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

April 8, 2022

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 08, 2022 (GLOBE NEWSWIRE) -- 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.

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.

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.

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.

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*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