Cortexyme Reports Safety and Pharmacokinetics Results from Single Ascending Dose Portion of its Phase 1 Clinical Trial of COR588

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COR588 well-tolerated in all dose cohorts

Human pharmacokinetics support once daily oral dosing

Multiple ascending dose data expected in the second quarter of 2022

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Mar. 8, 2022-- Cortexyme, Inc. (Nasdaq: CRTX), a clinical-stage biopharmaceutical company pioneering upstream therapeutic approaches to improve the lives of patients diagnosed with degenerative diseases, today announced results from the single ascending dose (SAD) portion of the Phase 1 clinical trial of its new drug candidate COR588, a next generation, oral, small-molecule lysine gingipain inhibitor in development for the treatment of diseases related to *P. gingivalis* infection. The SAD trial was designed to evaluate the safety and pharmacokinetics of COR588 in healthy volunteers.

In the SAD portion of the Phase 1 trial, preliminary results indicate COR588 was well-tolerated across all four cohorts in the dose range from 25 mg to 200 mg with no serious adverse events. No clinically significant findings were observed on other safety measures, including vital signs, laboratory findings, telemetry, or ECGs. In the study, COR588 exhibited an 11-to-12-hour half-life consistent with once daily dosing and a dose-proportional pharmacokinetic profile that achieved and exceeded the targeted exposure predicted for therapeutic efficacy.

“COR588 was designed to be a potent and selective molecule with pharmacokinetics supportive of once daily oral dosing and these data support continued development,” said Michael Detke, MD, PhD, Cortexyme’s chief medical officer. “We are encouraged by the initial safety results and look forward to sharing the full data set from the COR588 Phase 1 trial in the second quarter of 2022 once the multiple ascending dosing phase is complete.”

COR588 Phase 1 Trial Overview

COR588 is a selective, oral small-molecule inhibitor of lysine gingipains, protease virulence factors secreted by *P. gingivalis,* and is being developed for patients with disorders related to *P. gingivalis* infection, including Alzheimer’s disease. The clinical trial of COR588 has now progressed to the second portion of this Phase 1 study, with a multiple ascending dose (MAD) evaluation of three cohorts: 50 mg, 100 mg, and 200 mg of COR588 versus placebo, once daily for 10 days. Cortexyme expects to present the full data set from the COR588 Phase 1 clinical trial in the second quarter of 2022.

Sponsored by Cortexyme, the COR588 Phase 1 trial is a randomized, double-blind, placebo-controlled, first-in-human study to evaluate the safety, tolerability, and pharmacokinetics of single and multiple ascending doses of oral COR588 capsules in healthy adult participants. The SAD portion of the trial included 32 enrolled participants, and the full trial is listed under clinicaltrials.gov Identifier: NCT04920903. Future studies will evaluate the ability of COR588, an oral investigational medicine, to slow or halt the progression of Alzheimer’s disease, among other potential indications, by inactivating the proteases, or gingipains, released by the keystone bacterium *P. gingivalis*. Therapeutic effects of gingipain inhibitors have been demonstrated in humans in the GAIN Trial, in addition to both mouse (Dominy et al, 2019) and naturally occurring aged dog models (Arastu-Kapur et al, 2020).

About Cortexyme

Cortexyme, Inc. (Nasdaq: CRTX) is a clinical stage biopharmaceutical company pioneering upstream therapeutic approaches designed to improve the lives of patients diagnosed with Alzheimer’s and other degenerative diseases. Cortexyme’s lead program targets a specific, infectious pathogen called *P. gingivalis* found in the brain of Alzheimer’s patients and other organs and tied to degeneration and inflammation in humans and animal models. The company’s causation evidence for Alzheimer’s disease and the mechanism of its novel therapeutic has been independently replicated and confirmed by multiple laboratories around the world, as well as published in peer-reviewed scientific journals. To learn more about Cortexyme, visit www.cortexyme.com or follow @Cortexyme on Twitter.

Forward-Looking Statements

Statements in this news release contain “forward-looking statements” that are subject to substantial risks and uncertainties. Forward-looking statements contained in this news release may be identified by the use of words such as “anticipate,” “expect,” “will,” “may,” “should,” “estimate,” “project,” “potential,” “encouraged,” or other similar words. Examples of forward-looking statements include, among others, the strategic development path for COR588 including with regard to the Phase 1 clinical trial; its business plans, internal and external development of the pipeline, strategy, planned FDA submissions and clinical trials and timeline, prospects, and milestone expectations; the timing and success of the company’s clinical trials and related data, including plans and the ability to initiate, conduct and/or complete current and additional studies; the potential of COR588 to treat Alzheimer’s disease and other indications; the timing of announcements and updates relating to its clinical trials and related data; the potential therapeutic benefits, safety and efficacy of the company’s product candidate or library of compounds; and statements about its ability to obtain, and the timing relating to, further development of atuzaginstat and other programs or indications, regulatory submissions and interactions with regulators, and related response and decisions, and approvals with respect to the company’s drug product candidate. Forward-looking statements are based on Cortexyme’s current expectations and are subject to inherent uncertainties, risks, and assumptions that are difficult to predict and could cause actual results to differ materially from what the company expects. Further, certain forward-looking statements are based on assumptions as to future events that may not prove to be accurate. Factors that could cause actual results to differ include, but are not limited to, the risks and uncertainties described in the section titled “Risk Factors” in Cortexyme’s Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on March 1, 2022, its Quarterly Report on Form 10-Q filed with the SEC on October 29, 2021, and other reports as filed with the SEC. Forward-looking statements

contained in this news release are made as of this date, and Cortexyme undertakes no duty to update such information except as required under applicable law.

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