Cortexyme announces phase I data demonstrating COR388 is safe and well tolerated in healthy older volunteers and Alzheimer's patients

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-- Data on safety and exploratory cognitive testing presented in late-breaking poster at the 2018 Clinical Trials of Alzheimer's Disease Conference

-- Phase 2 enrollment expected to begin in 2019

South San Francisco, Calif. and Barcelona, Spain – October 24, 2018 –Cortexyme, Inc. today announced encouraging results from its phase 1 clinical trial of COR388, the company's lead small molecule in development as a potential treatment for Alzheimer's Disease (AD). The primary objectives of the trial were to assess the safety, tolerability, and pharmacokinetics of repeated doses of COR388 in older healthy volunteers and patients with AD, and to evaluate exploratory biomarkers and pharmacodynamic measures including cognition.

In a late-breaking poster presentation (LBP16) at the 11th Clinical Trials in Alzheimer's Disease (CTAD) Conference taking place this week, investigators reported COR388 was safe and well tolerated when given at a range of doses for up to 28 days. COR388 was detectable in the cerebral spinal fluid (CSF) along with fragmented DNA from the bacterium that COR388 targets. Additionally, while the study was not powered for significance, COR388 showed positive trends across several cognitive tests in patients suffering from AD. Based on these results, Cortexyme plans to initiate a large phase 2 clinical trial of COR388 in mild to moderate AD in 2019.

"The presentation of these results at CTAD is an important milestone for Cortexyme as we advance a potential new approach to tackling one of medicine's most pressing challenges," said Casey Lynch, Cortexyme's co-founder and chief executive officer. "We are committed to moving quickly to advance COR388 for the benefit of the global Alzheimer's community in need of new therapeutic options. Following the completion of our Series B financing this past summer, we are well resourced to advance COR388 into phase 2 clinical development."

COR388 is a first-in-class, orally administered bacterial protease inhibitor that targets Porphyromonas gingivalis (Pg), a bacterium discovered in the brains of patients with Alzheimer's by Cortexyme's co-founder and chief scientific officer, Stephen Dominy, M.D. COR388 was designed to inhibit Pg's neurotoxic proteases, or gingipains, found in the brains of AD patients with levels correlating to tau and ubiquitin pathology. By inhibiting these gingipains, COR388 aims to protect neurons from bacterial toxicity, lower neuroinflammation and reduce abeta42 production, thereby preventing further cognitive decline and dysfunction. If borne out in clinical testing, COR388 could represent a wholly new approach to addressing a disease estimated to affect more than 5.4 million people in the United States.[1]

Trial Design

The randomized, placebo controlled, repeat dose phase 1 study enrolled 33 subjects in four cohorts. Cohorts 1-3 enrolled healthy volunteers between the ages of 55 and 80 without evidence of dementia or major illness. Subjects in Cohorts 1, 2, and 3 received 25, 50, and 100 mg of COR388 or placebo every 12 hours for ten consecutive days, with multiple blood samples collected on Days 1 and 11 for measurements of plasma levels of COR388.

Cohort 4 enrolled subjects with AD between the ages of 55 and 85 who were in otherwise general good health. Inclusion criteria for this cohort included probable AD based on NINDS-ADRDA criteria, baseline MMSE between 14-25, screening MRI compatible with AD, and no other cause of dementia. Cohort 4 subjects could stay on stable doses of background medication, including symptomatic treatments for AD. Subjects received 50 mg of COR388 or placebo every 12 hours for 28 days as outpatients, returned for weekly safety assessments, and underwent lumbar puncture on Days 1 and 28. On Day 1, repeated blood and CSF samples were collected following the first dose of COR388.

Results

Cohorts 1-3 enrolled a total of 24 healthy volunteers, 55 percent of whom were male with a mean age of 60 years. Eighteen subjects received COR388 and six received placebo, with all but one subject completing the planned ten days of treatment. COR388 was found to be safe and well tolerated. Drug related treatment emergent adverse events (AEs) were mild and transient, including in two (33%) placebo subjects, two (33%) 50 mg treated subjects and three (50%) 100 mg treated subjects. There were no dose limiting toxicities or serious adverse events reported. No subjects withdrew from the study because of adverse events.

Cohort 4 enrolled nine AD patients, 56 percent of whom were male with a mean age of 72 years. Six subjects received COR388 and three received placebo. Drug related adverse events occurred in two (66.7%) patients on placebo and two patients (33.3%) on COR388. AEs were mild to moderate and transient. No serious adverse events were reported, and no subjects withdrew from the study because of adverse events. The pharmacokinetic (PK) profile of COR388 in AD subjects was similar to that in healthy volunteers, and CSF levels of COR388 were detected at levels similar to that seen in nonclinical studies that are associated with high brain penetration. All AD subjects analyzed had fragments of DNA from P. gingivalis in their CSF at baseline.

Although the primary focus of this phase 1 study is safety and PK, Alzheimer's patients in Cohort 4 underwent exploratory cognitive testing. MMSE and CANTAB measures of memory and reaction time showed improvement from baseline in the treatment group compared to placebo. The differences were not statistically significant. Additionally, Winterlight's Cognitive Test using speech and language assessments showed numerical improvements from baseline in a variety of parameters in the COR388 group compared to placebo, indicating a trend to improvement in the level of detail during picture description. Statistically significant improvement from baseline was seen on three measures in the treatment group and no measures in the placebo group.

"The results of this randomized, placebo-controlled phase 1 clinical trial demonstrate that COR388 is safe, well-tolerated, and has a favorable pharmacokinetic profile in the therapeutic dose range," said Samer Kaba, M.D., Cortexyme's chief medical officer. "Based on these data, we

anticipate starting a phase 2 clinical trial next year in order to further evaluate the potential efficacy of this novel mechanism for addressing Alzheimer's and other degenerative diseases."

About Cortexyme

Cortexyme is a privately held, clinical-stage pharmaceutical company developing therapeutics to alter the course of Alzheimer's and other degenerative disorders. Cortexyme is targeting a specific, infectious pathogen tied to neurodegeneration and chronic inflammation in humans and animal models. The company's lead compound, COR388, is entering phase 2 development; additional proprietary small molecules are moving forward in preclinical development. Cortexyme's investors include Sequoia Capital, Vulcan Capital, Verily Life Sciences, EPIQ Capital Group, RSL Investments, Lamond Family, Pfizer, Takeda Ventures, Breakout Ventures, Dolby Family Ventures, and Breakout Labs among others. For more information on Cortexyme, visit www.cortexyme.com.

[1]https://www.cdc.gov/chronicdisease/resources/publications/aag/alzheimers.htm