Brainstorm Cell Therapeutics Inc.
www.brainstorm-cell.com

Treating neurodegenerative diseases with stem cell therapy

Brainstorm Cell Therapeutics is looking for financial and corporate partners to help complete the development and launch of revolutionary neurodegenerative disease treatments.

Neurodegenerative diseases such as Alzheimer's, Parkinson's and Huntington's disease and amyotrophic lateral sclerosis (ALS) for the most part lack truly effective disease-modifying therapies. Not surprisingly, researchers have investigated the potential of cellular therapies to treat neurodegenerative diseases by using mesenchymal stem cells (MSCs). Stem cells can be used either to replace dead, damaged or dying neurons or to support damaged and dying neurons via a variety of routes, including dampening of the immune system and the secretion of neurotrophic factors.

Brainstorm Cell Therapeutics is pursuing a multistep approach that begins with the harvesting of undifferentiated MSCs from a patient's own bone marrow. The MSCs are then expanded *ex vivo* and induced to differentiate into cells capable of releasing several neurotrophic factors, including glial-derived neurotrophic factor, brain-derived neurotrophic factor, vascular endothelial growth factor and hepatocyte growth factor, which are critical for the growth, survival and differentiation of developing neurons. Differentiated neurotrophic-factor-secreting MSCs (MSC-NTFs) ('NurOwn') are then transplanted back into the original patient (**Fig. 1**).

"We believe that our NurOwn platform for propagating MSC and their differentiation into neurotrophic-factor-secreting cells, which can be transplanted at, or near to, the site of neuronal damage, offers hope to sufferers of neurodegenerative diseases," explained company COO and CMO Ralph Kern. The company has already shown that its MSC-NTFs are effective in animal models of ALS, Parkinson's disease, multiple sclerosis, optic nerve transection, Huntington's disease and autism.

The platform was developed in collaboration with Daniel Offen, of the Felsenstein Medical Research Center of Tel Aviv University, and the late Eldad Mohammed, former head of neurology at the Rabin Medical Center. Brainstorm Cell Therapeutics acquired the platform through an exclusive, worldwide licensing agreement with Ramot, the technology transfer company of Tel Aviv University.

ALS and the lead program

The progressive degeneration of motor neurons in ALS, which is also known as motor neuron disease or Lou Gehrig's disease, leads to progressive weakness, respiratory failure and eventually death, with a median survival for patients of 3–4 years from the time the first symptoms manifest. The disease affects approximately 4–7 per 100,000 people worldwide. The only ALS medications approved by the US Food and Drug Administration are Rilutek (riluzole), which extends the time to death by only several months, and Radicava (edaravone), which slows the rate of functional decline only modestly in ALS patients.

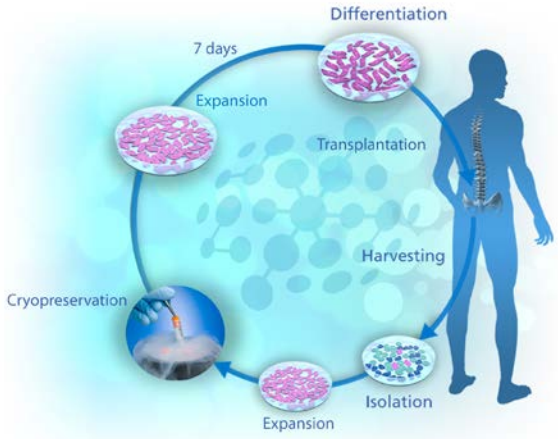

Figure 1: The NurOwn approach. The diagram shows the different steps of the NurOwn cycle, from cell harvesting to reimplantation.

The company's most advanced program is in ALS, and it has reported favorable findings. In a US phase 2 study in 48 ALS patients, the company not only achieved its primary endpoint of demonstrating that NurOwn cells are safe and well tolerated, but also noted clinically meaningful changes in the ALS functional rating responder score (ALSFRS-R). The company also reported encouraging cerebrospinal fluid biomarker profiles, with levels of neurotrophic factor increasing and those of inflammatory markers decreasing.

With the phase 2 data in hand, the company has moved quickly to initiate a phase 3 trial of NurOwn in ALS. The trial will enroll approximately 200 patients at six top ALS clinical sites in the United States. The primary endpoint will be the impact on ALSFRS-R. In July 2017, the company announced that its phase 3 ambitions in ALS will be supported by a $16 million nondilutive grant from the California Institute for Regenerative Medicine (CIRM), the world's largest institution dedicated to cell therapies.

To date, the company has entered into agreements with Massachusetts General Hospital, the University of Massachusetts, California Pacific Medical Center and the University of California–Irvine Medical Center to participate in the ALS phase 3 NurOwn trial—that started enrolling patients in October 2017. The company has also chosen Worldwide Clinical Trials as the clinical research organization that will manage the trial.

Next steps

Although the CIRM grant will cover much of the phase 3 trial expenses, Brainstorm is now looking for financial and corporate partners to help it pursue its long-term ambitions. "While we have more than a decade's experience in developing this clinically proven technology, we recognize that we won't be able to do it all on our own," said Kern.

Brainstorm is hoping to attract both health-care-focused venture capitalists who understand the potential value of cell-based therapies and corporate partners with the complementary skills and regulatory expertise needed to develop and commercialize cell-based therapies. Brainstorm is confident that the market potential for a disease-modifying treatment for ALS will be attractive to potential partners.

"There are not many late-stage opportunities focusing on brain diseases, and that is what we have to offer. We are looking for partners that are willing to take a long-term position with at least a two-year horizon," Kern added. Indeed, in addition to its active clinical program in ALS, Brainstorm Cell Therapeutics is looking to expand NurOwn's application to other neurodegenerative indications.

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