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

BrainStorm Cell Therapeutics, a leading developer of adult stem cell therapeutics for neurodegenerative diseases, 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 ^{3}35, 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.

Source: **BrainStorm Cell Therapeutics**