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CuraSen Therapeutics Announces Oral Presentation of Additional Positive Phase 2a Data with CST-2032/CST-107 in Patients with Alzheimer's or Parkinson's Disease at AD/PD™ 2024 International Conference

Drug Combination's Unique Mechanism of Action Enables Reactivation of Brain Adrenergic Function, Showing Improvements in Multiple Areas of Cognition

March 07, 2024 09:00 AM Eastern Standard Time

SAN CARLOS, Calif. & LISBON, Portugal--(BUSINESS WIRE)--CuraSen Therapeutics, Inc., a clinical-stage company developing small molecule therapies to treat neurodegenerative disease, announced that it will present additional positive Phase 2a data with its combination adrenergic activator, CST-2032/CST-107, in patients with mild cognitive impairment (MCI) or mild dementia from either Alzheimer's or Parkinson's disease. The oral presentation will take place at AD/PD™ 2024: The International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders, being held March 5-9, 2024, in Lisbon, Portugal.

CST-2032 is one of CuraSen's two lead product candidates being tested in patients with Alzheimer's and Parkinson's disease. Both CST-2032 and CST-103, the company's other lead clinical candidate, are oral, brain-permeant, beta2 adrenoceptor (β_2-AR) agonists delivered in combination with CST-107 (nadolol, a brain-sparing beta blocker) to inhibit peripheral effects of β_2-AR agonism. Both CST-2032 and CST-103 work by enabling reactivation of brain adrenergic function lost early in the neurodegenerative disease process.

The updated Phase 2a data with CST-2032/CST-107 showed statistically and clinically important effects across several cognitive domains in patients with Alzheimer's and Parkinson's disease, such as memory, attention, executive function, facial recognition and impulse control — areas known to be impacted by adrenergic function. Target effect sizes of 0.2-0.3 or higher, as seen in this study, predict success in larger, longer studies.

"These encouraging data build on earlier results presented at October 2023's CTAD conference, reinforcing that treatment with CST 2032/CST-107 can produce meaningful quality-of-life cognitive improvements for Alzheimer's and Parkinson's patients, particularly those with mild cognitive impairment, rapidly and safely," said Anthony Ford, PhD, chief executive officer of CuraSen. "The robust, collective data set from both CST-2032 and CST-103 demonstrate that this novel mechanism of action for restoring adrenergic function to the brain is a highly compelling strategy to address unmet symptoms of neurodegeneration. We plan to evaluate additional doses and refine optimal patient profiles in our upcoming Phase 2 studies, with the goal to significantly increase cognitive performance and ultimately, halt disease progression."

The randomized, placebo-controlled, double-blinded crossover study evaluated 64 patients with MCI or mild dementia from either Alzheimer's disease or Parkinson's diseases:

AD with MCI = 30 patients randomized; 25 completed
AD with dementia = 6 patients randomized; 5 completed
PD with MCI = 22 patients randomized; 21 completed
PD with dementia = 6 patients randomized; 4 completed

Data highlights included:

- Digit Symbol Substitution test, which measures complex attention, memory and executive function:
  AD patients with MCI = 0.36 effect size; p=0.02 on Day 14
- Facial Expression Recognition response time to accurately recognize facial expressions, which measures social cognition:
  AD patients with MCI = 0.66 effect size; p=0.04 on Day 14 for happy expression and 0.91 effect size; p = 0.01 on Day 14 for surprise expression
- Stop Signal test, which measures impulse control
  PD patients with MCI = 0.52 effect size; p=0.04 on Day 14
- Excellent safety and tolerability profile
  No serious adverse events: no increases in heart rate observed one to four hours after dose

The company plans to initiate longer studies with both CST-2032/CST-107 and CST-103/CST-107 in AD and PD patients with MCI later this year, as well as develop fixed-dose combination tablets for each of these drug candidates.

Study Objectives and Design

The study objectives were to establish safety and tolerability of CST-2032/CST-107, identify optimal dosing, and identify cognitive tests responsive to agonist stimulus within the two-week dosing period. Measures of cognition included the digit symbol substitution test, Cambridge neuropsychological test battery, and the facial expression recognition task. The study took place at multiple sites in the United States and New Zealand.

Patients received either daily 3 mg of CST-2032 with 3 mg of nadolol for 14 days, or matching placebo, followed by a wash-out period (≥7-d) before crossing over to the other treatment arm. Blood samples are being analyzed for AD biomarkers, and DNA samples for AD and PD genotyping.

Abstract Details

Title: “CST-2032, a Novel Beta-2 Adrenoceptor Agonist, Improves Cognition in Patients with Impairment Due to Alzheimer’s or Parkinson’s Disease”
Abstract #: PO34
Presenter: Gabriel Vargas, MD, PhD, chief medical officer, CuraSen Therapeutics
Session: Translational Drug Discovery and Experimental Models 05
Date: Saturday, March 9, 2024
Time: 17:25-17:40 UTC, session time,16:40 - 18:40 UTC
Location: Auditorium VII

About CuraSen Therapeutics

CuraSen is focused on the development of new treatments for neurodegenerative diseases, including Parkinson’s disease, Alzheimer’s disease and other related orphan conditions. CuraSen’s drugs are designed to activate certain receptor populations in the brain to compensate for critical neuronal and glial functions that have otherwise been lost due to degeneration and represent a unique approach in the field. The company is evaluating CST-103 and CST-2032, both

selective β_2-AR agonists, in combination with CST-107, a β-AR blocker, in multiple Phase 2 clinical studies. CST-3056, an α_{1A}-AR agonist, is in preclinical development for the treatment of Alzheimer's disease. For more information, please visit www.curasen.com.

Contacts

Susan Kinkead
Kinkead Communications
susan@kinkeadcomm.com
415-509-3610