Zentalis Pharmaceuticals Announces Updates Across its Pipeline Including Promising New Interim Clinical Data on ZN-c3 (WEE1i) and ZN-c5 (SERD) and Two Potentially Registrational Trials for ZN-c3, with the First Trial Already Initiated

June 28, 2021

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

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

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

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

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

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

NEW YORK and SAN DIEGO, June 28, 2021 (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 key clinical and regulatory updates across its pipeline.

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

ZN-c3: Oral WEE1 Inhibitor for Solid Tumors

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

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

pediatric disease priority voucher upon approval.

- Zentalis will also support two planned additional investigator-initiated trials: a trial with the Ivy Brain Center in glioblastoma multiforme (GBM) and a trial with immunotherapy with Dana Farber in triple negative breast cancer.
- Zentalis' China JV Zentera is advancing corresponding clinical trials in China with ZN-c3.

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

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

Monotherapy Trials (Expansion and Dose Escalation)

- In total, 56 patients with 2 median prior lines of treatment were evaluated for safety and efficacy. Across all doses from 50 mg QD to 300 mg QD, the observed CBR was 33% and the ORR was 5%. ZN-c5 generated 2 PRs at the 150 mg and 300 mg doses. Adverse events (AEs) were found in less than 10% of the patients and there were no observed cases of bradycardia, visual disturbances, QTC or dizziness. Of note, treatment related diarrhea adverse event rate was 3.6%, with only grade 1 or 2 events observed. The Phase 2 monotherapy trial has been initiated and Zentalis may take multiple doses into this study.
- An oral dose of 50 mg QD (n=16) demonstrated a CBR of 40%, with many patients in this dose cohort remaining on study drug and in the trial. Final determination of the monotherapy RP2D will occur following completion of this 50 mg QD dose cohort.

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

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

Window of Opportunity Trial

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

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

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

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

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

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

About Zentalis Pharmaceuticals

Zentalis Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company focused on discovering and developing small molecule therapeutics targeting fundamental biological pathways of cancers. The Company is developing a broad pipeline of potentially best-in-class oncology candidates, all internally discovered, which include ZN-c5, an oral selective estrogen receptor degrader (SERD) for ER+/HER2- breast cancer, ZN-c3, a WEE1 inhibitor for advanced solid tumors, ZN-d5, a BCL-2 inhibitor for hematologic malignancies, and ZN-e4, an EGFR inhibitor for non-small cell lung carcinoma (NSCLC). Zentalis has licensed ZN-c5, ZN-c3 and ZN-d5 to its majority-owned joint venture, Zentera Therapeutics, to develop and commercialize these candidates in China. Zentalis has operations in both New York and San Diego.

For more information, please visit www.zentalis.com. Follow Zentalis on Twitter at @ZentalisP and on LinkedIn at www.linkedin.com/company/zentalis-pharmaceuticals.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without

limitation statements regarding our expectations surrounding the development, potential, safety, efficacy, and regulatory and clinical progress of our product candidates in the Unites States and globally, and plans and timing for the initiation of and the release of data from our clinical trials and our ability to meet other key milestones. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the COVID-19 pandemic has adversely impacted and may continue to adversely impact our business, including our preclinical studies and clinical trials; our limited operating history, which may make it difficult to evaluate our current business and predict our future success and viability; we have and expect to continue to incur significant losses; our need for additional funding, which may not be available; our substantial dependence on the success of our lead product candidates; failure to identify additional product candidates and develop or commercialize marketable products; the early stage of our development efforts; potential unforeseen events during clinical trials could cause delays or other adverse consequences; risks relating to the regulatory approval process or ongoing regulatory obligations; failure to obtain U.S. or international marketing approval; our product candidates may cause serious adverse side effects; inability to maintain our collaborations, or the failure of these collaborations; our reliance on third parties; effects of significant competition; the possibility of system failures or security breaches; risks relating to intellectual property; our ability to attract, retain and motivate qualified personnel; and significant costs as a result of operating as a public company. These and other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2021 filed with the U.S. Securities and Exchange Commission (SEC) and our other filings with the SEC could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management’s estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

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