Zentalis Pharmaceuticals Announces Promising Initial Data Presented in a Late-Breaking Session at AACR on ZN-c3, its WEE1 Inhibitor, in Patients with Advanced Solid Tumors

April 10, 2021

ZN-c3 demonstrated single agent activity, generating Exceptional Responses in a range of heavily pre-treated solid tumors

ZN-c3 was safe and well-tolerated

Identified recommended Phase 2 dose for ZN-c3 to be 300 mg QD with continuous dosing

Announces plan to start Phase 1/2 osteosarcoma trial in Q3 2021

Company to host webcast event with key opinion leaders on Monday, April 12 at 4:00 p.m. EDT

NEW YORK and SAN DIEGO, April 10, 2021 (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 Phase 1 dose-escalation portion of its ongoing Phase 1/2 clinical trial of ZN-c3 in patients with advanced solid tumors who are refractory to or ineligible for standard therapy or for whom no standard therapy is available. Initial results showed that monotherapy ZN-c3 use resulted in Exceptional Responses in heavily pre-treated patients in a range of solid tumors, including Partial Responses (PRs) in ovarian cancer, colorectal cancer, non-small cell lung carcinoma and uterine serous carcinoma. Data were reviewed as a late-breaking abstract during the American Association of Cancer Research (AACR) Annual Meeting, being held virtually April 10-15, 2021 and May 17-21, 2021.

“The initial clinical data on our WEE1 inhibitor are extremely promising and showcase ZN-c3’s strong potential to improve outcomes in patients with advanced solid tumors who have exhausted available treatment options,” commented Dr. Anthony Sun, Chairman and Chief Executive Officer of Zentalis. “Our WEE1 candidate, which we believe is potentially a best-in-class small molecule, demonstrated favorable safety results with a wide therapeutic window, and resulted in Partial Responses in five patients with a range of cancers. Having identified a recommended dose for future studies, we look forward to advancing clinical trials in a larger number of patients, as well as novel biomarkers that may help select patients who are likely to respond to treatment with ZN-c3. We are looking to make Exceptional Responses commonplace.”

Initial Efficacy and Safety Data

In the Phase 1 dose-escalation trial, ZN-c3 was dosed starting at 25 mg and going as high as 450 mg QD in patients with advanced or metastatic solid tumors. At the time of the data cutoff on February 12, 2021, 55 patients were evaluated for safety, the primary endpoint. The study remains ongoing and based on the data presented at AACR, ZN-c3 generated 5 Partial Responses.

Best Overall Responses:

- Two confirmed PRs in ovarian cancer and colorectal cancer (CRC) patients
  - After receiving 18 prior lines of therapy, 11 prior lines in the advanced metastatic setting, a patient with Stage IV ovarian cancer had a RECIST-confirmed PR with a 56% reduction in overall target lesions. The patient also experienced a large rapid drop in CA-125 from 610 kU/L at baseline to 125 kU/L within 4 weeks on treatment, with her CA-125 level normalizing 3 weeks later. The patient was on study for 186 days and remains on study drug.
  - After receiving 5 prior lines of therapy in the advanced metastatic setting, a patient with Stage IV CRC had a RECIST-confirmed PR with a 42% reduction in overall target lesions, as well as a rapid decrease in CEA tumor marker from 327 ng/mL at baseline to <50 ng/mL after 3 weeks on treatment. The patient remained on study for 169 days until clinical disease progression.
- In addition, three unconfirmed PRs—one in non-small cell lung carcinoma (NSCLC) and two in uterine serous carcinoma (USC) patients
  - After receiving 3 prior lines of therapy in the advanced metastatic setting, a patient with Stage IV NSCLC had an unconfirmed (per RECIST) PR with a 50% reduction in overall target lesions. The patient was on study for 145 days and remains on study drug.

ZN-c3 was generally well-tolerated as a single agent. As of the cutoff date, the most common treatment-related adverse events were mainly Grade 1/2, including nausea (49.0% of patients), diarrhea (32.7% of patients), fatigue (29.0% of patients) and vomiting (29.0% of patients) across all doses. Significant hematological adverse events were limited; treatment-related white blood cell count decrease / neutropenia (7.2% all Grades, 3.6% Grade ≥3), anemia (7.2% all Grades, 5.4% Grade ≥3) and thrombocytopenia (7.2% all Grades, 3.6% Grade ≥3).

Results from this study indicate that an oral dose of 300 mg QD with continuous dosing is the recommended Phase 2 dose of ZN-c3 when used as a monotherapy. The 300 mg QD dose demonstrated high plasma exposure levels, while minimizing adverse events. In addition, the pharmacodynamic marker of pCDK1 levels in skin punch biopsies showed active target engagement at relevant pharmacological doses. The Company initiated the Phase 1 expansion portion of the trial with the 300 mg QD dose earlier in 2021 and is exploring this candidate’s potential in combination trials including

in ovarian cancer and osteosarcoma. Using this recommended dose, Zentalis will also coordinate with Zentera Therapeutics, Zentalis' majority-owned joint venture, to initiate a Phase 1b trial investigating ZN-c3 as a single agent in China.

"WEE1 is a promising target for cancer therapy, and this dataset provides further validation on the importance of candidates like ZN-c3 that are designed to inhibit the DNA damage checkpoint, resulting in tumor cell death," said Dr. Anthony Tolcher, CEO, Founder and Director of Clinical Research at NEXT Oncology. "ZN-c3 was shown to be tolerable in this heavily pretreated patient population. Furthermore, this candidate's early signals of anti-tumor activity are very exciting, and I am even more optimistic that WEE1 inhibition may become an important treatment approach for a wide range of cancers."

KOL Webcast Event:

Zentalis will host a webcast event with key opinion leaders Monday, April 12, 2021 at 4:00 p.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 ZN-c3

ZN-c3 is an 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. Zentalis is currently conducting a Phase 1/2 clinical trial in patients with advanced solid tumors and reported initial data from the Phase 1 portion at the AACR Annual Meeting 2021. In addition, the Company is also conducting a Phase 1b trial evaluating ZN-c3 in combination with chemotherapy in patients with advanced ovarian cancer, with plans to initiate a Phase 1/2 in combination with chemotherapy in osteosarcoma and a Phase 2 trial investigating ZN-c3 as a monotherapy in patients with uterine serous carcinoma in 2021.

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, 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 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, 2020 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.

Investor Contact:
Thomas Hoffmann
Solebury Trout
1.646.378.2931
thoffmann@soleburytrout.com

Media Contact:
Julia Deutsch
Solebury Trout
1.646.378.2967
jdeutsch@soleburytrout.com