Cortexyme Presents Data Linking P. gingivalis Infection to Cardiovascular Disease Severity and Alzheimer's Disease, Along With Evidence That Treatment With Atuzaginstat (COR388) Improves Biomarkers Associated With Both Diseases

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-- Researchers presented new preclinical data on atuzaginstat and the potential impact on cardiovascular disease and AD-associated neurodegeneration in two poster presentations at AAIC 2020

-- Cortexyme also presented phase 1b clinical data demonstrating atuzaginstat's therapeutic potential in blocking AD-associated ApoE fragmentation

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jul. 28, 2020-- Cortexyme, a clinical stage biopharmaceutical company pioneering upstream therapeutic approaches to improve the lives of patients diagnosed with Alzheimer's and other degenerative diseases, today announced new preclinical data demonstrating the role of the bacterium *P. gingivalis* in Alzheimer's disease (AD) and cardiovascular disease, providing a potential explanation for why the two diseases often occur together. Cortexyme also provided data demonstrating the therapeutic potential of its lead compound, atuzaginstat (COR388), in treating both diseases. This data, along with two other poster presentations on atuzaginstat, are being presented by Cortexyme at the Alzheimer's Association International Conference® 2020 (AAIC®), which is taking place virtually from July 27-31.

"Atuzaginstat is the subject of the GAIN Trial, a Phase 2/3 clinical trial evaluating its potential to slow or halt Alzheimer's disease progression by blocking the toxic proteases, or gingipains, released by *P. gingivalis* as it invades the brain," said Casey Lynch, Cortexyme's chief executive officer and co-founder, and a co-author of all three presentations. "As evidence mounts regarding *P. gingivalis'* role in a variety of serious health conditions, including cardiovascular disease, we are pleased to play a leading role in the research and development of gingipain inhibitors, and believe that this novel class of compounds may have significant therapeutic breadth and applicability."

The Role of *P. gingivalis* and Potential for Atuzaginstat in Cardiovascular Disease

Previous research led by Cortexyme has demonstrated a causative association between the bacterial pathogen *P. gingivalis* and AD. Cortexyme's lead gingipain inhibitor atuzaginstat has been shown to block the neuropathology triggered by *P. gingivalis* in animal models. Researchers have also found an association between *P. gingivalis* and the atherosclerotic plaques associated with cardiovascular disease, with a 2017 study by Mougeot *et al.* demonstrating *P. gingivalis* as the pathogen found most abundantly in coronary and femoral artery tissues in atherosclerosis and linked to the development of this disease pathology.

In a poster presented at AAIC today, "Targeting *Porphyromonas gingivalis* to treat Alzheimer's disease and comorbid cardiovascular disease" (Abstract 47058P3), researchers demonstrated that oral infection with *P. gingivalis* accelerated atherosclerosis in a rabbit model of disease and showed that atuzaginstat reduced inflammation and the formation of unstable atherosclerotic plaques. Specifically, the gingipain inhibitor reduced deposits of lipids in the aortas of infected animals and prevented the progression of atherosclerosis linked to *P. gingivalis* infection.

"Building on strong prior research linking *P. gingivalis* to cardiovascular disease, our research shows improvements in lipid deposition, progression of atherosclerosis and levels of systemic inflammation in the *P. gingivalis*-infected groups treated with atuzaginstat," said Hatice Hasturk, D.D.S., Ph.D., director of the Center for Clinical and Translational Research at the Forsyth Institute and a principal investigator of the research presented today. "These data are highly suggestive that atuzaginstat may have therapeutic potential in mitigating cardiovascular disease in people with *P. gingivalis* infection, a common oral infection thought to effect more than 50% of the adult population, which is capable of promoting systemic infection and inflammation."

"We are proud to lead global research demonstrating the role of *P. gingivalis* in Alzheimer's disease and, in turn, the therapeutic potential for the gingipain inhibitor atuzaginstat in treating and preventing Alzheimer's pathology," said Stephen Dominy, M.D., Cortexyme's chief scientific officer and co-founder, and co-author on the presentation. "We are encouraged by this new data demonstrating the potential impact of atuzaginstat on cardiovascular disease, a condition where *P. gingivalis* has previously been implicated, and believe this therapeutic approach warrants further study."

Cortexyme's work was featured in two additional poster presentations at the virtual AAIC 2020 event:

Atuzaginstat Protects Against AD-Associated Synaptic Loss

In a poster titled "Comprehensive Alzheimer's pathology is induced by *Porphyromonas gingivalis* infection: atuzaginstat (COR388) and other proprietary gingipain inhibitors protect against synaptic loss" (Abstract 44023P1), researchers showed additional evidence supporting COR388 as a potential AD therapy. This study, conducted in neuron cultures and neuron-astrocyte-microglia co-cultures, showed that atuzaginstat and proprietary gingipain inhibitors protected neurons infected with *P. gingivalis* from synapse loss. Additionally, atuzaginstat reduced the bacterial load in neurons, astrocytes and microglia infected with *P. gingivalis* and protected against deficits in other pathways impacted by the bacterium, including synaptic transmission.

Atuzaginstat Also Decreases ApoE Fragmentation

The third Cortexyme presentation, titled "COR388 (atuzaginstat), a novel gingipain inhibitor, decreases ApoE fragmentation in the CNS of Alzheimer's disease patients" (Abstract 40578P3), presents data indicating *P. gingivalis* gingipains target and cleave ApoE proteins in the nervous system of AD patients. Data from Cortexyme's Phase 1b trial of atuzaginstat show that gingipains preferentially fragment the ApoE4 protein variant, suggesting why the *APOE4* gene variant may increase the risk of developing AD, i.e., the protein is more susceptible to gingipain cleavage and, in turn, AD-associated neurodegeneration.

To view the full poster presentations, please visit the Presentations page under the News & Events heading of the Cortexyme investor site

(ir.cortexyme.com).

About Forsyth Institute

Founded in 1910, The Forsyth Institute is the only independent research organization in the United States dedicated to understanding the important connections between oral health and overall wellness. Forsyth scientists have identified and characterized many of the oral bacteria that play role in oral health and have capacity to increase risk for other diseases in the body. Forsyth Institute is a not-for-profit organization that is also committed to treating underserved populations in local communities and on a national and global scale. To learn more about Forsyth, visit www.forsyth.org

About Cortexyme, Inc.

Cortexyme (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. Based upon the evidence generated to date, Cortexyme is currently advancing its lead therapeutic candidate, atuzaginstat (COR388), in the GAIN Trial, an ongoing Phase 2/3 clinical trial in patients with mild to moderate Alzheimer's disease. Cortexyme is targeting a specific, infectious pathogen found in the brain of Alzheimer's patients and tied to neurodegeneration and neuroinflammation in animal models. 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, the translation to humans of pre-clinical data; the pre-clinical results for our product candidates, the timing and success of our clinical trials and related data, the potential of atuzaginstat to treat Alzheimer's disease and cardiovascular disease, our ability to fund planned operating and capital expenditures, 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, our Quarterly Report on Form 10-Q filed with the SEC on May 12, 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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