



Cortexyme Provides Business Update and Reports First Quarter 2021 Results

May 10, 2021

Top-line data from 643-subject Alzheimer's disease pivotal GAIN Trial expected in fourth quarter 2021

Top-line data from 233-subject periodontal disease Phase 2 REPAIR sub-study of the

GAIN Trial expected in fourth quarter 2021

COR588 on track to initiate first-in-human studies in third quarter 2021

Current cash position sufficient to fund operations through 2023

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--May 10, 2021-- Cortexyme, Inc. (Nasdaq: CRTX), 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 and other degenerative diseases, today provided an update on expected clinical data readouts and reported first quarter 2021 financial results.

"We are pleased by our continued progress and remain on track for another exciting year with important data readouts from our pivotal GAIN Trial in Alzheimer's and periodontal disease expected in the fourth quarter of 2021," said Casey Lynch, Cortexyme's chief executive officer, co-founder, and chair. "The foundational evidence of *P. gingivalis* as a causal agent of Alzheimer's and other degenerative diseases continues to expand and further validate our disruptive science targeted at high unmet need indications. We have the strategic vision to reach beyond our multiple upcoming milestones and enter this next stage of development with a strong cash position sufficient to fund operations through 2023."

Pipeline Updates

- The GAIN Trial continues to progress toward top-line data in the fourth quarter 2021. The study is designed to be powered at approximately 90% and approximately one-third of patients are pending completion in the study.
- Cortexyme successfully completed a radiolabeled (¹⁴C) human mass balance study for atuzaginstat (Study COR388-003), a key clinical pharmacology study necessary for a New Drug Application (NDA).
- The company successfully completed a six-month transgenic mouse carcinogenicity study for atuzaginstat, another key requirement for an atuzaginstat NDA, with no findings of carcinogenicity.
- The GAIN Trial includes a periodontal sub-study named REPAIR (REduction of *P. GingivAalls* To ImpRove Pocket Depth) that includes 233 subjects with the standard regulatory efficiency endpoints of pocket depth and clinical attachment level at six months and one year. Top-line data for the REPAIR sub-study, which evaluates atuzaginstat in treating periodontitis, is expected in the fourth quarter 2021.
- COR588 IND-enabling studies are proceeding with a first-in-human study expected to begin in the third quarter 2021. COR588 is a unique small molecule lysine gingipain inhibitor with once-daily oral dosing that Cortexyme intends to advance in periodontal disease and potentially other new indications
- Two arginine gingipain inhibitors, COR788 and COR822, have been selected as lead compounds to progress toward IND-enabling studies, including manufacturing scale-up and dose range-finding toxicology studies. Arginine gingipain is a distinct target associated with *P. gingivalis* that contributes to bacterial survival, replication, and toxicity. An arginine gingipain inhibitor may be used as monotherapy in new indications or potentially additively with lysine gingipain inhibitors like atuzaginstat and COR588. Both molecules have novel composition of matter (patents pending), are brain-penetrant, and orally available.

Scientific Updates

- Cortexyme announced that *Cell Reports Medicine* selected its research paper, "Gingipains identified in Alzheimer's disease brains differentially fragment ApoE proteins" (CR-MEDICINE-D-21-00188), for peer review and made the article, as originally submitted, available via [Cell Press Sneak Peek](#). Further documenting the pathogenic role of *P. gingivalis* in Alzheimer's, the research demonstrates that gingipains in Alzheimer's disease brains preferentially fragment ApoE4 over ApoE3 and ApoE2, linking *P. gingivalis* to the strongest genetic risk factor for sporadic Alzheimer's. Additionally, analysis of cerebrospinal fluid (CSF) from Alzheimer's subjects administered the gingipain inhibitor atuzaginstat reveals a decrease in ApoE fragments and a slowing in decline of Ab₁₋₄₂.
- Abstracts have been accepted for presentations at upcoming scientific meetings, including the 2021 American Society of Clinical Psychopharmacology (ASCP) Annual Meeting on June 1-4, 2021; the International Association for Dental Research (IADR) General Session & Exhibition on July 21-24, 2021; the Alzheimer's Association International Conference (AAIC) on July 26-30, 2021; and the Annual Biomarkers for Alzheimer's Disease Summit on August 24-26, 2021. Cortexyme plans to present additional baseline data from the GAIN Trial, as well as further evidence to support *P. gingivalis* as an important upstream driver of disease pathology and the efficacy of proprietary gingipain inhibitors at these meetings.
- Adding to the growing body of evidence linking *P. gingivalis* and neurodegeneration, Cortexyme presented new [research](#) at

AD/PD 2021 in March 2021, further reinforcing the company's foundational evidence on *P. gingivalis*' role in Alzheimer's disease (AD) and new techniques to detect its presence in the human brain. Scientists at the University of Auckland and Cortexyme reported new techniques to determine the ultrastructural localization of the arginine-gingipain (Rgp) virulence factor secreted by *P. gingivalis* in the human AD brain using electron microscopy. The researchers reported on the intracellular organelles in AD brain cells that Rgp co-localizes with, providing insight for the first time into why some sub-cellular organelles in AD neurons and astrocytes are damaged.

First Quarter 2021 Financial Results

- **Cash Position:** Cash, cash equivalents, and short and long-term marketable securities as of March 31, 2021 were \$170.8 million and include approximately \$117.6 million of net proceeds raised in Cortexyme's private placement offering completed in February 2020. Cortexyme expects its cash position to be sufficient to fund its operating and capital expenditures through 2023.
- **Research and Development (R&D) Expenses:** For the quarter ended March 31, 2021, R&D expenses were \$16.8 million, primarily due to costs related to the research and development of atuzaginstat, the GAIN Trial, and stock-based compensation expense of \$3.5 million.
- **General and Administrative (G&A) Expenses:** For the quarter ended March 31, 2021, G&A expenses were \$6.5 million. The expenses were primarily attributable to personnel-related expenses, insurance, professional and legal fees, and stock-based compensation of \$3.5 million.
- **Net Loss:** For the quarter ended March 31, 2021, the company's net loss was \$23.1 million, or a loss of \$0.78 per basic share. Weighted average shares outstanding for the quarter ended March 31, 2021 were 29,554,921.

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; its ability to fund planned operating and capital expenditures; the timing of announcements and updates relating to its clinical trials and related data; the timing of and its ability to enroll patients into its clinical trials; the potential therapeutic benefits, safety and efficacy of the company's product candidate or library of compounds; statements about its ability to obtain, and the timing relating to, regulatory submissions and approvals with respect to the company's drug product candidate; and expected cash runway and financial update. 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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