Zentalis Pharmaceuticals Announces First ZN-c3 Clinical Development Collaboration with Pfizer

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Companies will collaborate on Phase 1/2 dose escalation study of ZN-c3, a selective Wee1 inhibitor, in combination with encorafenib and cetuximab in patients with BRAF V600E-mutated colorectal cancer

NEW YORK and SAN DIEGO, Oct. 24, 2022 (GLOBE NEWSWIRE) -- Zentalis™ Pharmaceuticals, Inc. (Nasdaq: ZNTL), a clinical-stage biopharmaceutical company focused on discovering and developing clinically differentiated small molecule therapeutics targeting fundamental biological pathways of cancers, today announced plans to initiate the first study of its collaboration with Pfizer on Zentalis' product candidate ZN-c3, a selective Wee1 inhibitor designed to induce synthetic lethality in cancer cells. The study is one component of Zentalis' strategic collaboration with Pfizer, which was previously announced along with Pfizer's $25 million equity investment in Zentalis.

Zentalis and Pfizer will initiate a Phase 1/2 dose escalation study of ZN-c3 in combination with encorafenib and cetuximab—an FDA-approved standard of care known as the BEACON regimen—in patients with BRAF V600E-mutated metastatic colorectal cancer (mCRC). Published studies indicate that up to 21% of mCRC patients have BRAF mutations and that the V600E mutation accounts for more than 95% of BRAF mutations.[1] BRAF-mutated mCRC constitutes a more aggressive malignancy than non-BRAF-mutated mCRC, generally conferring worse survival outcomes. While the BEACON regimen established a new standard of care for patients with BRAF V600E-mutated mCRC—demonstrating statistically significant and clinically meaningful improvement in overall survival—all patients taking this regimen eventually progress, at which point they have limited additional treatment options. BRAF-mutated mCRC therefore continues to represent an area of significant unmet medical need.

"We are extremely excited to announce this investigational study, which we believe will benefit greatly from the expertise and support gained through our collaboration with Pfizer," said Carrie Brownstein, M.D., Chief Medical Officer of Zentalis. "Combining ZN-c3 with the BEACON agents in this study represents an opportunity in our ZN-c3 clinical development program, alongside ongoing studies in both the monotherapy and chemotherapy combination settings in multiple tumor types. If successful in clinical trials and approved, the combination of ZN-c3 with targeted / DNA damage response (DDR) agents could be another potential treatment option to help improve the lives of people living with BRAF-mutated metastatic colorectal cancer."

"We are excited to unite Pfizer's capabilities and development expertise with Zentalis' innovation to aid the success of this important study," said Adam Schayowitz, Ph.D., MBA, Vice President and Development Head for Breast Cancer, CRC and Melanoma at Pfizer, who joined the Zentalis Scientific Advisory Board as part of the Pfizer/Zentalis collaboration. "Through this collaboration, we have the opportunity to accelerate the foundational science Pfizer has created in this space and potentially bring a second generation of therapies to patients facing BRAF-mutated colorectal cancer."

Preclinical evidence supports the rationale for combining inhibition of BRAF, Wee1 and EGFR. Wee1 inhibition has shown synergy with many targeted agents in mutationally driven cancers, and the addition of ZN-c3 to encorafenib and cetuximab enhanced anti-tumor activity in a cell-line-derived xenograft (CDX) model. These observations highlight the potential synergy combining a number of molecularly targeted therapies.

Zentalis anticipates initiating patient enrollment in the first quarter of 2023.

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-d5, a BCL-2 inhibitor for hematologic malignancies and related disorders and a heterobifunctional degrader of BCL-xL for solid and hematological malignancies. The Company has licensed ZN-c3, ZN-d5 and ZN-c5 to its joint venture, Zentera Therapeutics, Ltd., 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 U.S. 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 plans to initiate a clinical study; potential benefits of Pfizer's expertise and support; potential benefits of combining ZN-c3 with BEACON agents; the potential for the combination of ZN-c3 with targeted DNA DDR agents to be a treatment option for people living with BRAF-mutated mCRC; the opportunity to accelerate Pfizer's foundational science; the potential to bring a second generation of therapies to patients facing BRAF-mutated mCRC; the potential synergy of combining a number of molecularly targeted therapies; and the timing of initiating patient enrollment in a study. The terms "believe," "could," "may," "opportunity," "plans," "potential," "will" and similar references are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. 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: 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; the outcome of preclinical testing and early trials may not be predictive of the

success of later clinical trials; failure to identify additional product candidates and develop or commercialize marketable products; 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 risks relating to management transitions; significant costs as a result of operating as a public company; the COVID-19 pandemic has adversely impacted and may continue to adversely impact our business, including our preclinical studies and clinical trials; and the other important factors discussed under the caption “Risk Factors” in our most recently filed periodic report on Form 10-K or 10-Q and subsequent filings 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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[1] Sorbye H, Dragomir A, Sundström M, et al. High BRAF Mutation Frequency and Marked Survival Differences in Subgroups According to KRAS/BRAF Mutation Status and Tumor Tissue Availability in a Prospective Population-Based Metastatic Colorectal Cancer Cohort. PLoS One. 2015;10(6):e0131046.

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