# Cortexyme Provides New GAIN Trial Data at AD/PD 2022 Demonstrating Potential Benefit of Lysine Gingipain Inhibition in Mild to Moderate Alzheimer's Population

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*Target engagement and biomarker data expands understanding of the role of P. gingivalis and the potential benefit of lysine gingipain inhibition*

*Biomarker data and correlations to clinical outcomes consistent with the gingipain hypothesis*

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Mar. 21, 2022-- Cortexyme, Inc. (Nasdaq: CRTX), a clinical-stage biopharmaceutical company pioneering upstream therapeutic approaches to improve the lives of patients diagnosed with degenerative diseases, presented new target engagement and biomarker data from the GAIN Trial at the AD/PD™ 2022 International Conference on Alzheimer's and Parkinson's Diseases.

"Our understanding of the impact of lysine gingipain inhibition on neurodegeneration and other Alzheimer's disease markers continues to expand. The evidence demonstrates our target – *P. gingivalis* – may play a key upstream role in both of these areas, and correlations between *P. gingivalis* biomarkers and clinical assessments show that our ability to inhibit this target potentially leads to improved patient outcomes," said Michael Detke, MD, PhD, Cortexyme's chief medical officer. "These additional data from the GAIN Trial provide critical insights to help us advance our gingipain inhibitor pipeline, expanding upon and supporting clinical evidence of this target and atuzaginstat's mechanism of action, in addition to helping us better identify which patients are most likely to benefit."

**New GAIN Trial Data Highlights from AD/PD 2022**

In its presentation titled "Data from the Phase 2/3 GAIN Trial of COR388 (Atuzaginstat) for the Treatment of Mild to Moderate Alzheimer's Disease," Cortexyme shared new target engagement and biomarker data, including correlations between biomarkers and clinical outcomes, detailed below. This presentation is the first of multiple presentations this year which are expected to include incremental analysis and biomarker data from the GAIN Trial.

- **Target Engagement Supportive of Mechanism of Action:** GAIN Trial findings support that atuzaginstat engaged the target, inhibiting lysine gingipains, which are essential to the survival of *P. gingivalis*. Lysine gingipain inhibition by atuzaginstat resulted in a 30% to 50% slowing of cognitive decline in the participants with high *P. gingivalis* load.
- **Trends to Benefit on Traditional CSF Biomarker Measures:** GAIN Trial data included the measurement of traditional Alzheimer's disease biomarkers, including cerebral spinal fluid (CSF) biomarkers phospho-tau 181 and total tau. By engaging a novel upstream target, atuzaginstat demonstrated numerical trends to benefit in tau biomarkers, which is consistent with the observed slowing of Alzheimer's disease progression. These beneficial trends were also present in the *P. gingivalis* DNA status (PG-DS) prespecified subgroup, which are the most likely responders, consistent with the gingipain hypothesis and atuzaginstat's efficacy.
- **Trends to Benefit on Novel Brain Volumetric Biomarker Measures:** The GAIN Trial also included exploratory MRI brain volumetric measures as biomarkers of disease modification in Alzheimer's disease, including bilateral hippocampal volume, cortical thickness, and whole brain volume. All three brain volumetric measures demonstrated consistent numerical trends with lower rates of decline on atuzaginstat, particularly in the PG-DS prespecified subgroup. Importantly, these brain volumetric measures also showed correlation with the clinical co-primary endpoints ADAS-Cog11 and ADCS-ADL. These findings further support a role of *P. gingivalis* in disease progression.

To access Cortexyme's AD/PD 2022 presentation, please visit the Science or Investors sections of the company's website at www.cortexyme.com.

**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 degenerative diseases, including Alzheimer's disease, periodontitis, and oral potentially malignant disorders, among others. Cortexyme's innovative approach targets a specific, infectious pathogen called *P. gingivalis* found in the brain of Alzheimer's patients 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 "supportive," "benefit," "outcomes," "potential," "correlations," "efficacy" or other similar words. Examples of forward-looking statements include, among others, the strategic development path for atuzaginstat; its business plans, internal and external development of the pipeline, strategy, planned FDA submissions and clinical trials and timeline, prospects, and milestone expectations; the timing and success of the company's clinical trials and related data, including plans and the ability to initiate, conduct and/or complete current and additional studies; 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, further development of atuzaginstat and other programs or indications, regulatory submissions and interactions with regulators, and related response and decisions, 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, 2022, its Quarterly Report on Form 10-Q filed with the SEC on October 29, 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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