDSCAPE

- Current standard of care for third line, USC is single-agent chemotherapy, with some limited use of bevacizumab and pembrolizumab monotherapies[5]
- There is a **high need** for a therapeutic option in later line patients **after prior platinum containing chemotherapy and pembrolizumab + lenvatinib treatment**[1]
  - Another Wee1 inhibitor (adavosertib) is also in late-stage clinical evaluation
- ZN-c3 is potentially a best in-class treatment option for USC

ZN-c3's efficacy and tolerability profile are well positioned for the USC population

(1) Muggia, J Clin Oncol, 2002 (2) Hamilton CA et al. Br J Cancer. 2006 Mar 13;94(5):642-6. (3) Liu JF et al. J Clin Oncol. 2021 Mar 11:JCO2003167. (4) Decision Resources Group; data on file. (5) CancerMPact, Future Trends and Insights Endometrial cancer June 2021; data on file.

Safety and clinical activity of single-agent ZN-c3, an oral Wee1 inhibitor, in a Phase 1 trial in subjects with recurrent or advanced uterine serous carcinoma (USC)

F. Meric-Bernstam[1], P. Chalasani[2], H. Mamdani[3], C. Zheng[4], M. Viana[4], R. Lambersky[4], P. Pultar[4], A. Tolcher[5]

[1]MD Anderson Cancer Center, Houston, TX, USA; [2]University of Arizona Cancer Center, Tucson, AZ, USA; [3]Karmanos Cancer Center, Detroit, MI, USA; [4]Zentalis Pharmaceuticals, New York, NY, USA; [5]Texas Oncology Babcock, San Antonio, TX, USA

Updated monotherapy data from USC cohort dose ≥300mg QD will be presented as part of a mini-symposium on Monday, April 11th at 2:50pm CT

zentalis

ZN-c3: Chemo Combination in Ovarian Cancer

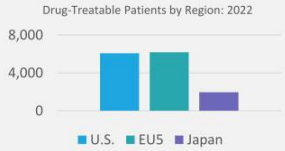
Platinum-Resistant/Refractory Ovarian Cancer Remains an Unmet Need

UNMET NEED

- Platinum-resistant and -refractory ovarian cancer represents a **high unmet need**
- It is associated with a poor prognosis and limited treatment options
  - **ORR of 11.8% with SOC[1] for platinum resistant patients**
- **Improvement in efficacy with acceptable safety profile** would make a meaningful difference for patients

PATIENT POPULATION

- In 2022, the total number of drug-treatable second line platinum-resistant ovarian cancer patients is estimated to be **>14,000 in the United States, EU5 and Japan[2]**



COMPETITIVE LANDSCAPE

- Current standard of care for second line platinum-resistant ovarian patients is single-agent chemotherapy ± bevacizumab[3]
- Ongoing pivotal trials focus on novel MOAs, including ADCs, and combinations with either PARPi or chemotherapy.[3] Of note, ADCs only work in a sub-population of patients
- ZN-c3 is potentially a first-in-class treatment option that works synergistically with other anticancer therapies

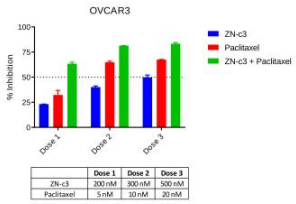
ZN-c3's efficacy and tolerability profile are well-positioned for the platinum-resistant/refractory ovarian population

(1) Pujade-Lauraine et al. J Clin Oncol 2014; 32:1302-1308; AURELIA study (2) Decision Resources Group; data on file. (3) CancerMPact Treatment Architecture Ovarian cancer July 2021; data on file.

ZN-c3 Combined with Chemotherapy is Highly Active *in vitro* Against OVCAR3 Ovarian Cancer Cells

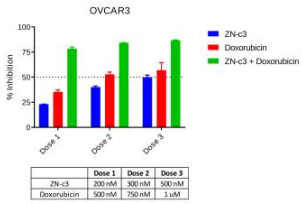
- Inhibition of Wee1, combined with DNA-damaging agents (**doxorubicin** and **carboplatin**) or inducers of replication stress (**paclitaxel** and **gemcitabine**), causes mitotic entry without completion of DNA repair, leading to mitotic catastrophe[1-3]
  - **Paclitaxel:** shown to induce degradation of the Wee1 protein by causing mitotic arrest
  - **Gemcitabine:** inhibits the enzyme RRM2* essential for synthesis of deoxyribonucleotides and causes replication stress
- In addition, Wee1 inhibition elicits an immune response which may synergize with the immune activation mediated by chemotherapy (Immunogenic Cell Death)

ZN-c3 + Paclitaxel



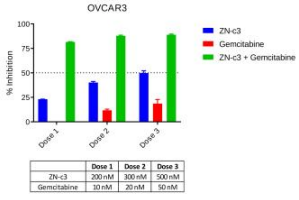
	Dose 1	Dose 2	Dose 3
ZN-c3	200 nM	300 nM	500 nM
Paclitaxel	5 nM	10 nM	20 nM

ZN-c3 + Doxorubicin



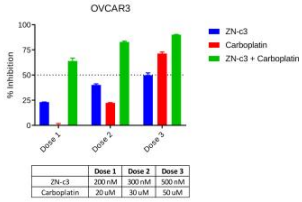
	Dose 1	Dose 2	Dose 3
ZN-c3	200 nM	300 nM	500 nM
Doxorubicin	500 nM	750 nM	1 uM

ZN-c3 + Gemcitabine



	Dose 1	Dose 2	Dose 3
ZN-c3	200 nM	300 nM	500 nM
Gemcitabine	10 nM	20 nM	50 nM

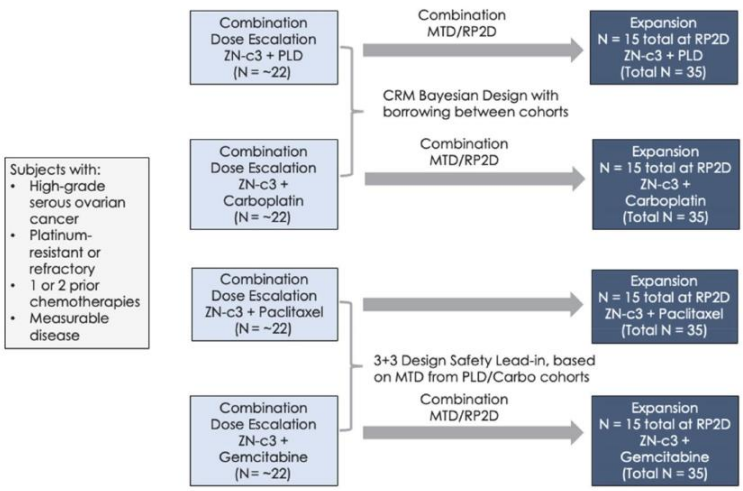
ZN-c3 + Carboplatin



	Dose 1	Dose 2	Dose 3
ZN-c3	200 nM	300 nM	500 nM
Carboplatin	20 uM	30 uM	50 uM

(1) L Ghelli et al. J Hematol Oncol. 2020; 13:126
(2) NYL Ngoi et al. Trends Cancer. 2021; 7:930-957
(3) M Aarts et al. Cancer Discov. 2012;2:524-39
* Ribonucleoside-diphosphate reductase subunit M2

ZN-c3-002: Study Design



MTD= maximum tolerated dose; N= number of subjects; RP2D= recommended Phase 2 dose; CRM= continual reassessment method; PLD= liposomal doxorubicin

ZN-c3-002: Baseline Characteristics

Baseline Characteristics (All Cohorts)

Characteristic	ZN-c3 + PLD (n = 30)	ZN-c3 + Carboplatin (n = 17)	ZN-c3 + Paclitaxel (n = 9)	Total[1,2] (N = 56)
Median age, years (range)	55 (34–75)	61 (49–74)	67 (51–74)	58.5 (34–75)
Race, n (%)				
White	29 (97)	17 (100)	8 (89)	54 (96)
Asian	1 (3)	0 (0)	1 (11)	2 (4)
ECOG status, n (%)				
0	20 (67)	8 (47)	8 (89)	36 (64)
1	10 (33)	9 (53)	1 (11)	20 (36)
Prior lines of therapy, n (%)				
1	19 (63)	9 (53)	5 (56)	33 (59)
2	11 (37)	8 (47)	4 (44)	23 (41)
Prior bevacizumab, n (%)	13 (43)	9 (53)	4 (44)	26 (46)
Prior PARP inhibitor, n (%)	3 (10)	4 (24)	1 (11)	8 (14)
Prior therapy status, n (%)				
Resistant	24 (80)	15 (88)	9 (100)	48 (86)
Platinum refractory	6 (20)	2 (12)	0 (0)	8 (14)

100% of patients became resistant/refractory to platinum within the first 2 lines of therapy indicating an aggressive phenotype

(1) No subjects have been enrolled in the gemcitabine arm as of January 28, 2022.
(2) Full patient genetic background analysis ongoing.

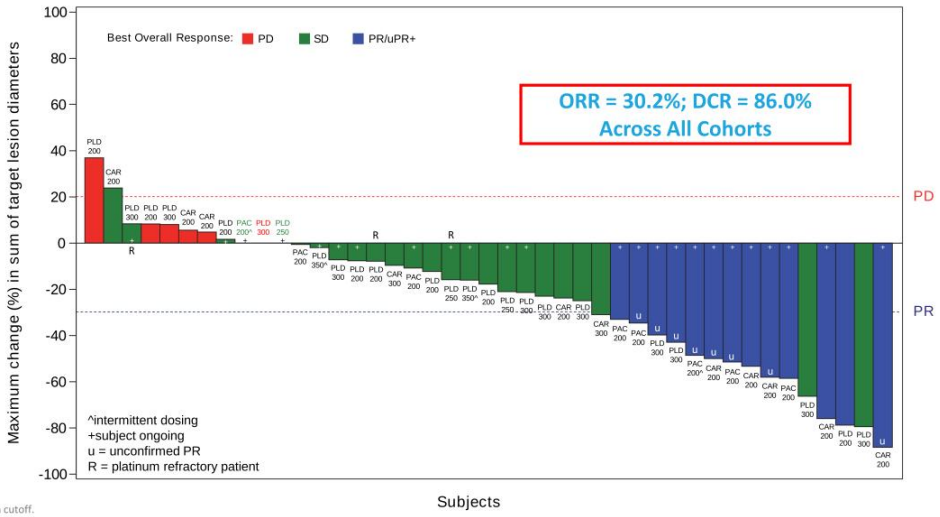
Expectations for Efficacy in Recurrent Ovarian Cancer Patients

Study Name / Author	Drug	Platinum Refractory	Prior Bevacizumab Treatment	ORR	Overall Survival for Wee1 Inhibitor
AURELIA (Phase 3, Randomized Trial) [1]	Chemotherapy (PLD, paclitaxel, topotecan) in control arm	Not included	None	11.8%	N/A
Moore KM, CCR (Phase 2, Open Label) [2]	Adavosertib + chemotherapy	Not included	34% overall	11-33% range (High dose C2 arm not tolerated)	N/A
Lheureux S, Lancet (Phase 2, DB, PC, Randomized Trial) [3]	Adavosertib + gemcitabine	Included Plat Refractory (10%)	Unknown	23% (6% chemo alone)	**mOS = 11.4 mos; HR = 0.56 vs gemcitabine alone (p=0.017)**
ZN-c3-002	ZN-c3 + chemotherapy	Included Plat Refractory (7%)[4]	46% overall		

A response rate >20% may lead to significant PFS and OS advantages in larger trials

(1) Pujade-Lauraine E et al. [AURELIA study] *J Clin Oncol* 2014; 32:1302-1308.
(2) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(3) Lheureux S et al. *Lancet* 2021; 397: 281–92
(4) Platinum refractory population of 7% in evaluable population

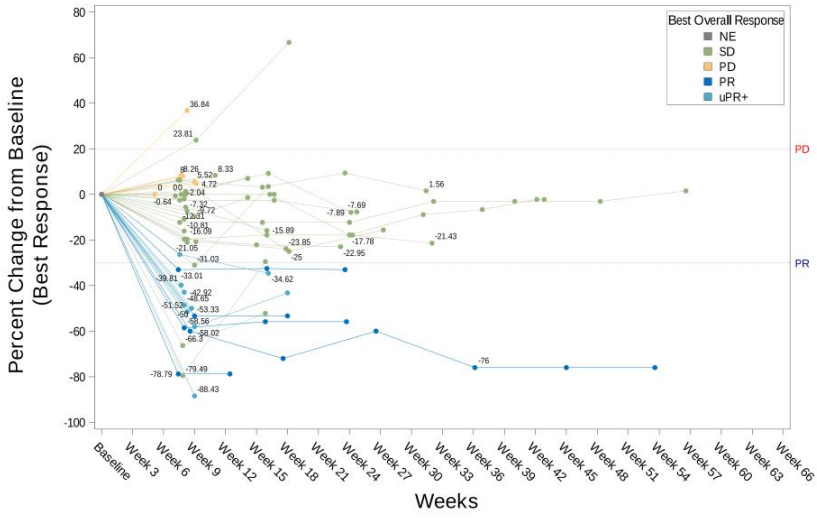
ZN-c3-002: Maximum Reduction in Sum of Target Lesion Diameters All Patients (n=43*)(1)



(1) January 28, 2022 data cutoff.
Note: Excluding platinum refractory patients ORR = 32.5% and DCR = 85%.
* Evaluable patients; Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1; Patients with measurable disease and at least one post-baseline scan

ZN-c3-002: Robust Disease Control Rate Observed Across All Cohorts

Responders experienced a meaningful duration of response



Data cutoff January 28, 2022.

ZN-c3-002: Responder #1 Background

Ovarian Cancer – Platinum-resistant

- 52-year-old female, Stage III Ovarian Cancer, metastases to the liver, abdomen, mesentery (lymph node). ECOG PS 0
- Two prior lines of therapy in the advanced/ metastatic setting
- ZN-c3 starting dose: 200 mg QD + Paclitaxel 80 mg/m^2
- The subject remained on the study for 214 days (Cycle 7) until clinical disease progression
- Patient experienced decreased CA-125 tumor marker from 1122 ng/mL at baseline to 254 ng/mL at Cycle 4

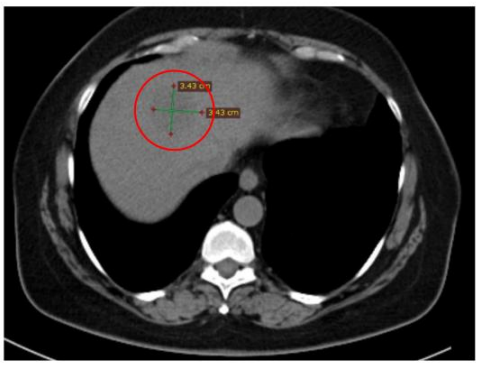
Confirmed PR with 56% reduction overall

Previous Therapy Experience

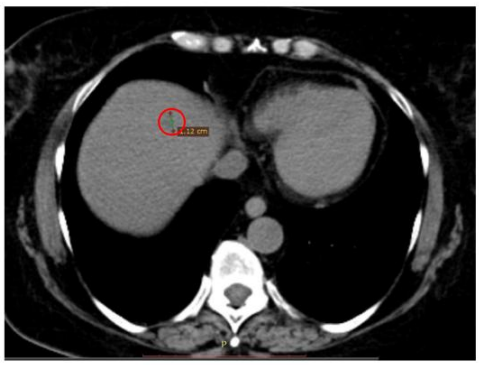
Intent of Treatment	Regimen	Start	Stop	Best Response
Advanced/ Metastatic	Carboplatin / Paclitaxel	Jul-17	Sep-17	SD
Advanced/ Metastatic	Carboplatin / Doxorubicin	Dec-20	Apr-21	PD

ZN-c3-002: Responder #1 Baseline and Follow-up (Liver Lesion)

Baseline (July 2021)



4th Assessment (Jan 2022)



ZN-c3-002: Responder #2 Background

Ovarian Cancer – Platinum-resistant

- 72-year-old female, Stage IV Ovarian Cancer, metastases to the greater omentum, spleen capsule, pararectal, Liver capsule, peritoneum. ECOG PS 0
- Two prior lines of therapy in the advanced/ metastatic setting
- ZN-c3 starting dose: 300 mg QD + PLD 40 mg/m^2
- The subject remains on the study, currently Cycle 5
- Patient experienced decreased CA-125 tumor marker from 381 ng/mL at baseline to <50 ng/mL at Cycle 5

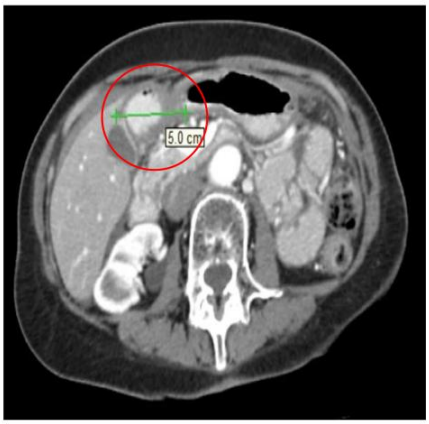
Confirmed PR with 46% reduction overall

Previous Therapy Experience

Intent of Treatment	Regimen	Start	Stop	Best Response
Advanced/ Metastatic	Carboplatin / Paclitaxel	Oct-19	Mar-20	SD
Advanced/ Metastatic	Carboplatin / Paclitaxel	Dec-20	May-21	PD

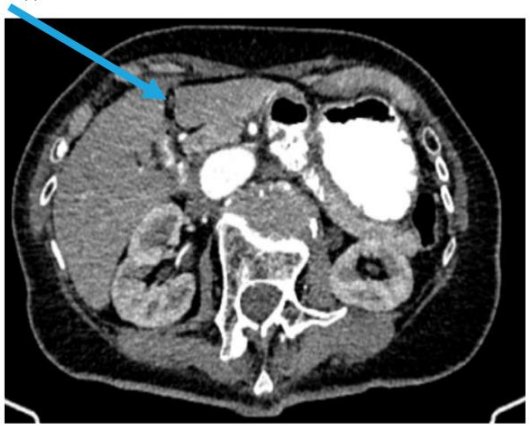
ZN-c3-002: Responder #2 Baseline and Follow-up (Liver Lesion)

Baseline (October 2021)



Complete disappearance

2nd Assessment (December 2021)



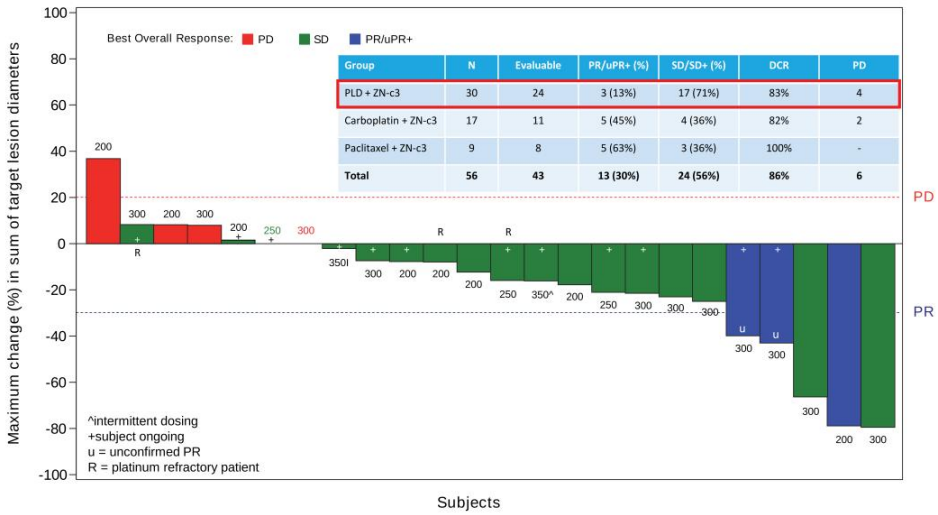
ZN-c3-002: Summary of Clinical Activity

Summary of Clinical Activity (All Cohorts)

Group	N	Evaluable* (n)	PR/uPR+ (n)	SD/SD+ (n)	PD (n)	DCR (%)	ORR (%)
Total	56	43	13	24	6	86.0	30.2
ZN-c3 + PLD	30	24	3	17	4	83.3	12.5
ZN-c3 + Carboplatin	17	11	5	4	2	81.8	45.5
ZN-c3 + Paclitaxel	9	8	5	3	–	100	62.5

Measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1
* Patients with measurable disease and at least one post-baseline scan
Of evaluable subjects, ORR is percentage with PR/uPR; and DCR is percentage with ORR + SD/SD+
+ Indicates treatment is ongoing for this subject
PR = partial response; uPR = unconfirmed partial response; ORR = objective response rate; DCR = disease control rate; SD = stable disease; PD = progressive disease
Data cutoff January 28, 2022

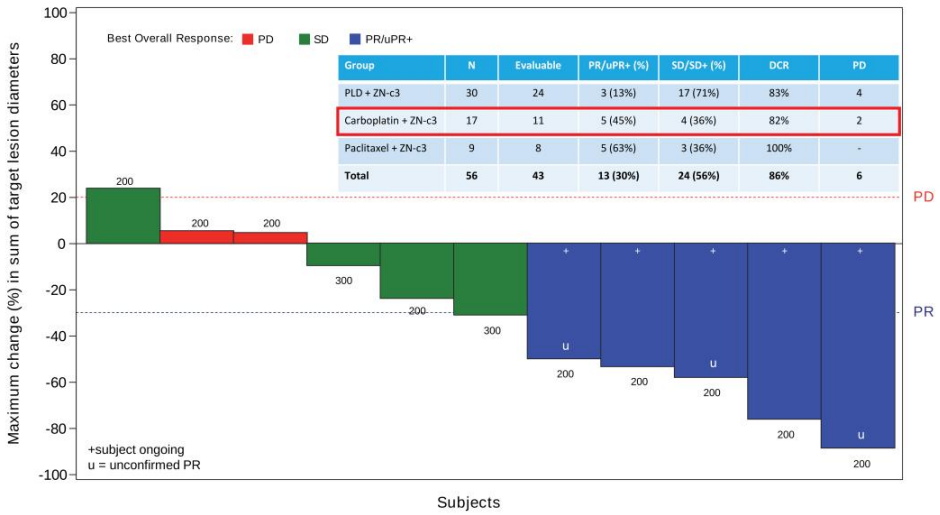
ZN-c3-002: Maximum Reduction in Sum of Target Lesion Diameters PLD Patients(1)



Group	N	Evaluable	PR/uPR+ (%)	SD/SD+ (%)	DCR	PD
PLD + ZN-c3	30	24	3 (13%)	17 (71%)	83%	4
Carboplatin + ZN-c3	17	11	5 (45%)	4 (36%)	82%	2
Paclitaxel + ZN-c3	9	8	5 (63%)	3 (36%)	100%	-
Total	**56**	**43**	**13 (30%)**	**24 (56%)**	**86%**	**6**

(1) January 28, 2022 data cutoff.
Note: Excluding platinum refractory patients ORR = 14.3% and DCR = 81%.

ZN-c3-002: Maximum Reduction in Sum of Target Lesion Diameters Carboplatin Patients[1]



Group	N	Evaluable	PR/uPR+ (%)	SD/SD+ (%)	DCR	PD
PLD + ZN-c3	30	24	3 (13%)	17 (71%)	83%	4
Carboplatin + ZN-c3	17	11	5 (45%)	4 (36%)	82%	2
Paclitaxel + ZN-c3	9	8	5 (63%)	3 (36%)	100%	-
Total	**56**	**43**	**13 (30%)**	**24 (56%)**	**86%**	**6**

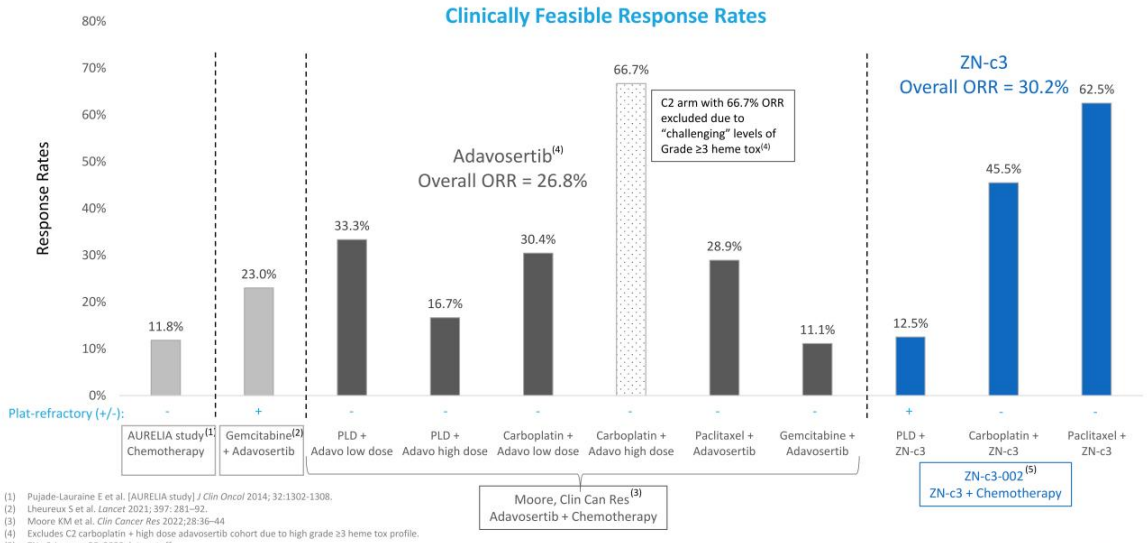
(1) January 28, 2022 data cutoff.

ZN-c3-002: Maximum Reduction in Sum of Target Lesion Diameters Paclitaxel Patients(1)

Group	N	Evaluable	PR/uPR+ (%)	SD/SD+ (%)	DCR	PD
PLD + ZN-c3	30	24	3 (13%)	17 (71%)	83%	4
Carboplatin + ZN-c3	17	11	5 (45%)	4 (36%)	82%	2
Paclitaxel + ZN-c3	9	8	5 (63%)	3 (36%)	100%	-
Total	**56**	**43**	**13 (30%)**	**24 (56%)**	**86%**	**6**

(1) January 28, 2022 data cutoff.

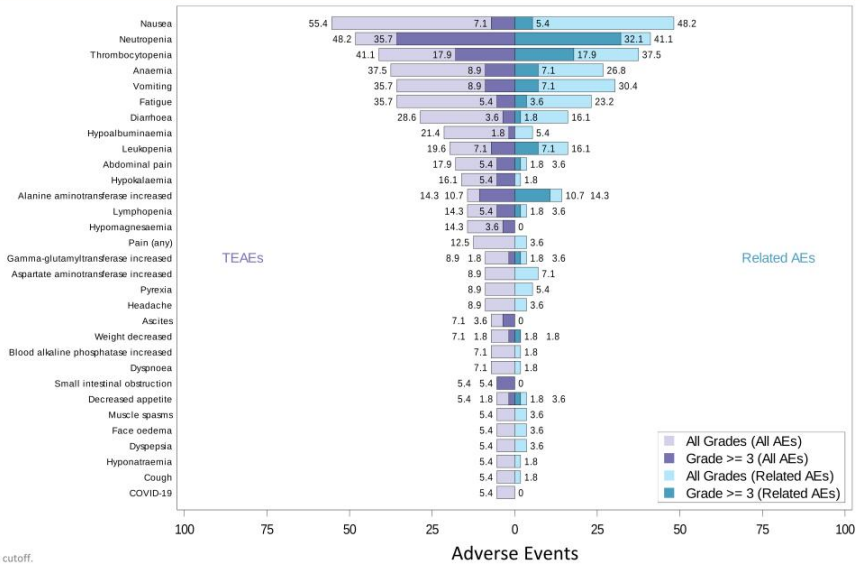
Clinically Feasible Response Rates for ZN-c3 and Competitors in Ovarian Cancer*



(1) Pujade-Lauraine E et al. [AURELIA study] *J Clin Oncol* 2014; 32:1302-1308.
(2) Lheureux S et al. *Lancet* 2021; 397: 281–92.
(3) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(4) Excludes C2 carboplatin + high dose adavosertib cohort due to high grade ≥3 heme tox profile.
(5) ZN-c3 January 28, 2022 data cutoff.

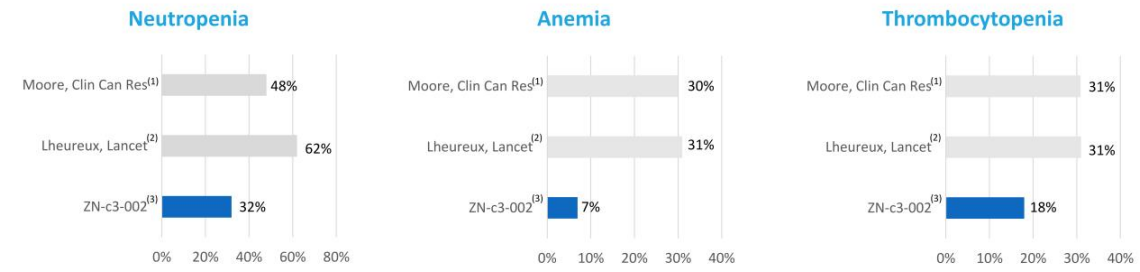
* Non-head-to-head comparison. Results of a head-to-head comparison may differ significantly from those set forth herein. In addition, because our Phase 1 clinical trial for ZN-c3 and the clinical trials of those other compounds above were separate trials, differences between the results of the trials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

ZN-c3-002: TEAEs ≥5% for All Patients (N=56)[1]



(1) January 28, 2022 data cutoff.

ZN-c3 Exhibits Lower Hematologic Toxicity vs Adavosertib When Combined with Chemotherapy – Grade ≥ 3 TRAEs*

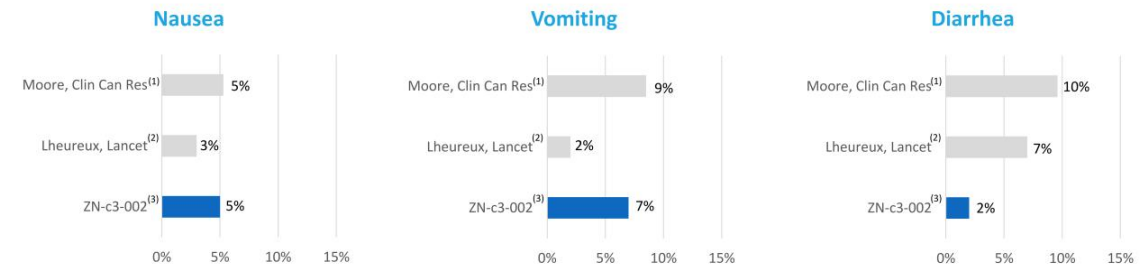


- Target ZN-c3 dosing was QD continuously throughout the treatment cycle across all chemotherapy cohorts
- Adavosertib's dosing schedule was intermittent to manage expected tolerability concerns, creating hurdles for commercial adoption

ZN-c3 demonstrated a potentially best-in-class hematologic tolerability profile versus adavosertib even with a higher total drug load

(1) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(2) Lheureux S et al. *Lancet* 2021; 397: 281–92 (as reported)
(3) ZN-c3-002 data cutoff January 28, 2022.
* 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.

ZN-c3 GI Tolerability Profile is Better than Adavosertib When Combined with Chemotherapy – Grade ≥ 3 TRAEs*



- Target ZN-c3 dosing was QD continuously throughout the treatment cycle across all chemotherapy cohorts
- Adavosertib's dosing schedule was intermittent to manage expected tolerability concerns, creating hurdles for commercial adoption

ZN-c3's GI tolerability profile is potentially better than adavosertib even with a higher total drug load

(1) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(2) Lheureux S et al. *Lancet* 2021; 397: 281–92 (as reported)
(3) ZN-c3-002 data cutoff January 28, 2022.
* 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.

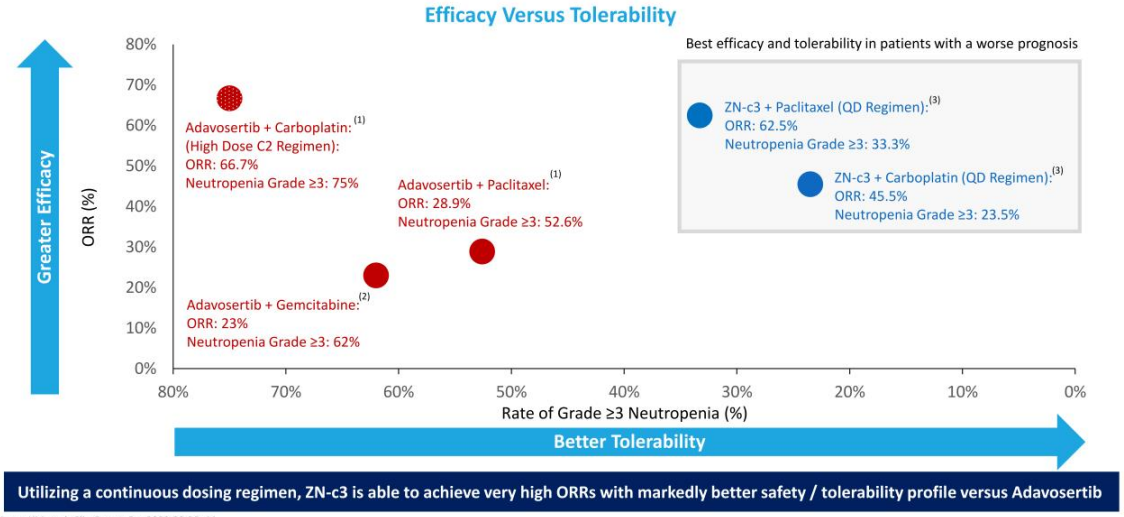
ZN-c3 Oral Dosing Regimen is Convenient and Currently in Dose Escalation

	Paclitaxel	Carboplatin	PLD
	Wee1i Dose *(per cycle-28D)*	Wee1i Dose *(per cycle-21D)*	Wee1i Dose *(per cycle-28D)*
ZN-c3-002[1] (Dose escalation)	200 mg QD	200 mg QD	300 mg QD
Adavosertib (High Dose)[2]	225 mg BID Days 1-3, 8-10, 15-17	225 mg BID Days 1-3, 8-10, 15-17	225 mg BID Days 1-3
Adavosertib (Low Dose)[2]	N/A	225 mg BID Days 1-3	175 mg BID Days 1-3

- Oral continuous dosing regimen for ZN-c3 is enabled by its potentially best-in-class tolerability profile
- Continuous ZN-c3 dosing in combination with chemotherapy is better tolerated than intermittent dosing with an adavosertib/chemotherapy combination
- ZN-c3-002 is an ongoing trial and continues to enroll patients in dose escalation

(1) ZN-c3 January 28, 2022 data cutoff.
(2) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
Note: 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.

ZN-c3 Demonstrates Superior Efficacy with Greater Safety/ Tolerability in Patients with a Worse Prognosis*



Utilizing a continuous dosing regimen, ZN-c3 is able to achieve very high ORRs with markedly better safety / tolerability profile versus Adavosertib

(1) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(2) Lheureux S et al. *Lancet* 2021; 397: 281–92
(3) ZN-c3 January 28, 2022 data cutoff.
* 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.

ZN-c3-002: Summary of Chemotherapy Combination in Ovarian Cancer

CLINICAL ACTIVITY

- **Strong clinical activity** in combination with chemotherapy agents for platinum-resistant ovarian cancer patients (ORR = 30%)
  - Paclitaxel combo: ORR = 63%
  - Carboplatin combo: ORR = 46%
- ZN-c3-002 enrolled a **more advanced patient population** (higher prior bevacizumab treatment and allowed platinum-refractory patients) than related adavosertib trial [1,3]

SAFETY PROFILE

- ZN-c3 is **well-tolerated** in combination with chemotherapy at oral doses ≥ 200 mg QD in subjects with platinum-resistant or -refractory ovarian cancer
- **Superior tolerability** profile for ZN-c3 enabled continuous initial dosing and **higher dose intensity** than adavosertib [1,2]
- Overall **lower rates** of hematological adverse events compared to adavosertib combinations [1-3]
- Dosing regimen for ZN-c3 is **more patient friendly**, which should boost compliance

REGULATORY PATH

- **Promising interim results** support development of a Phase 3 study for potential approval of ZN-c3 in ovarian cancer
- Randomized **Phase 3 study in planning** to support full approval
  - 2nd line platinum-resistant ovarian cancer – in combination with chemotherapy (*tbd*)
- Future development plan details forthcoming

ZN-c3 is well-tolerated with chemotherapy and supports potential use in additional indications

(1) Moore KM et al. *Clin Cancer Res* 2022;28:36–44
(2) Lheureux S et al. *Lancet* 2021; 397: 281–92

(3) 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.

zentalis

ZN-c5: Oral SERD Data Update

ZN-c5 Combination with CDK 4/6i – Efficacy Data

Palbociclib Combination

Phase 1 Dose (mg/day)	N	ORR	CBR	mPFS (months)
25 mg QD + Palbo	10	1/7* (14%)	2/7*(29%)	**
50 mg QD + Palbo	18	2/13 (15%)	6/18 (33%)	3.6
>50 mg + palbo (includes 25 BID)	22	0/14	8/22 (36%)	3.7
Overall	**50**	**3/34 (9%)**	**16/47 (34%)**	**3.7 [95% CI: 2.2-5.7]**

Data as of Jan 31, 2022
*# of subjects with 24 weeks + 10 days opportunity for f/u
** median not estimable due to very few PD events
ClinicalTrials.gov Identifier: NCT03560531

- At the selected doses the combination of ZN-c5 and Palbociclib had a clinical benefit rate of 34% in ER+/HER2- breast cancer patients
- DDI was seen at 50 mg of ZN-c5 with a 35% decrease in palbociclib exposure relative to historical patient data

Abemaciclib Combination

Dose (mg/day)	N	ORR	CBR*	mPFS (months)
50 mg ZN-c5 QD + 150 mg abema BID	4	-	0/4	2.0
25 mg ZN-c5 QD + 150 mg abema BID	5	-	1/1	Not estimable
25 mg ZN-c5 QD + 150 mg abema BID (fed conditions)	1	-	-	No on-treatment scans yet
Overall	**10**	**-**	**1/5 (20%)**	**4.0**

Data as of Jan 11, 2022
*Subjects with opportunity for follow-up > 24 weeks
ClinicalTrials.gov Identifier: NCT04514159

- In a small Phase 1 cohort of ER+/HER2- breast cancer patients receiving ZN-c5 and abemaciclib, a 20% CBR rate was observed, based on interim immature data
- DDI was seen at the 50 mg dose of ZN-c5 with a 67% decrease in abemaciclib exposure at steady state

ZN-c5 Combination with CDK 4/6i – Tolerability Profile (TEAE ≥20%)

Palbociclib Combination (N=50)

Treatment Emergent Adverse Events	All Grades (%)	Grade ≥ 3 (%)
Any adverse event	98.0	66.0
Neutrophil count decreased	72.0	40.0
While blood cell count decreased	72.0	24.0
Anemia	52.0	0.0
Fatigue	36.0	0.0
Lymphocyte count decrease	32.0	10.0
Nausea	32.0	0.0
Hyperglycemia	32.0	0.0
Arthralgia	30.0	4.0
Platelet count decreased	28.0	0.0
Hypertriglyceridema	22.0	0.0

Data as of Jan 31, 2022
ClinicalTrials.gov Identifier: NCT03560531

Abemaciclib Combination (N=10)

Treatment Emergent Adverse Events	All Grades (%)	Grade ≥ 3 (%)
Any adverse event	90.0	50.0
Neutropenia	60.0	20.0
Diarrhea	60.0	0.0
Nausea	40.0	0.0
Fatigue	30.0	10.0
Anemia	20.0	0.0
Hypertension	20.0	20.0

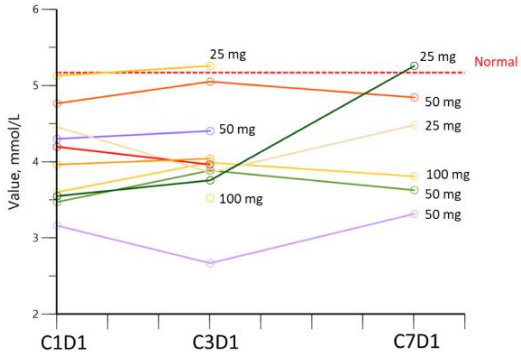
Data as of Jan 11, 2022
ClinicalTrials.gov Identifier: NCT04514159

ZN-c5 is well-tolerated across all dose cohorts and in combination with selected CDK 4/6 inhibitors

ZN-c5 is not Expected to have DDI with Commonly Used Medicines at Relevant Doses

- We have not identified potential for any relevant interaction of ZN-c5 with drugs from 50 most prescribed drugs list
- Well established drugs such as apalutamide and enzalutamide are known CYP3A inducers
- Atovarstatin is a CYP3A substrate and is one of the most prescribed drugs in the United States

Example: For subjects taking atovarstatin, Cholesterol remains well-controlled regardless of ZN-c5 dose

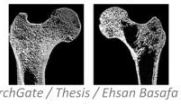


Based on modeling no significant DDI expected in the ZN-c5 + ZN-c3 combination studies

(1) Ibrance™ Clin Pharmacology Review 2014 Aug 13. Weighted average from Pfizer studies-1001c and 1003d (AUC 1801 hr*ng/mL)

ZN-c5 Safety Profile and Bone Protective Activity Versus Other Oral SERDs Supports Use in Adjuvant Settings

- Loss of estrogen associated with osteoporosis in post-menopausal women[1]

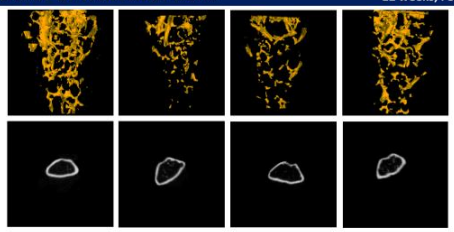


ResearchGate / Thesis / Ehsan Basafa (2013)

- Advanced breast cancer patients suffer from osteolytic bone metastasis[1]
- Treatment with fulvestrant is associated with osteolysis[1]
- ZN-c5 opportunity:
  - **ZN-c5 combines anti-tumor effect with bone-protective effect**

Micro-CT of Trabecular Bone

12 weeks; Femur

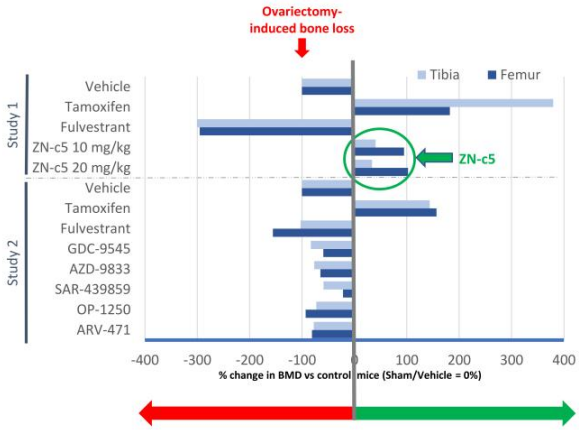


Sham Vehicle | OVX Vehicle | OVX Fulvestrant | OVX ZN-c5 10mpk

Note: Fulvestrant was dosed sc QW, ZN-c5 was dosed po QD

(1) Bado, I. et. al., Oncogene 2017; 36, 4527-4537

Bone Mineral Density in Ovariectomized Mice (Interim Look, 9 weeks)

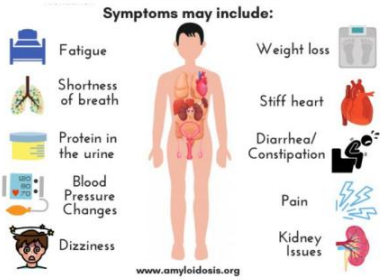


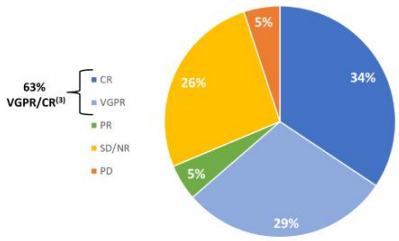
Starting 2-3 weeks after ovariectomy, mice were treated with compounds for 12 weeks. Study 2, investigating oral SERDs, is still ongoing. The 2 independent studies are compared after 9 weeks of treatment and have been normalized to maximum bone mass density loss by ovariectomy (-100%) in each study. SERDs and tamoxifen were dosed daily PO at 10 mg/kg (+ 20 mg/kg for ZN-c5, twice daily for SAR-439859), fulvestrant was dosed once weekly SC at 25 mg/kg

zentalis

ZN-d5: BCL2 Inhibitor

ZN-d5 in AL (Primary) Amyloidosis





- AL Amyloidosis: Deposition of immunoglobulin light chains
  - Clonal plasma cell population secretes misfolding light chain
  - Progressive systemic amyloid accumulation causes widespread organ damage
  - **High morbidity and mortality**
- Orphan disease
  - Estimated worldwide prevalence is 75,000(1)
  - About 4k new cases/year in the US(2)
- Not a cancer, but treated like one
  - Agents active in multiple myeloma used in first-line and relapsed/refractory settings
  - Daratumumab only approved therapy, for first-line use with CyBorD
- **Relapsed/refractory setting is a high unmet medical need**

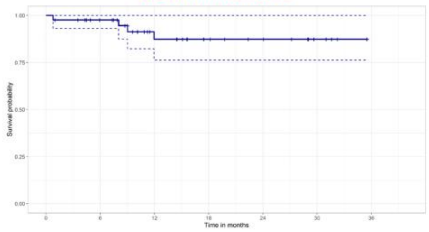
AL Amyloidosis study is currently enrolling patients

(1) Zhang et al. Clin Lymphoma Myeloma Leuk. 2019;19(suppl 10):e339
(2) Kyle et al, Mayo Clin Proc. 2019;94:465-471
(3) Premkumar et al, Blood Cancer J 2021;11:10; hematologic response rate in 38 evaluable patients.

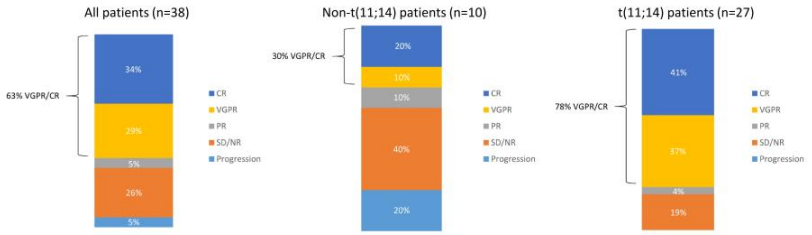
BCL-2 Inhibition has Shown Robust Clinical Activity in AL Amyloidosis

- Patients with the t(11;14) translocation have a worse prognosis than the general AL amyloidosis community
- BCL-2 inhibition showed an improved response rate in the t(11;14) cohort with a trend towards better survival

OS for All Patients



Best Response in Evaluable Patients



(1) Premkumar et al, Blood Cancer J 2021;11:10; hematologic response rate in 38 evaluable patients.

zentalis

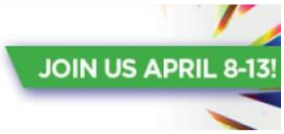
ZN-d5 + ZN-c3: Activity in Hematologic Malignancies and Solid tumors

AACR American Association for Cancer Research ANNUAL MEETING 2022 New Orleans

BH3 mimetics synergize with the Wee1 inhibitor ZN-c3 by activating caspases which induce DNA damage and degrade key proteins

Hooman Izadi, Noah Ibrahim, Tiffany Hoang, Jianhui Ma, Petrus R. De Jong, Joseph Pinchman, Kevin D. Bunker, Ahmed A. Samatar, Fernando Doñate

AACR American Association for Cancer Research ANNUAL MEETING 2022 New Orleans

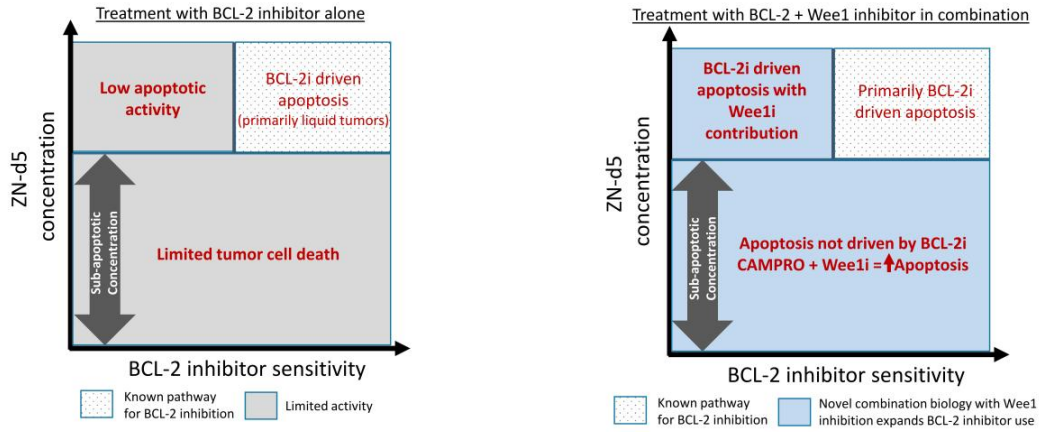


Combination of the BCL-2 inhibitor ZN-d5 with the Wee1 inhibitor ZN-c3 shows additive or synergistic anti-tumor activity in acute myeloid leukemia (AML)

Hooman Izadi, Noah Ibrahim, Tiffany Hoang, Jianhui Ma, Petrus R. De Jong, Jiali Li, Joseph Pinchman, Brant C. Boren, Kevin D. Bunker, Ahmed A. Samatar, Fernando Doñate

Novel Biology Supports Synergy of BCL-2 and Wee1 Inhibition – *CAMPRO (CAspase Mediated PROteolysis)*

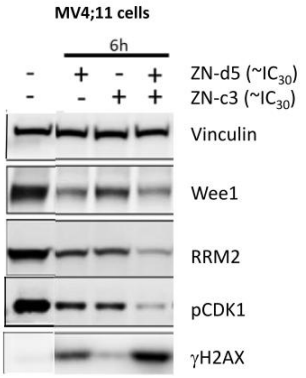
BCL-2 inhibition (BCL-2i) induces CAMPRO of multiple proteins, including DNA damage repair (DDR) proteins



This novel synergistic finding supports the use of ZN-d5 + ZN-c3 in both sensitive and less sensitive tumor cells, opening a large market opportunity across both solid and liquid tumors

ZN-d5 + ZN-c3 Combination Treatment Also Results in Decreased Levels of DDR Proteins

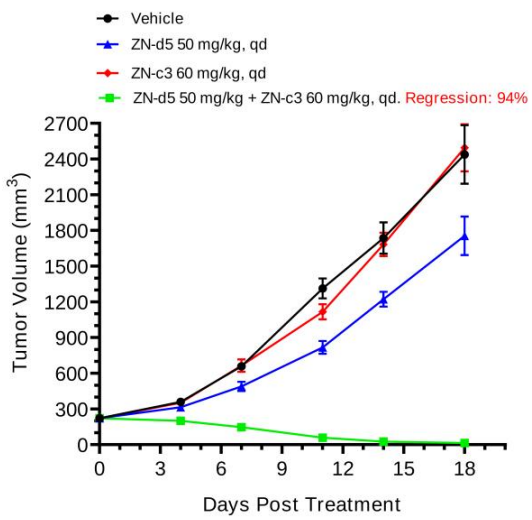
- **ZN-d5 at subtherapeutic doses activates caspases leading to:**
  - DNA damage (increased in γH2AX)
  - Degradation or decrease of DDR related proteins (Wee1 and RRM2)
  - **These effects are increased when combined with ZN-c3**
- **This, in turn, results in inhibition of multiple relevant pathways (e.g. pCDK1) and synergistic anti-tumor activity when combined with ZN-c3**



The Combination of BCL-2 and Wee1 Inhibitor Results in Synergism in Several Tumor Models Including AML

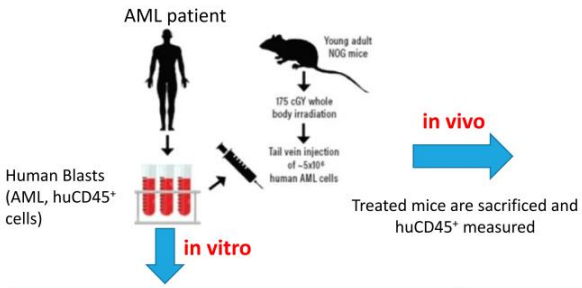
ZN-d5 + ZN-c3

HL-60 AML model



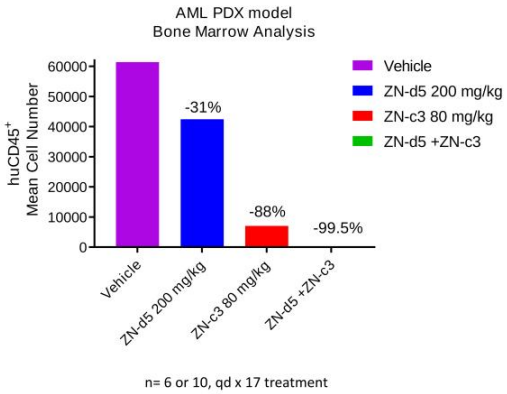
- The combination of ZN-d5 and ZN-c3 represents a novel therapeutic approach
- Significant enhancement of activity than single agent in several indications, including AML
- Combination regimen was well-tolerated in mice
- **Zentalis is the only company known to have both inhibitors in clinical development**

ZN-d5 Combined with ZN-c3 is Active in Patient-Derived AML Samples



Clinical				In vitro (ZN-d5+ZN-c3)	
Patient	Blasts % (before treatment)	Post- Collection Treatment	Blasts % (After Treatment)	ZN-d5/ZN-c3 Treatment (nM)	Blasts % (After Treatment)
3930	93.4	Vidaza/Venetoclax	Residual AML (33% blast) (~2 months post-treatment)	120/500	4.6
3977	62.1	Vidaza/Venetoclax	Residual AML (68% blast) (~2 months post-treatment)	65/100	0
3978	41.1	Gilteritinib/Venetoclax	Residual AML (32% blast) (~1 month post-treatment)	65/500	3.6

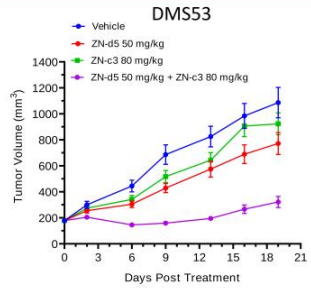
- The combination of ZN-d5+ ZN-c3 is active *in vitro* in **3/3 samples from patients who progressed on venetoclax**
- The combination of ZN-d5 + ZN-c3 is active *in vitro* in 29 patient's derived AML samples independently of TP53 mutation

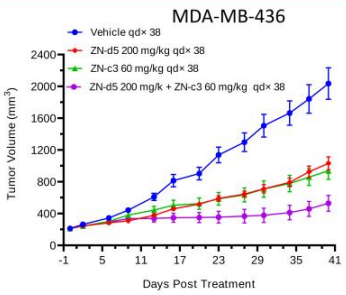


n= 6 or 10, qd x 17 treatment

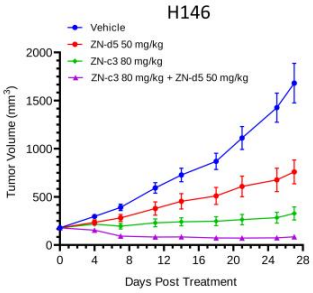
ZN-d5 + ZN-c3 shows promising activity in samples from AML patients progressing on venetoclax

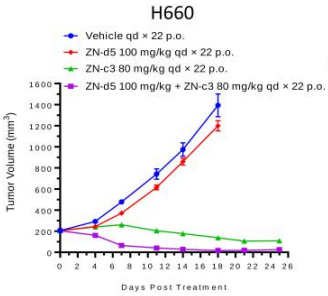
Antitumor Activity in Solid Tumor Models with the ZN-d5 + ZN-c3 Combination Represents Market Expansion Opportunities





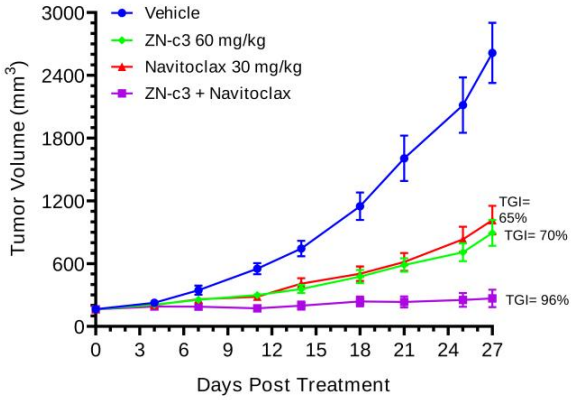
Cell Line	Indication
DMS53	SCLC
MDA-MB-436	TNBC





Cell Line	Indication
H146	NSCLC
H660	Neuroendocrine Prostate

ZN-c3 Combined with a Low Dose of Navitoclax (BCL-xL Inhibitor) Results in Enhanced Anti-tumor Activity in the ALL model MOLT-4



The MOA of the combination of ZN-d5 and ZN-c3 represents a novel therapeutic approach which also applies to combinations of ZN-c3 with other inhibitors of anti-apoptotic proteins

- Navitoclax enhances the anti-tumor activity of ZN-c3 at one-third of the active dose used as a single agent in xenografts (30 versus 100 mg/kg)
- Opportunity to overcome the toxicity observed with navitoclax

TGI: Tumor Growth Inhibition
ALL: Acute Lymphoblastic Leukemia
MOLT-4 model is BCL-xL dependent, but is not on BCL-2

zentalis

Summary

Summary

ZN-c3 Wee1 Inhibitor: A Potential Cornerstone Treatment

- ZN-c3 showed **strong clinical activity** and **good tolerability** in USC and in combination with chemotherapy in ovarian cancer
- Observed overall potential superior profile compared to adavosertib[1-3] in both monotherapy and in combination
- ZN-c3 is currently in a potentially registrational trial in USC; planning is underway for a Phase 3 trial in combination with chemotherapy in ovarian cancer
- In addition, ZN-c3 has **shown broad preclinical activity across multiple models** in both monotherapy and in combination:
  - Osteosarcoma, colorectal, prostate, *neuroendocrine prostate*, breast cancer (ER+, HER2+, and TNBC), AML, NHL, *ALL*, *SCLC*, NSCLC
- ZN-c3's potentially best-in-class/first-in-class profile and underlying biology may establish it as a potential cornerstone treatment, creating a significant market opportunity across a broad range of solid and liquid tumors

ZN-c5 Oral SERD

- ZN-c5 continues to show clinical activity and potentially best-in-class tolerability data, suggesting potential superiority amongst the oral SERDs
  - Decision made to not to pursue CDK 4/6i combination
- ZN-c5 showed bone protective activity in a preclinical model - unlike other investigational SERDs - positioning ZN-c5 well for an adjuvant setting
- Initiating combination of ZN-c5 + ZN-c3 in $ER^+/HER2^-$ CDK 4/6i-resistant patients in 2022

ZN-d5 Bcl-2 Inhibitor

- Preclinical combination data of ZN-d5 + ZN-c3 utilizing novel biology showed synergistic and additive activity across multiple indications in both solid and liquid tumors, often at subtherapeutic doses
- First patient enrolled in a potentially registrational study evaluating ZN-d5 monotherapy in AL amyloidosis

(1) Liu JF et al. J Clin Oncol. 2021 Mar 11:JCO2003167
(2) Moore KM et al. Clin Cancer Res 2021.
(3) Lheureux et al. Lancet 2021.
Italics indicate new data presented today

Key Milestones

ZN-c3: Wee1 Inhibitor

1H 2022	✓	Initial readout on Phase 1 USC expansion cohort
1H 2022	✓	Initial readout on Phase 1b ovarian chemotherapy combo
2H 2022		Initial enrollment/safety update on Phase 2 USC trial[+]
2H 2022		Initial readout on Phase 1/2 chemotherapy combo in osteosarcoma*

ZN-c5: Oral SERD

1H 2022	✓	Phase 1b combination study topline results with Pfizer's palbociclib
1H 2022	✓	Phase 1b combination study topline results with Lilly's abemaciclib
2H 2022		Initiate Phase 1b combination study of ZN-c5 + ZN-c3 in CDK4/6i resistant breast cancer

ZN-d5: BCL-2 Inhibitor

1Q 2022	✓	Initiate Phase 1/2 monotherapy study in amyloidosis*
1H 2022		Initiate Phase 1/2 combination study of ZN-d5 + ZN-c3 in AML
2H 2022		Updated results from Phase 1 dose escalation study in AML and NHL

ZN-e4: EGFR Inhibitor

2H 2022		Report results on Phase 1 NSCLC trial

Integrated Discovery Engine

2022		Initiate IND enabling studies for an internal program

Zentera

2022		Maximize value from investment in and partnership with Zentera

[+] Registrational trial with FDA Fast Track designation
* Potentially registrational trial

zentalis

Anthony Sun, M.D.,
CEO and Chairman

asun@zentalis.com
(212) 433-3780

Melissa Epperly,
Chief Financial Officer

mepperly@zentalis.com
(215) 290-7271

Corporate Office

1359 Broadway
Suite 1710
New York, NY 10018

Science Center

10275 Science Center Drive
Suite 200
San Diego, CA 92121