Ceregene, Inc., is a private, venture capital backed San Diego-based biotechnology company that is the leader in developing therapies utilizing neurotrophic factors to treat major neurodegenerative disorders. The company’s president and CEO is Jeffrey M. Ostrove, Ph.D., who has 25+ years working on the development of biopharmaceuticals. Ceregene’s executive vice president and chief scientific officer is Raymond T. Bartus, Ph.D., a world renowned neuroscientist with over 250 publications in the field of drug development and neurodegenerative diseases and several successful products. The team at Ceregene has been working for the past 11 years to develop and optimize CERE-120, an AAV2-vector expressing the neurotrophic factor neurturin (NRTN) to treat patients with Parkinson’s disease and CERE-110, an AAV2-vector expressing Nerve Growth Factor (NGF) for the treatment of Alzheimer’s disease. Our scientists have carried out extensive toxicology, efficacy and biodistribution/Expression studies in multiple animal species and models of disease. Over a dozen of these studies have been published in the medical scientific literature. The Ceregene team has also developed a cost-effective cGMP manufacturing process that can be used for Phase 3 studies and commercialization. Ceregene has carried out 7 clinical studies on these products and is now looking for a partner to advance them into Phase 3 and commercialization.

Opportunity Overview

Neurodegenerative diseases such as PD result from the degeneration of specific neuronal populations in the central nervous system. Substantial scientific evidence has shown that neurotrophic factors can have remarkable restorative effects on degenerating neurons in numerous models of human disease. However, the inability to accurately, safely and effectively target their delivery has limited their successful translation to the clinic. Ceregene’s proprietary AAV-based gene delivery approach solves this problem, providing targeted delivery of the neurotrophic factors in a safe and sustained fashion for the lifetime of the patient following a single dosing procedure. The Company has demonstrated human clinical proof of concept in a Phase 2a study in Parkinson’s disease (PD) with their lead product CERE-120, an AAV2-based vector expressing the neurotrophic factor neurturin (NRTN). CERE-120, which acts to repair damaged and dying dopamine-secreting neurons, has the potential to both treat the symptoms as well as slow disease progression of PD.

Ceregene has amassed a large body of data supporting its approach, including:

- Extensive validation in preclinical testing. Over 2 dozen studies in rodents and nonhuman primates demonstrate the safety, efficacy and long-term, controlled expression of the product.
- Successful completion of 3 clinical studies that further support the safety and efficacy in PD patients, while providing unique insight for enhancing the effects. Specifically, CERE-120 has been administered to approximately 75 patients with Parkinson’s disease, involving a 12-patient Phase 1 safety study, a 58 patient, multi-center, placebo-controlled Phase 2a trial, and a follow-on, 6-patient Phase 1 study. A multi-center, sham-surgery controlled Phase 2b study is ongoing. These studies demonstrate:
  - The safety of CERE-120 to date, with no unexpected or serious consequences of administering the viral vector, or expressing NRTN protein in any of the 75 subjects given CERE-120, some as long as 7 years ago.
  - ‘Proof of Concept’ of efficacy in a double-blind, controlled study. Statistically significant and/or clinically meaningful efficacy was observed on several endpoints at the 12 month primary time point, with not a single measure favoring the sham control group. Importantly, the subset of patients who had blinded assessments at the protocol-prescribed 18 month secondary time point demonstrated a statistically significant improvement (p=0.23) on the UPDRS III (i.e., primary endpoint), as well as on numerous additional endpoints.
  - Confirmation of sustained, stable expression of NRTN expression in the targeted regions of the PD brain up to 4 years, post-dosing.
Details of MJFF Grant

Ceregene has been working with the MJFF since 2005 and has received the following 5 grants:

1. A Phase I Clinical Trial of Neurturin (NTN) Gene Therapy for Parkinson's Disease
   Date: November 17, 2005
   Amount: $740,436.48

2. A Phase II Clinical Trial of Neurturin (NTN) Gene Therapy for Parkinson's Disease
   Date: October 9, 2006
   Amount: $1,617,968.75

3. CERE-120 Long-Term Subject Follow-Up
   Date: June 1, 2009
   Amount: $719,874.97

4. A Sham-Surgery Controlled Phase 2 Trial Testing AAV2-Neurturin (CERE-120) in Moderately Advanced Parkinson’s Disease
   Date: May 20, 2010
   Amount: $2,500,000.00

5. Supplemental funding for "A Sham-Surgery Controlled Phase 2 Trial Testing AAV2-Neurturin (CERE-120) in Moderately Advanced Parkinson's Disease"
   Date: July 12, 2011
   Amount: $1,000,000.00

Results and Potential Next Steps

Ceregene is currently conducting a Phase 2b study designed to maximize the benefit of CERE-120 and provide additional safety information and pivotal efficacy data. The clinical benefit observed at 12 months in the blinded Phase 2a trial (see Opportunity Overview), along with evidence for amplified benefit with longer, post-CERE-120 time points and insight gained from the autopsy data, led to the development of a revised dosing paradigm employed in the current Phase 2b clinical trial. The primary change in dosing involved adding CERE-120 injections directly into the substantia nigra, in addition to the putamen. The nigral injections are intended to directly target the degenerating cell bodies (located in the nigra), where NRTN elevations must occur if repair genes located in the nucleus of those cell bodies are to be activated. Additionally, the CERE-120 dose delivered to the terminal fields of the degenerating neurons (in the putamen) was increased 4-fold (compared to the initial Phase 2a trial), on the basis of the additional long-term/high dose animal safety/tox data generated since the time the initial Phase 2a trial was launched, as well cumulative safety data for CERE-120 in Parkinson’s patients.

If the ongoing Phase 2b trial is successful in demonstrating a significant clinical benefit (data available in early 2013), as measured by the UPDRS III, the Company believes that an additional clinical study encompassing fewer than 250 additional CERE-120 patients would likely be needed to secure registration in the U.S., at a total projected spend of approximately $50 - 60 million. This allows for an FDA filing and potential approval by 2016, assuming fast track treatment at the Agency.

Intellectual Property Status

Ceregene has over 100 issued patents covering: a) Neurotrophic Factors; b) The AAV vectors used to manufacture CERE-120; c) Methods for delivering neurotrophic factors to the brain to treat Parkinson’s and Alzheimer’s disease; d) Components the molecular structure of CERE-120 expressing NRTN; and e) The device used by neurosurgeons to deliver CERE-120 to Parkinson’s patients and CERE-110 to Alzheimer’s patients.