Cortexyme Provides Business Update and Reports Second Quarter 2021 Results

August 9, 2021

GAIN Trial top-line data for disease modification in Alzheimer's expected by mid-November 2021

Phase 2 REPAIR sub-study results evaluating periodontal disease expected by mid-November 2021

Current cash position sufficient to fund operations through 2023

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Aug. 9, 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 provided an update on expected clinical top-line data and reported second quarter 2021 financial results.

"Evidence demonstrating a causal link between the infectious pathogen *P. gingivalis* and neurodegeneration continues to grow. We are pleased with the rigorous and efficient execution of the GAIN trial and are excited to be rapidly approaching such a significant milestone for our industry. By following the evidence, we have developed a potential therapeutic with a breakthrough mechanism of action upstream of multiple aspects of Alzheimer's disease pathology including inflammation and neurodegeneration. We look forward to sharing a robust top-line data set by mid-November 2021," said Casey Lynch, Cortexyme's chief executive officer, co-founder, and chair.

"We believe positive data from the GAIN Trial could fundamentally shift the paradigm of neurodegeneration research and disease-modifying treatment in the Alzheimer's field and we intend to rapidly pursue collaboration with the FDA for the benefit of patients. Cortexyme is confident that we have enrolled the right population and that the study is powered to show a meaningful treatment effect. We remain steadfast in our mission to provide real change for Alzheimer's patients and their caregivers," said Michael Detke, MD, PhD, Cortexyme's chief medical officer.

Pivotal GAIN Trial Top-line Data Expected by Mid-November 2021

Cortexyme is pioneering an innovative, upstream, disease-modifying therapeutic approach to Alzheimer's disease with the company's pivotal Phase 2/3 GAIN Trial that enrolled 643 patients with mild to moderate Alzheimer's disease, in addition to its Phase 2 periodontal disease REPAIR sub-study in 233 patients. Less than 100 participants are pending treatment completion in the study. The following are key highlights as the company readies for its GAIN and REPAIR top-line data:

- The GAIN Trial is powered at approximately 90% to show a 50% slowing of decline as measured by the cognitive and functional co-primary clinical endpoints of ADAS-Cog11 and ADCS-ADL.
- Top-line data will also include other secondary and exploratory clinical measures and biomarker data to support disease modification in addition to key safety and tolerability outcomes.
- The Phase 2 periodontal disease REPAIR sub-study of the GAIN Trial evaluates standard clinical endpoints of periodontitis, including gingival pocket depth, clinical attachment level, and bleeding on probing.
- GAIN Trial baseline demographics confirm a representative patient population of mild to moderate Alzheimer's participants, including the ratio of female patients (57% female to 42% male), a balance of mild and moderate patients (50% mild and 50% moderate based on MMSE measure), a representative proportion of ApoE4 carriers (64%), and approximately three-fourths (74%) of patients using cholinesterase inhibitors/memantine for the treatment of Alzheimer's disease symptoms. Importantly, the GAIN Trial includes higher than average diversity with approximately 20% representation from Black and African American, Hispanic and Latino, and patients of other racial and ethnic backgrounds.

Scientific and Pipeline Updates

- Cortexyme continued to expand its evidence base by presenting new data at the International Association for Dental Research (IADR) 2021 demonstrating atuzaginstat disrupts biofilms and is efficacious in preclinical models of periodontal disease. Atuzaginstat penetrates and disrupts bacterial biofilms, a key feature for efficacy in treating *P. gingivalis* driven disease. Data presented also demonstrated that atuzaginstat reverses alveolar bone loss in mice after oral *P. gingivalis* infection at doses relevant for therapeutic efficacy in periodontal disease.
- At the Alzheimer's Association International Conference® 2021 (AAIC®), Cortexyme presented preclinical data linking *P. gingivalis* to elevated levels of p-tau217, reinforcing evidence of the infectious pathogen as a causative agent of Alzheimer's disease, and these elevations were prevented by treatment with atuzaginstat. In addition, newly presented GAIN Trial baseline data demonstrates that a majority of patients have elevated serum Von Willebrand factor, a marker of endothelial cell injury, and alpha-2-macroglobulin, an endogenous protease inhibitor.
- Cortexyme successfully completed IND enabling studies of COR588, including nonclinical safety and two-month toxicology studies. First-in-human studies are on schedule to begin in the third quarter 2021.

- The company announced the selection of a lead 3CLpro inhibitor (COR803) for the treatment of coronavirus infections, including COVID-19 disease, caused by SARS-CoV-2 infection. COR803 is a novel patent-pending small molecule 3CLpro inhibitor. 3CLpro, or Mpro, is a viral cysteine protease and validated drug target shown to be essential in replication of SARS-CoV-2. We believe COR803 has potentially beneficial properties over other COVID-19 therapeutics and 3CLpro inhibitors in development including: covalent irreversible binding of the viral 3CLpro enzyme; high potency; antiviral EC90 of 30 nM in human lung cell viral replication assays; highly selective for 3CLpro versus other cellular proteases including Cathepsin L; and excellent systemic exposure utilizing intranasal or subcutaneous administration, allowing for clinical use in multiple settings such as outpatient and inpatient.

Second Quarter 2021 Financial Results

- Cash Position: Cash, cash equivalents, and short and long-term marketable securities as of June 30, 2021, were $153.5 million. Cortexyme expects its cash position to be sufficient to fund its operating and capital expenditures through 2023.
- Research and Development (R&D) Expenses: For the quarter ended June 30, 2021, R&D expenses were $14.7 million primarily due to costs related to the research and development of atuzaginstat, the GAIN Trial, COR588, and personnel-related expenses.
- General and Administrative (G&A) Expenses: For the quarter ended June 30, 2021, G&A expenses were $7.1 million. The expenses were primarily attributable to personnel-related expenses, insurance, and professional and legal fees.
- Net Loss: For the quarter ended June 30, 2021, the company's net loss was $21.8 million, or a loss of $0.74 per basic share. Weighted average shares outstanding for the quarter ended June 30, 2021, were 29,587,352.

About The GAIN Trial

Cortexyme's seminal discovery, along with confirmatory clinical and preclinical studies, demonstrate that the intracellular pathogen, *P. gingivalis*, is found in the brain of more than 90% of Alzheimer's patients and that an oral infection with *P. gingivalis* in animals results in brain infiltration and downstream hallmark Alzheimer's pathologies, including Aβ42 production, tau hyperphosphorylation, microglial activation, and neurodegeneration. The company's lead drug candidate, atuzaginstat (COR388), is a first-in-class, orally administered, brain penetrant small molecule targeting *P. gingivalis,* which is upstream of neuronal death and Alzheimer's disease pathology. Atuzaginstat blocks gingipains, protease virulence factors secreted *by P. gingivalis*, which are required for its survival and responsible for its toxicity. The GAIN Trial also includes a REPAIR sub-study of 233 patients targeting *P. gingivalis* – most commonly known as a keystone bacterium associated with periodontal disease – and measuring the efficacy of atuzaginstat on clinical endpoints of periodontal disease. Cortexyme's innovative therapeutic approach continues to be supported by research from laboratories around the world published in peer-reviewed scientific journals.

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 the sufficiency of its cash position to fund its operations; its business plans, strategy, timeline, prospects, and milestone expectations; 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 potential of COR803 to treat coronavirus infections; 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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