Cortexyme Presents New Data Demonstrating Atuzaginstat Disrupts Biofilms and is Efficacious in Preclinical Models of Periodontal Disease at IADR 2021

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Leading drug candidate penetrates and disrupts bacterial biofilms, a key feature for efficacy in treating P. gingivalis driven disease

Atuzaginstat reverses alveolar bone loss in mice after oral P. gingivalis infection at doses relevant for therapeutic efficacy in periodontal disease

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jul. 21, 2021-- Cortexyme, Inc. (Nasdaq: CRTX), a company advancing a pivotal trial in Alzheimer's disease with top-line data expected in the fourth quarter of 2021 and a growing pipeline of therapeutics for degenerative diseases **,** announced new preclinical data demonstrating efficacious dose range finding data for its lead drug candidate atuzaginstat (COR388) in periodontal disease in conjunction with its participation at the International Association for Dental Research (IADR) 2021 General Session & Exhibition, a virtual event. Periodontal disease represents a significant unmet market of 65 million people in the U.S. alone.

New data presented at the IADR 2021 conference by Cortexyme showed its lead clinical small molecule, atuzaginstat, was able to engage and inhibit its target, lysine-gingipain from *P. gingivalis*, within a biofilm and disrupt the biofilm integrity. The inability of traditional antibiotics to penetrate oral biofilms at therapeutic concentrations is a major reason for their lack of efficacy in treating chronic periodontitis. The company also confirmed that a second-generation lysine-gingipain inhibitor, COR588, demonstrated biofilm penetration and target engagement similar to atuzaginstat and is planned to begin Phase I studies in the third quarter 2021. In a second presentation at IADR 2021, Cortexyme presented data from preclinical studies demonstrating that atuzaginstat was efficacious in reversing alveolar bone loss induced by oral *P. gingivalis* infection.

"As top-line data for our GAIN Trial rapidly approaches in the fourth quarter 2021, Cortexyme is in a unique position with a pivotal clinical study of our lead drug candidate atuzaginstat that targets the infectious pathogen *P. gingivalis* not only as the causative agent of Alzheimer's disease, but also its well-established role as a keystone bacterium for periodontal disease. This presents us with the potential to provide innovative and breakthrough treatments in two high unmet clinical need areas with a first-in-class, orally administered small molecule," said Casey Lynch, Cortexyme's chief executive officer, co-founder and chair. "The 233-patient periodontal disease REPAIR sub-study of the GAIN Trial evaluates standard clinical endpoints of periodontitis, including gingival pocket depth, clinical attachment, and bleeding on probing. We look forward to reporting top-line data from the REPAIR sub-study in the fourth quarter 2021."

New data will be featured in two poster sessions at IADR 2021:

- **Atuzaginstat Penetrates Biofilms for Periodontal Disease Therapeutic Efficacy:** At Cortexyme's IADR 2021 poster session titled "Gingipain Inhibitors Penetrate And Inhibit Gingipains In *Porphyromonas gingivalis* Biofilms" (Abstract #3571509) taking place Friday, July 23, 2021, starting at 3:45 p.m. ET, new data will be presented demonstrating the efficacy of atuzaginstat and COR588 to penetrate *in vitro* surface attached biofilms. Biofilms are one of the primary reasons that other molecules like broad spectrum antibiotics are ineffective against *P. gingivalis*. Biofilm cultures demonstrated decreased potency of the broad-spectrum antibiotic amoxicillin relative to planktonic growth as expected for robust biofilms. Atuzaginstat and the company's second generation COR588 exhibited significant time and concentration-dependent inhibition of lysine-gingipain activity, while maintaining their target selectivity within the biofilms to inhibit lysine-gingipain. Other similarly potent gingipain inhibitors were less capable of activity within the biofilm.

- **Atuzaginstat Efficacious in Mouse Model of Periodontal Disease:** At Cortexyme's IADR 2021 poster session titled "Novel lysine-gingipain inhibitor atuzaginstat (COR388) is efficacious in a mouse model of periodontal disease" (Abstract #1756) taking place Friday, July 23, 2021, starting at 11:00 a.m. ET, new data will be presented that demonstrates that atuzaginstat, a first-in-class brain-penetrant lysine-gingipain inhibitor, was effective in reversing alveolar bone loss in mice after repeated oral *P. gingivalis* infection. Mice were orally infected with *P. gingivalis* for 42 days and treated from day 35 through day 70 with oral administration of atuzaginstat. Multiple studies were used to determine an effective exposure and dose regimen. A previously peer-reviewed publication established efficacy of atuzaginstat in reducing oral infection and periodontal disease in a naturally occurring aged dog model (Aratsu-Kapur et al. 2021).

KOL Webinar: Innovation in Periodontal Disease – A Major Unmet Medical Need

In conjunction with its participation at IADR 2021, Cortexyme is hosting a key opinion leader (KOL) webinar titled "Innovation in Periodontal Disease – A Major Unmet Medical Need" on Friday, July 23, 2021, at 10:00 a.m. ET. The webinar will feature KOL Mark Ryder, D.M.D., (University of California, San Francisco) who will discuss the unmet medical need in treating patients with *P. gingivalis*-induced periodontal disease and Cortexyme management will present new data from the company's IADR 2021 abstracts. An update on the REPAIR Phase 2 periodontal sub-study of atuzaginstat as part of its pivotal Phase 2/3 GAIN Trial in Alzheimer's disease will also be presented. Dr. Ryder and Cortexyme's management will be available to answer questions following the formal presentations. To register for this webinar, please click here.

Mark Ryder, D.M.D., is a Professor of Periodontology and former Chair of Periodontology and Director of the Postgraduate program in Periodontology at the University of California, San Francisco where he has been a faculty member for the past 41 years. He received his dental and specialty training from the Harvard School of Dental Medicine. He is the author of over 190 articles, abstracts, and book chapters and has lectured extensively on a variety of research and educational topics. He serves as an Associate Editor of *the Journal of Periodontal Research* and is on the Editorial Board of several dental research journals. He has also served as a chair and/or reviewer on several NIH study sections and other national and international

peer review grant organizations, in addition to serving as a consultant for several national and international accreditation programs for dental education. His current research interests include connections between periodontal diseases and Alzheimer's Disease, the links between oral and systemic health in HIV patients, and basic research and clinical trials on novel periodontal therapies.

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 in the fourth quarter of 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," or other similar words. Examples of forward-looking statements include, among others, statements we make regarding our 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; 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 May 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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Stacy Roughan
Cortexyme, Inc.
Vice President, Corporate Communications & Investor Relations
ir@cortexyme.com

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