BrainStorm Cell Therapeutics Announces Peer-reviewed Publication of Biomarker Data from NurOwn's® Phase 3 Clinical Trial in ALS

NurOwn treatment resulted in a positive impact on important CSF biomarkers relevant to ALS compared to placebo. Significant changes in multiple ALS disease pathways support NurOwn's mechanism of action and complement clinical effects observed in ALS.

NEW YORK, April 10, 2024 /PRNewswire/ -- BrainStorm Cell Therapeutics Inc. (NASDAQ: BCLI), a leading developer of cellular therapies for neurodegenerative diseases, today announced the peer-reviewed publication of Phase 3 biomarker data in *Muscle and Nerve*. The paper, entitled "Debamestrocel multimodal effects on biomarker pathways in amyotrophic lateral sclerosis are linked to clinical outcomes", can be found online through the Muscle and Nerve website. This study suggests that debamestrocel or NurOwn®, an investigational cell therapy, may impact key biomarkers in amyotrophic lateral sclerosis (ALS) that are predictive of disease progression.

The study analyzed forty-five biomarkers and identified three that are predictive of clinical outcomes in debamestrocel-treated participants, including neurofilaments light (NfL), LAP/TGFb1 and Galcetin-1. Treatment with debamestrocel led to significant changes in 64% of the forty-five analyzed biomarkers, spanning various pathways involved in ALS pathology. These changes included increases in anti-inflammatory and neuroprotective markers suggesting a potential ability to reduce inflammation and protect neurons, and decreases in inflammatory and neurodegenerative markers indicating a possible reduction in disease activity and nerve cell damage.

"The publication of these findings is important, because it demonstrates a potential biologic mechanism by which modified mesenchymal stem cells (debamestrocel) may benefit patients with ALS," said Dr. Anthony J. Windebank, MD, Professor of Neurology and Judith and Jean Pape Adams Professor of Neuroscience, Mayo Clinic College of Medicine and Science. "There was a strong signal in the phase III trial suggesting a benefit of these cells in a sub-group of patients with less advanced disease. The fact that BrainStorm has reached agreement with FDA through a special protocol assessment (SPA) is also very encouraging that the agency is firmly committed to working with the company to rigorously evaluate the clinical benefit of debamestrocel."

Stacy Lindborg, PhD, Co-Chief Executive Officer ofBrainStorm Cell Therapeutics, added: "Biomarkers are becoming an increasingly important part of drug development in ALS. Having these data peer reviewed and published in a prestigious journal is an important milestone in the NurOwn® development program. We look forward to confirming these findings in our upcoming Phase 3b trial, which is in planning for the most expeditious path forward to bring NurOwn to people living with ALS."

About the Biomarker Study

The study was conducted by researchers atMassachusetts General Hospital, University of Massachusetts, Mayo Clinic, University of California Irvine, California Pacific Medical Center, and Cedars-Sinai Medical Center, evaluating the effect of NurOwn on cerebrospinal fluid (CSF) biomarkers, offering valuable insights into the potential mechanisms of action and suggests a possible, related clinical impact. Merit Cudkowicz, MD, Chair of Neurology Massachusetts General Hospital, Julieanne Doran, Professor of Neurology Harvard Medical School and Robert Brown, MD, Donna and Robert J. Manning Chair in Neuroscience Director, Program in Neurotherapeutics UMass Chan Medical School, share the senior author position on the paper.

Data from the paper are from a randomized, double-blind, placebo-controlled Phase 3 trial, evaluating the safety and efficacy of repeat intrathecal doses of NurOwn® in study participants.

"These findings are encouraging and provide preliminary evidence that debamestrocel may be effective in treating ALS. The impact on biomarkers suggests debamestrocel targets inflammation and neurodegeneration," said Chaim Lebovits, President and CEO of BrainStorm Cell Therapeutics. "We are grateful to the trial participants, lead authors Dr. Merit Cudkowicz and Dr. Robert Brown, in addition to all of the Phase 3 Principal Investigators. This manuscript, nor the insights into known and emerging ALS biomarkers wouldn't exist without them."

About NurOwn®

The NurOwn® technology platform (autologous MSC-NTF cells) represents a promising investigational therapeutic approach to targeting disease pathways important in neurodegenerative disorders. MSC-NTF cells are harvested from each person with ALS and are manufactured using an innovative and proprietary process, to secrete neurotrophic factors to target specific neurodegenerative diseases. The lead program for NurOwn is for the treatment of ALS. BrainStorm's long-term commitment to ALS is demonstrated in preclinical research and a series of clinical studies, all of which have been published in peer-reviewed

journals.

The NurOwn clinical program has generated valuable insights into the pathology of ALS, as well as disease progression and treatment. Since the initial Phase 3 readout, BrainStorm has shared the full dataset through rigorous peer-reviewed analysis, including: quantification of Floor Effect, which had been noted, but never before explored in depth; evaluation of multiple pre-specified biomarkers, collected at seven different points across 20 weeks during the trial, allowing a longitudinal view; and analysis of genetic data, which represents one of the first ALS trials to prospectively invoke pharmacogenomic analysis of clinical outcome, offering great promise for the development of future treatments for ALS.

About BrainStorm Cell Therapeutics Inc.

BrainStorm Cell Therapeutics Inc. is a leading developer of innovative autologous adult stem cell therapeutics for debilitating neurodegenerative diseases. BrainStorm holds the rights to clinical development and commercialization of the NurOwn® technology platform used to produce autologous MSC-NTF cells through an exclusive, worldwide licensing agreement. Autologous MSC-NTF cells have received Orphan Drug designation status from the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for the treatment of amyotrophic lateral sclerosis (ALS). BrainStorm has completed a Phase 3 trial in ALS (NCT03280056); this trial investigated the safety and efficacy of repeat administration of autologous MSC-NTF cells and was supported by a grant from the California Institute for Regenerative Medicine (CIRM CLIN2-0989), and another grant from the ALS Association and I AM ALS. BrainStorm completed under an investigational new drug application a Phase 2 open-label multicenter trial (NCT03799718) of autologous MSC-NTF cells in progressive MS and was supported by a grant from the National MS Society (NMSS).

Notice Regarding Forward-Looking Statements

This press release contains "forward-looking statements" that are subject to substantial risks and uncertainties, including statements regarding meetings with the U.S. Food and Drug Administration (FDA), Special Protocol Assessment (SPA), ADCOM meeting related to NurOwn, the timing of a PDUFA action date for the BLA for NurOwn, the clinical development of NurOwn as a therapy for the treatment of ALS, the future availability of NurOwn to patients, and the future success of BrainStorm. All statements, other than statements of historical fact, contained in this press release are forward-looking statements. Forward-looking statements contained in this press release may be identified by the use of words such as "anticipate," "believe," "contemplate," "could," "estimate," "expect," "intend," "seek," "may," "might," "plan," "potential," "predict," "project," "target," "aim," "should," "will" "would," or the negative of these words or other similar expressions, although not all forward-looking statements contain these words. Forward-looking statements are based on BrainStorm's current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. These potential risks and uncertainties include, without limitation, management's ability to successfully achieve its goals, BrainStorm's ability to raise additional capital, BrainStorm's ability to continue as a going concern, prospects for future regulatory approval of NurOwn, whether BrainStorm's future interactions with the FDA will have productive outcomes, and other factors detailed in BrainStorm's annual report on Form 10-K and quarterly reports on Form 10-Q available at http://www.sec.gov. These factors should be considered carefully, and readers should not place undue reliance on BrainStorm's forward-looking statements. The forward-looking statements contained in this press release are based on the beliefs, expectations, and opinions of management as of the date of this press release. We do not assume any obligation to update forward-looking statements to reflect actual results or assumptions if circumstances or management's beliefs, expectations or opinions should change, unless otherwise required by law. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance, or achievements.

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Manuscript Summary

Treatment with debamestrocel led to significant changes in 64% of the forty-five analyzed biomarkers, spanning various pathways involved in ALS pathology.
These changes included increases in anti-inflammatory and neuroprotective markerssuggesting a potential ability to reduce inflammation and protect neurons, and decreases in inflammatory and neurodegenerative markers indicating a possible reduction in disease activity and nerve cell damage. For example, a significant reduction from baseline of 11% in neurofilaments light (NfL), a marker of nerve cell damage, was observed with NurOwn compared to placebo ($p<0.05$).

Predictive Biomarkers: Certain biomarkers, such as baseline NfL, LAP/TGFb1 and Galectin- 1, were found to be predictive of clinical outcomes in debamestrocel-treated participants.

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https://ir.brainstorm-cell.com/2024-04-10-BrainStorm-Cell-Therapeutics-Announces-Peer-reviewed-Publication-of-Biomarker-Data-from-NurOwns-R-Phase-3-Clinical-Trial-in-ALS