Cortexyme Expands Proprietary Development Pipeline with Initiation of Phase 1 Clinical Trial of COR588

September 8, 2021

First participants dosed in clinical trial of second-generation gingipain inhibitor differentiated by novel compound properties and anticipated once daily administration

Clinical advancement of pipeline delivers on commitment to bring innovation to an increasing range of P. gingivalis-related disease indications with high unmet clinical needs

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Sep. 8, 2021-- Cortexyme, Inc. (Nasdaq: CRTX), a company advancing a pivotal trial in Alzheimer's disease with top-line data expected by mid-November 2021 and a growing pipeline of therapeutics for degenerative diseases, today announced that the first cohort of healthy participants have been dosed in the Phase 1 clinical trial of its new drug candidate, COR588. COR588 is a second-generation small-molecule lysine-gingipain inhibitor differentiated from the company's lead drug candidate atuzaginstat (COR388) by its improved pharmacokinetic properties and anticipated once daily oral administration. Delivering on its commitment to bring innovation to high unmet clinical needs, Cortexyme expects COR588 to be targeted for use in the treatment of periodontal disease and other *P. gingivalis*-related indications.

"Advancing COR588 into the clinic as planned marks an important milestone for Cortexyme as we expand our proprietary drug pipeline and strategically advance our first-in-class gingipain inhibitors for additional indications where the evidence demonstrates *P. gingivalis* plays a critical role in disease progression," said Casey Lynch, Cortexyme's chief executive officer, co-founder, and chair. "Based on this wealth of research, we believe our innovative upstream therapeutic approach has the potential to shift the paradigm for the treatment of diseases with high unmet clinical need in distinct market segments. Building on the momentum of our successfully completed IND-enabling studies of COR588, we look forward to completing the Phase 1 study and advancing the clinical studies of this promising potential therapeutic."

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 patients. The trial will enroll up to 64 participants and 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 periodontal disease, among other potential indications, by inactivating the toxic proteases, or gingipains, released by the keystone bacterium *P. gingivalis*. Periodontal disease represents a major unmet medical need impacting 65 million Americans. Therapeutic effects of gingipain inhibitors have been demonstrated in both mouse and naturally occurring aged dog models (Arastu-Kapur et al, 2020).

Cortexyme is evaluating the efficacy of its lead lysine-gingipain inhibitor, atuzaginstat, in the company's pivotal GAIN Trial evaluating the role of *P. gingivalis* in the progression of Alzheimer's disease in mild to moderate patients, which includes a 233-patient sub-study in periodontal disease called REPAIR (REduction of *P. GingivAlIs* to ImpRove Pocket Depth). Top-line data from the GAIN Trial and REPAIR sub-study are expected by mid-November 2021.

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. The company is advancing its disease-modifying pivotal GAIN Trial in mild to moderate Alzheimer's disease with top-line data expected by mid-November 2021, in addition to growing a proprietary pipeline of first-in-class small molecule therapeutics for Parkinson's disease, periodontitis, and other diseases with high unmet clinical need. Cortexyme's lead program targets a specific, infectious pathogen called *P. gingivalis* found in the brain 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," "believe," "will," "may," "should," "estimate," "project," "outlook," "forecast," "potential" or other similar words. Examples of forward-looking statements include, among others, statements Cortexyme makes regarding its business plans, strategy, timeline, prospects, and milestone expectations; the characteristics and potential benefits of COR588, including for the treatment of periodontal disease; the timing and success of the company's clinical trials and related data, including with respect to the GAIN and REPAIR Trials, as well as enabling and human studies of COR588; the potential of atuzaginstat to treat Alzheimer's disease, periodontal disease, and other potential 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, regulatory submissions 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, 2021, its Quarterly Report on Form 10-Q filed with the SEC on August 6, 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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Source: Cortexyme, Inc.