BrainStorm Cell Therapeutics Announces Peer Reviewed Publication of Results from the NurOwn® Phase 2 Progressive MS Trial in Multiple Sclerosis Journal

Data demonstrate NurOwn's safety and provide preliminary evidence of efficacy in patients with progressive multiple sclerosis

Biomarker analyses show consistent treatment effects in neuroinflammation and neuroprotection pathways

NEW YORK, Sept. 15, 2022 /PRNewswire/ -- BrainStorm Cell Therapeutics Inc. (NASDAQ: BCLI), a leading developer of cellular therapies for neurodegenerative diseases, today announced the peer reviewed publication of data from the Phase 2 trial of NurOwn in progressive multiple sclerosis (MS) in *Multiple Sclerosis Journal*. The publication, entitled "Evaluation of neurotrophic factor secreting mesenchymal stem cells in progressive multiple sclerosis", can be found here.

Results from the Phase 2, single-arm, open-label study demonstrated NurOwn's safety and provided preliminary evidence of its efficacy in people with progressive MS. Additionally, biomarker analyses confirmed NurOwn's proposed mechanism of action by showing consistent treatment effects in neuroinflammation and neuroprotection pathways.

Twenty participants were enrolled into the Phase 2 trial, with seventeen receiving all three scheduled NurOwn treatments. The mean age of study participants was 47 years with a mean expanded disability status scale (EDSS) score of 5.4 at screening. Results from the trial were compared to 48 matched control patients who were selected from the from the Comprehensive Longitudinal Investigation of Multiple Sclerosis (CLIMB) registry (Brigham and Women's Hospital and the Ann Romney Center for Neurologic Diseases) at the beginning of the trial.

Treatment with NurOwn resulted in large, clinically meaningful improvements in some patients, as defined by response criteria, across all endpoints measured. These endpoints included timed 25-foot walk speed (T25FW), 9-hole peg test (9HPT), multiple sclerosis walking scale (MSWS), symbol digit modality test (SDMT), and low contrast letter acuity (LCLA). These observed improvements diverged from what was seen in matched patients with progressive MS from the CLIMB registry. Key data from the trial, as well as relevant comparisons to the matched CLIMB registry patients, are shown below.

- 19% of treated trial participants were responders (as defined by prespecified ≥25% improvement in T25FW or 9HPT at 28 weeks compared to baseline), compared to 4% of the matched CLIMB registry patients.
- 38% of treated trial participants showed a ≥10-point improvement from baseline in the 12-item MSWS (data for this endpoint were not collected by the CLIMB registry).
- 27% of treated trial participants showed a ≥8-letter improvement in LCLA binocular at a 2.5% contrast threshold, compared to 6% of the matched CLIMB registry patients.
- 67% of treated trial participants showed a ≥3-point improvement in the SDMT, compared to 18% of the matched CLIMB registry patients.
- 47% of treated trial participants showed a ≥8-point improvement in LCLA binocular at a 1.25% contrast threshold (data for this endpoint were not collected by the CLIMB registry).

Across all participants, improvements in function as measured by LCLA, SDMT and MS Functional Composite (MSFC) were observed. Mean ***improvements*** from baseline of 3.3 points in the LCLA binocular (2.5% contrast), 3.8 points on the SDMT, and 0.18 points in MSFC were observed in treated trial participants. The corresponding changes in matched CLIMB registry patients estimated at 28 weeks showed ***declines*** in function on the LCLA and MSFC. The average change in function decline as measured by T25FW, 9HPT, and EDSS across all treated trial participants demonstrated stabilization of functional decline, with similar or slightly worse findings observed in the matched CLIMB registry patients for the same endpoints.

There were no adverse events related to worsening of MS disease and no clinically significant changes in safety lab results/vital signs, confirming NurOwn's favorable safety profile. Two patients developed symptoms of low back and leg pain, consistent with arachnoiditis, occurring in one of three treatments in both participants.

Treatment also consistently resulted in increases in cerebrospinal fluid neuroprotective factors (VEGF–A, HGF, NCAM-1, Follistatin, LIF and Fetuin–A) and reductions in inflammatory biomarkers (MCP-1, sCD27, SDF-1, and Osteopontin), confirming NurOwn's proposed mechanism of action in progressive MS.

"We were pleased that the study's initial results showed efficacy in patients with progressive MS," said Jeffrey Cohen, M.D., Hazel Prior Hostetler Endowed Chair Professor, Cleveland Clinic Lerner College of Medicine, Director, Experimental Therapeutics, Mellen Center for MS Treatment and Research, and the paper's lead author. "There are both promising biological and preliminary clinical signals of a treatment effect that will require confirmation in a randomized trial."

"There is a high unmet need for better treatments for progressive forms of MS and we congratulate the Brainstorm Cell Therapeutics team for the successful completion and publication of this important study. We look forward to future studies that will help to fully understand the potential of NurOwn and other cell-based therapies for this hard-to-treat form of disease" said Bruce Bebo, EVP Research National MS Society.

Chaim Lebovits, Chief Executive Officer, BrainStorm Cell Therapeutics stated, "Having these data peer reviewed and published in the prestigious *Multiple Sclerosis Journal* is an important step in the evaluation of NurOwn in progressive MS. We appreciate the expertise and commitment of the study investigators and contributions of study participants to advance our understanding of NurOwn's cellular technology platform. Thanks to their efforts and those of the BrainStorm team, we believe we are closer to providing a meaningful treatment option for those with progressive MS".

Ralph Kern, M.D., MHSc, President and Chief Medical Officer of BrainStorm Cell Therapeutics and co-author of the paper commented, "This publication provides preliminary evidence of NurOwn's potential to modify functional outcomes in progressive MS, which we believe warrants further study. In addition, consistent changes in cerebrospinal fluid neuroinflammation and neuroprotection biomarkers reveal how NurOwn may impact disease mechanisms in progressive MS and are complementary to biomarker results observed in our Phase 3 ALS trial. These observations provide further support for NurOwn as a platform technology with potential broad applications and will bolster BrainStorm's efforts to bring much needed solutions to patients with progressive MS, ALS, and other neurodegenerative diseases."

Study Design

The Phase 2 study (BCT-101) was designed to evaluate the safety, efficacy, and biomarker effects of three intrathecal administrations of NurOwn (MSC-NTF cells), given at two-month intervals, to adults with progressive MS. The trial was conducted at four MS centers of excellence: Cleveland Clinic Mellen Center for MS, Icahn School of Medicine at Mount Sinai, Keck School of Medicine of the University of Southern California, and Stanford University School of Medicine. Twenty participants ages 18-65 with progressive MS were enrolled and 17 received all three treatments and were followed for up to 28 weeks. Participants had baseline EDSS scores of between 3.0 and 6.5, were able to walk 25 feet in 60 seconds or less and had not experienced an MS relapse in the 6 months prior to study enrollment.

The primary efficacy outcome was pre-specified improvement (≥25%) in T25FW or 9-HPT. Additional efficacy endpoints included pre-specified improvements in EDSS, SDMT, LCLA, and MSWS-12. The efficacy outcomes were compared to a pre-specified matched group of progressive MS patients from CLIMB registry (n=48) (Tanuja Chitnis, M.D. Brigham and Women's Hospital and the Ann Romney Center for Neurologic Diseases). The study was sponsored by Brainstorm Cell Therapeutics with additional financial support for biomarker analyses received from the National Multiple Sclerosis Society, Fast-Forward Commercial Research Funding Program. For more information on the trial, visit https://clinicaltrials.gov/ct2/show/NCT03799718.

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 produced from autologous, bone marrow-derived mesenchymal stem cells (MSCs) that have been expanded and differentiated ex vivo. MSCs are converted into MSC-NTF cells by growing them under patented conditions that induce the cells to secrete high levels of neurotrophic factors (NTFs). Autologous MSC-NTF cells are designed to effectively deliver multiple NTFs and immunomodulatory cytokines directly to the site of damage to elicit a desired biological effect and ultimately slow or stabilize disease progression.

About BrainStorm Cell Therapeutics Inc.

BrainStorm Cell Therapeutics Inc. is a leading developer of innovative autologous adult stem cell therapeutics for debilitating neurodegenerative diseases. The Company 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 pivotal 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). 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).

Safe-Harbor Statement

Statements in this announcement other than historical data and information, including statements regarding future clinical trial enrollment and data, constitute "forward-looking statements" and involve risks and uncertainties that could cause BrainStorm Cell Therapeutics Inc.'s actual results to differ materially from those stated or implied by such forward-looking statements. Terms and phrases such as "may," "should," "would," "could," "will," "expect," "likely," "believe," "plan," "estimate," "predict," "potential," and similar terms and phrases are intended to identify these forward-looking statements. The potential risks and uncertainties include, without limitation, BrainStorm's need to raise additional capital, BrainStorm's ability to continue as a going concern, prospects for future regulatory approval of BrainStorm's NurOwn® treatment candidate, the success of BrainStorm's product development programs and research, regulatory and personnel issues, development of a global market for our products and services, the ability to secure and maintain research institutions to conduct our clinical trials, the ability to generate significant revenue, the ability of BrainStorm's NurOwn® treatment candidate to achieve broad acceptance as a treatment option for ALS or other neurodegenerative diseases, BrainStorm's ability to manufacture and commercialize the NurOwn® treatment candidate, obtaining patents that provide meaningful protection, competition and market developments, BrainStorm's ability to protect our intellectual property from infringement by third parties, heath reform legislation, demand for our services, currency exchange rates and product liability claims and litigation; the impacts of the COVID-19 pandemic on our clinical trials, supply chain, and operations; 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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