BrainStorm Cell Therapeutics Provides Update on FDA Advisory Committee Meeting to Review NurOwn for the Treatment of ALS

NEW YORK, Sept. 27, 2023 /PRNewswire/ -- BrainStorm Cell Therapeutics Inc. (NASDAQ: BCLI), a leading developer of adult stem cell therapeutics for neurodegenerative diseases, today announced the outcome of the U.S. Food and Drug Administration's Cellular, Tissue and Gene Therapies Advisory Committee meeting to review the Biologics License Application (BLA) for NurOwn®, an investigational mesenchymal stem cell therapy for the treatment of amyotrophic lateral sclerosis (ALS).

Today the Committee voted that NurOwn did not demonstrate substantial evidence of effectiveness for treatment of mild to moderate ALS.

"The Committee's vote was a sad outcome for the ALS community, who have too few options to help manage this merciless and deadly disease," said Stacy Lindborg, PhD, co-CEO of BrainStorm. "We firmly believe that the totality of data presented for NurOwn today provide a compelling case for approval, with clinical evidence in those with less advanced disease supported by strong and consistent biomarker data that are predictive of clinical response. We truly did our best to make the NurOwn data clear to the FDA Advisory Committee. Unfortunately, had more time and opportunity been allowed, many remaining questions posed by Advisory Committee members could have been sufficiently addressed."

Chaim Lebovits, President and Chief Executive Officer of BrainStorm, added: "The discussion in today's Advisory Committee meeting, and the heartrending testimony of those living with ALS and their loved ones, underscores not only the need for regulatory flexibility but also for continuing research in the field. The people of BrainStorm will do everything in our power to fulfill the obligation we deeply feel we owe to the ALS community, and in the coming weeks we will explore all options available to us."

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, which is under FDA review. 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 Phase 3 pivotal trial of NurOwn did not reach statistical significance on the primary or secondary endpoints, likely due to a "floor effect," which confounds measurement of disease progression in patients with more advanced disease. A thorough analysis of NurOwn Phase 3 data shows evidence of clinically meaningful effectiveness in ALS participants who have not progressed to advanced levels of disease progression. In a pre-specified group of participants with an ALSFRS-R score ³35, there was a larger treatment effect across all endpoints with NurOwn compared to placebo, which aligned with historical trials and the study power assumptions and resulted in a statistically significant difference on a key endpoint (change from baseline in ALSFRS-R). Additionally, a post-hoc sensitivity analysis of patients across threshold of >26 through ≥35 on the ALSFRS-R highlighted that NurOwn-treated patients retain, on average, two points of function more compared to placebo–clinically meaningful preservation and important for quality of life for a person living with ALS and their loved ones.

NurOwn's clinical program also included most robust cerebrospinal fluid (CSF) biomarker study ever done in ALS, strong and consistent biomarker data, which are predictive of clinical response in the trial, span pathways that are important to ALS (neuroinflammation, neurodegeneration, neuroprotection), and align with NurOwn's mechanism of action. Biomarker data in all trial participants showed consistent biological patterns of NurOwn reducing markers of inflammation and neurodegeneration and increasing neuroprotective markers relative to placebo. Biomarker patterns were consistent across all NurOwn-participants, including in those with Advanced ALS disease where clinical scales, such as the ALS Functional Rating Scale, have demonstrated measurement challenges. Three CSF biomarkers were predictive of clinical outcomes in NurOwn-treated participants–NfL, galectin-1, latency associated peptide of TGF-beta1 (LAP or TGF-b).

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.

BrainStorm previously announced the FDA's intention to hold an ADCOM meeting to review NurOwn for the treatment of ALS. BrainStorm filed a BLA for NurOwn on September 9, 2022, and received a Refusal to File (RTF) letter from FDA on November 8, 2022. Following a Type A meeting and subsequent discussions with the FDA BrainStorm requested that CBER utilize the FDA's "File Over Protest" procedure, which offers the shortest amount of time to complete the regulatory process. The BLA was filed over protest, allowing completion of the regulatory process in the shortest time possible, and active review resumed on February 7, 2023.

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 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).

Notice Regarding Forward-Looking Statements
This press release contains "forward-looking statements" that are subject to substantial risks and uncertainties, including statements regarding the upcoming 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.

CONTACTS

Investor Relations:
John Mullaly
LifeSci Advisors, LLC
Phone: +1 617-429-3548
jmullaly@lifesciadvisors.com

Media:
Lisa Guiterman
Phone: +1 202-330-3431
lisa.guiterman@gmail.com

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