Cortexyme Presents Data Linking P. Gingivalis to Elevated Levels of Phospho-tau217 Reinforcing Evidence of Pathogen as Causative Agent of Alzheimer's Disease at AAIC 2021

July 26, 2021

New GAIN Trial baseline data demonstrates majority of patients have elevated Von Willebrand factor and alpha-2-macroglobulin

Cortexyme to host AAIC symposium titled "Getting to the Root Cause of Alzheimer's Disease: An Innovative, Upstream Approach for Disease Modification" on Tuesday, July 27

Join KOL webinar on atuzaginstat titled "Innovation in Alzheimer's Disease – Getting to the Root Cause of Neurodegeneration" on Friday, July 30 at 10 a.m. ET

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jul. 26, 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 the presentation of new preclinical data linking *P. gingivalis* to increased levels of phospho-tau217, an emerging biomarker for Alzheimer's disease. This research, along with new baseline data from its pivotal GAIN Trial, is being presented by the company at the Alzheimer's Association International Conference® 2021 (AAIC®) taking place July 26-30, 2021, in Denver, Colorado, as well as virtually. In addition to its presentations, Cortexyme will host a corporate sponsored symposium held in conjunction with the conference titled "Getting to the Root Cause of Alzheimer's Disease: An Innovative, Upstream Approach for Disease Modification" on Tuesday, July 27, 2021, from 5:30 p.m. to 7:30 p.m. MT.

"Cortexyme continues to conduct research that validates and reinforces the gingipain hypothesis and *P. gingivalis*' role as a causative agent of Alzheimer's disease," said Casey Lynch, Cortexyme's chief executive officer, co-founder, and chair. "The GAIN Trial, which is designed to be 90% powered to show a 50% slowing of disease, will read out on the gold standard measures of disease modification as Cortexyme looks to shift the paradigm in effective Alzheimer's treatment."

Cortexyme is pioneering an innovative, upstream, and disease-modifying therapeutic approach to Alzheimer's disease. The Phase 2/3 GAIN Trial is a potentially pivotal study in 643 patients with mild to moderate Alzheimer's Disease. 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 a simple 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.

Cortexyme's work will be featured in two poster presentations at AAIC 2021:

- **Increased Levels of Phospho-tau217 Linked to *P. gingivalis* Reduced by Atuzaginstat:** In its poster "Increased levels of phospho-tau217 in neuron cultures and CVN mice infected with *Porphyromonas gingivalis*" (Poster #52438), Cortexyme demonstrates *P. gingivalis* infected neuronal cell cultures and chronically infected CVN mice display elevated tau phosphorylation at T217 (phospho-tau217). Using IPSC-derived neuron cultures, neuron-astrocyte-microglia co-cultures, and CVN mice (APPSwDI/NOS2 bigenic) as model systems for *P. gingivalis*-induced Alzheimer's disease, the company demonstrated that phospho-tau217 was susceptible to *P. gingivalis*-induced and gingipain dependent digestion in a dose-dependent manner. At lower infection levels, tau protein persisted and an elevated phospho-tau217/total tau ratio was observed in a manner that might reflect the physiological level of gingipain exposure. In CVN mice chronically infected with *P. gingivalis*, the phospho-tau217/total tau ratio was elevated in the brain in infected compared to uninfected mice. Furthermore, after five weeks of treatment with atuzaginstat, the level of phospho-tau217 was similar to that seen in uninfected controls, while tau degradation was completely inhibited by treatment with atuzaginstat.

- **New Baseline Data from GAIN Trial:** In its poster titled "An update and baseline data from the Phase 2/3 GAIN trial of COR388 (atuzaginstat) a novel bacterial virulence factor inhibitor for the treatment of Alzheimer's Disease" (Poster #50624), Cortexyme shares updated and new baseline biomarker data from the full set of patients in the study that supports that this is an appropriate population for testing atuzaginstat for Alzheimer's disease. In addition to demonstrating that 100% of patients have evidence of systemic *P. gingivalis* exposure, GAIN baseline biomarker highlights include traditional CSF biomarkers Aβ, total tau, and phospho-tau 181. New data shows that a majority of patients have elevated Von Willebrand factor (vWF), a vascular injury marker, and alpha-2-macroglobulin (A2M), an endogenous protease inhibitor, in serum. GAIN baseline demographics also demonstrate that 90% of its periodontal disease REPAIR sub-study patients have moderate to severe periodontitis without requiring it as a criterion for study participation.

Cortexyme AAIC Symposium – Getting to the Root Cause of Alzheimer's Disease

Cortexyme will host a corporate sponsored symposium and dinner held in conjunction with AAIC 2021 titled "Getting to the Root Cause of Alzheimer's

Disease: An Innovative, Upstream Approach for Disease Modification" on Tuesday, July 27, 2021, from 5:30 p.m. to 7:30 p.m. MT at the Hilton Denver City Center. Led by Cortexyme's chief executive officer and co-founder Casey Lynch and chief medical officer Michael Detke, M.D., Ph.D., the symposium will provide an informative presentation on how Cortexyme is moving beyond the prevailing targets to deliver a game-changing shift in Alzheimer's disease treatment. For AAIC 2021 registered participants wishing to attend Cortexyme's symposium in person, please email info@cortexyme.com to sign up. The symposium also may be accessed online by registering to attend AAIC 2021 through its virtual conference experience here.

KOL Webinar: Innovation in Alzheimer's Disease – Getting to the Root Cause of Neurodegeneration

In conjunction with its participation at AAIC 2021, Cortexyme is hosting a key opinion leader (KOL) webinar titled "Innovation in Alzheimer's Disease – Getting to the Root Cause of Neurodegeneration" on Friday, July 30, 2021, at 10:00 a.m. ET. The webinar will feature KOL Marwan Noel Sabbagh, M.D., (Cleveland Clinic) who will discuss the current treatment landscape of Alzheimer's disease and dementia, the unmet medical need, as well as recent activity and evidence to support the role of *P. gingivalis* as an important upstream driver of Alzheimer's disease pathology. Dr. Sabbagh will also address new baseline data from Cortexyme's pivotal Phase 2/3 GAIN Trial of atuzaginstat for the treatment of Alzheimer's disease being presented at AAIC 2021. Cortexyme's management team will provide an update on its ongoing pivotal Phase 2/3 GAIN Trial, which builds on Phase 1 data demonstrating atuzaginstat was well tolerated in both healthy subjects and in patients with Alzheimer's disease. Dr. Sabbagh and Cortexyme's management will be available to answer questions following the formal presentations. To register for this webinar, please click here.

Marwan Noel Sabbagh, M.D., board certified neurologist and geriatric neurologist, hopes to work himself out of a job. Considered one of the leading experts in Alzheimer's and dementia, he is the Camille and Larry Ruvo Endowed Chair for Brain Health and Director of Translational Research at Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas. Dr. Sabbagh has dedicated his career to finding a cure for Alzheimer's and other age-related neurodegenerative diseases. Dr. Sabbagh is a leading investigator for many prominent national Alzheimer's prevention and treatment trials. Dr. Sabbagh is on the editorial board for *Journal of Alzheimer's Disease* and *BMC Neurology*. He is now editor in chief of *Neurology and Therapy*. He has authored and co-authored almost 370 medical and scientific articles on Alzheimer's research. Dr. Sabbagh is the author of *The Alzheimer's Answer: Reduce Your Risk and Keep Your Brain Healthy* , with foreword by Justice Sandra Day O'Connor, and *The Alzheimer's Prevention Cookbook: 100 Recipes to Boost Brain Health*. He has edited *Palliative Care for Advanced Alzheimer's and Dementia: Guidelines and Standards for Evidence Based Care and Geriatric Neurology* published in 2014 and *Fighting for my Life: living in the shadow of Alzheimer's disease* published in 2019. He has been recognized with numerous awards, including WestMarc Innovator Award, 2015; Fellow of the American Academy of Neurology, 2004. Dr. Sabbagh earned his undergraduate degree from the University of California, Berkeley and his medical degree from the University of Arizona in Tucson. He received his residency training in neurology at Baylor College of Medicine, Houston, Texas, and completed his fellowship in geriatric neurology and dementia at the University of California, San Diego School of Medicine, where he served on the faculty as assistant professor. Before joining the faculty of the Cleveland Clinic, he was at the Barrow Neurological Institute where he served for three years, and prior to that he was the director of the Banner Sun Health Research Institute for 15 years.

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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