Cortexyme Presents Data Supporting Role of P. Gingivalis in Alzheimer's Pathology at Advances in Alzheimer's and Parkinson's Therapies Virtual Focus Meeting 2020

April 2, 2020

-- New results demonstrate P. gingivalis' ability to infect neurons and cause characteristic Alzheimer's pathology

-- Cortexyme's lead compound, COR388, targets gingipains produced by P. gingivalis and is currently under investigation in the Phase 2/3 GAIN Trial

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Apr. 2, 2020-- Cortexyme, Inc. (Nasdaq: CRTX), a clinical stage biopharmaceutical company pioneering a novel disease-modifying therapeutic approach to treat Alzheimer's and other degenerative diseases, today announced new data supporting the ability of the pathogen *Porphyromonas gingivalis* to invade brain cells and trigger characteristic Alzheimer's pathology including synaptic loss, ultrastructural changes, and inflammation. The data is being presented this week as part of the Advances in Alzheimer's and Parkinson's Disease (AAT-AD/PD) Focus Meeting 2020, which was converted to a virtual meeting due to the COVID-19 pandemic and is being held April 2-5.

"Over the past several years, Cortexyme and scientists around the world have been publishing evidence on the role of *P. gingivalis* in Alzheimer's disease. Our goal is to continue to understand the unique ability of this pathogen to induce cellular damage related to Alzheimer's disease, and how we can best target it to treat the disease," said Stephen Dominy, M.D., Cortexyme's chief scientific officer, co-founder, and a co-author of today's presentation. "With this latest evidence of *P. gingivalis* infection of brain cells in vitro, we are seeing verification that the pathogen is able to infiltrate neurons and catalyze the corresponding characteristic pathology, reinforcing the fact that this is an essential upstream target for Alzheimer's treatment."

P. gingivalis is best known in published literature as the keystone pathogen in the development of periodontal disease. *P. gingivalis* produces toxic virulence factors known as gingipains, and previous research from Cortexyme has demonstrated the presence of gingipains in greater than 90% of post-mortem brains of Alzheimer's disease (AD) patients. In addition, Cortexyme and others have shown in animal models that oral infection with *P. gingivalis* results in brain infection and classic AD pathology, which can be blocked with gingipain inhibitors.

The research presented at AAT-AD/PD investigates changes induced by *P. gingivalis* at the cellular level. The data shows the expression of *P. gingivalis* and gingipains inside of co-cultured brain cells after infection, including neurons, astrocytes, and microglial cells and the display of cellular pathology consistent with AD. This outcome reinforces the findings of previous research on the impact of *P. gingivalis* in the in vivo biological environment of the central nervous system. It also provides support for the premise of Cortexyme's ongoing GAIN Trial studying the efficacy of COR388, a gingipain inhibitor, in improving downstream pathology of the bacterium and alleviating AD symptoms.

"The Phase 2/3 GAIN Trial of COR388 is supported by years of research that the neurodegeneration associated with Alzheimer's may be caused by a bacterium and the gingipains it releases within the central nervous system," said Casey Lynch, Cortexyme's CEO, co-founder and chair. "The data presented today adds to the preclinical and clinical evidence supporting our approach to this devastating disease. We are committed to optimizing the therapeutic potential of COR388 and the potential benefits this approach could have for the millions of people affected by Alzheimer's disease."

To view the poster, please visit the Presentations page under the News & Events heading of the Cortexyme investor site (ir.cortexyme.com).

About the Research Presented at AAT-AD/PD

In the study, infected neurons displayed AD-like neuropathology, including accumulation of autophagic vacuoles and multivesicular bodies, the same structures found in dystrophic, or dysfunctional, neurites in AD brains. The neuron cultures also demonstrated cell loss, tau phosphorylation, neurofilament changes, and a significant loss of synapse density after infection with *P. gingivalis*, mirroring the changes seen in AD brains.

The neuron-astrocyte-microglia co-culture model also allowed researchers to observe that, in infected cultures, *P. gingivalis* was taken up by microglia, where it caused increases in Il-6, Il-8, TNFα and Il-1β cytokines, notable markers of inflammation, signaling an inflammatory immune response similar to that seen in the Alzheimer's-affected brain. At the same time, researchers saw reduced levels of Trem-2, a microglia-secreted protein, and ApoE, a known gingipain substrate, in these infected cultures.

The results from this in vitro model reinforce the results of previous in vivo studies of *P. gingivalis*, demonstrating that the pathogen is able to infiltrate the central nervous system and provide support for the role of *P. gingivalis* in inducing AD pathology.

About the GAIN Trial

The GAIN (GingipAIN Inhibitor for Treatment of Alzheimer's Disease) Trial is a randomized, double-blind, placebo-controlled Phase 2/3 trial is evaluating the efficacy, safety, and tolerability of COR388, Cortexyme's investigational gingipain inhibitor, in patients with mild to moderate Alzheimer's disease. The GAIN Trial also includes a sub-study measuring the efficacy of COR388 on symptoms of periodontal disease including gingival pocket depth. The GAIN Trial has been ongoing since the second quarter of 2019, with top-line results expected in the fourth quarter of 2021. For more information on the trial, visit www.gaintrial.com.

About Cortexyme, Inc.

Cortexyme (Nasdaq: CRTX) is a clinical stage biopharmaceutical company pioneering a novel, disease-modifying therapeutic approach to treat what it believes to be a key underlying cause of Alzheimer's disease and other degenerative diseases. Cortexyme is targeting a specific, infectious pathogen found in the brain of Alzheimer's patients and tied to neurodegeneration and neuroinflammation in animal models. The company's lead investigational medicine, COR388, is the subject of the GAIN Trial, an ongoing Phase 2/3 clinical study in patients with mild to moderate Alzheimer's. To learn more about Cortexyme, visit www.cortexyme.com or follow @Cortexyme on Twitter.

Forward-Looking Statements

Statements in this press release contain “forward-looking statements” that are subject to substantial risks and uncertainties. Forward-looking statements contained in this press 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 and prospects, cash forecasts, the timing and success of our clinical trials and related data, the timing of announcements and updates relating to our clinical trials and related data, the timing of and our ability to enroll patients into our clinical trials, and the potential therapeutic benefits, safety and efficacy of our product candidate or library of compounds. 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 we expect. 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 our Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on March 16, 2020, and other reports as filed with the SEC. Forward-looking statements contained in this press 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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