# Cortexyme Presents an Update and Baseline Data from the Phase 2/3 GAIN Trial of Atuzaginstat at CTAD 2020, the Clinical Trials on Alzheimer's Disease Conference

November 5, 2020

*-- Data demonstrate that patients enrolled in the GAIN Trial have baseline biomarkers consistent with Alzheimer's disease and potential responders to atuzaginstat --*

*-- Press release issued in advance of CTAD presentation as an SEC exemption to the embargo policy, granted by the conference's organizers --*

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Nov. 5, 2020-- Cortexyme, Inc. (Nasdaq: CRTX), a clinical stage biopharmaceutical company pioneering potential therapeutics for Alzheimer's and other degenerative diseases, announced the presentation of data demonstrating that in a subset of samples analyzed to date, a very high proportion of the adults with mild to moderate Alzheimer's disease (AD) enrolled in the ongoing Phase 2/3 GAIN Trial of atuzaginstat have biomarker profiles consistent with AD, and all patients analyzed to date have evidence of immune response to systemic *Porphyromonas gingivalis* (*P. gingivalis*) infection, a bacteria believed to play a role in AD pathology. Atuzaginstat is a gingipain inhibitor designed to selectively block *P. gingivalis* toxicity and reduce bacterial load. The data (Abstract #OC19) are being presented today in an oral session at the 13th Clinical Trials on Alzheimer's Disease Conference (CTAD 2020), which is taking place as a digital event November 4-7.

"The baseline biomarker and *P. gingivalis* characteristics reported today give us confidence that we have enrolled an appropriate patient population for testing the efficacy of atuzaginstat in the GAIN Trial," said Michael Detke, M.D. Ph.D., Cortexyme's Chief Medical Officer. "A variety of AD-associated biomarkers have been identified in the vast majority of patients enrolled in the trial to date. Additionally, all patients enrolled in the trial and analyzed to date have evidence of immune response to systemic *P. gingivalis* infection. More than 90 percent of patients in the trial's dental sub-study had moderate to severe periodontal disease at baseline. Cortexyme remains on track to conduct an interim analysis of the GAIN Trial in December 2020."

The ongoing Phase 2/3 GAIN Trial is rooted in a strong body of research outlining the role of *P. gingivalis* in the neurodegeneration associated with AD. *P. gingivalis*, which is most commonly associated with periodontal disease, has been discovered in greater than 90% of post-mortem brains of patients with AD and has been shown to produce Alzheimer's pathology in infected animals. The GAIN Trial is evaluating the potential of Cortexyme's lead compound, atuzaginstat, to inhibit the toxic proteases, or gingipains, produced by *P. gingivalis* in patients with mild to moderate AD and to potentially slow or halt AD progression. The trial has completed enrollment, and 643 subjects have been randomized to one of two doses of atuzaginstat (40mg or 80mg twice daily) or placebo. The co-primary endpoints are mean change in cognition (ADAS-Cog 11) and function (CDR-SB or ADCS-ADL) from baseline to 48 weeks compared to placebo. Secondary and exploratory endpoints include change in Winterlight Speech Assessment, cerebral spinal fluid biomarkers, volumetric MRI, and other measures. The GAIN Trial also includes a sub-study measuring the efficacy of COR388 on symptoms of periodontal disease, including gingival pocket depth. An interim analysis of the GAIN Trial is expected in December 2020. Top-line data from the trial's final analysis are expected in the fourth quarter of 2021.

Key findings reported in today's presentation, titled "Phase 2/3 GAIN trial of atuzaginstat (COR388), a novel bacterial virulence factor inhibitor for the treatment of Alzheimer's disease: Update and baseline data," include:

- Approximately 75% of analyzed subjects have an amyloid β (Aβ) 42/40 ratio below the assay cut-off (<0.095) associated with AD, and approximately 88% have an Aβ 42/40 ratio associated with Aβ positivity on PET scan (<0.129).
- 89% of analyzed subjects have total Tau levels above the assay AD cut-off (>290 pg/ml), and 86% have pTau 181 levels consistent with AD in the Amyloid/Tau/Neurodegeneration (ATN) designation (>61 pg/ml).
- All subjects analyzed to date had evidence of *P. gingivalis*-specific IgG at baseline, with 72% exhibiting high antibody titers associated with more severe periodontal disease and 97% with titers associated with at least mild periodontal disease according to third party research.[1] Previous research has demonstrated that IgG titers roughly correlate to infection load.[2]
- More than 90% subjects in the periodontal sub-study included at the time of data cut-off had moderate to severe periodontal disease at baseline.
- Approximately 65% of the trial participants carry at least one ApoE4 gene and these participants are stratified across the three treatment groups.

Baseline biomarker analyses presented at CTAD include 40-50% of the enrolled subjects with data available at the time of data cutoff. The presentation with additional detail is now available at https://ir.cortexyme.com/news-and-events/presentations.

**About Cortexyme, Inc.**

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. 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 timing and success of our clinical trials and related data including the outcome of the interim analysis, the potential of atuzaginstat to treat Alzheimer’s 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 August 14, 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.

[1] Offenbacher et al., Journal of Periodontology 2007 Oct;78(10):1911

[2] Kojima et al., Journal of Periodontology 1997. 68 (7): 618

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