INTERNATIONAL ALLIANCE OF ALS/MND ASSOCIATIONS

# BrainStorm Cell Therapeutics – NurOwn
# November 2020

## Background

The BrainStorm treatment regimen consists of a person's own stem cells (called autologous) being removed from bone marrow and then grown outside of the body in the presence of a chemical owned by the company called NurOwn, which aims to increase the stem cells' ability to make and secrete protective substances called growth factors. The stem cells are then injected into the fluid that bathes the brain and spinal cord (called cerebrospinal fluid or CSF) with a needle (called intrathecal or IT injection) at multiple intervals. The hope is that these treated stem cells will be able to slow the progression of motor neuron degeneration and hence, the progression of ALS symptoms.

In 2016, the first peer reviewed publication appeared, demonstrating preliminary, positive safety data in combination with BrainStorm completing a phase 2 clinical trial at three renowned US clinical sites.

The phase 2 trial data involved 48 ALS patients (36 treated and 12 placebo) and was published in December 2019 in the journal Neurology, titled "A single-dose transplantation of MSC-NTF cells is safe and demonstrated early promising signs of efficacy."

A phase 3 clinical trial testing multiple doses of NurOwn in 200 participants at six sites in the United States was started in 2017. The trial was double-blinded, meaning neither researchers nor participants knew if they were on active treatment or placebo. The primary measurements were to examine safety of repeated intrathecal injections of NurOwn and the ability of NurOwn to slow progression of ALS/MND using a scale called the ALSFRS-R. To determine if NurOwn-treated stem cells were providing the intended biological effect, the CSF was measured for biomarkers including neurotrophic factors (aiming for increased levels) and neurodegenerative/neuroinflammatory factors (aiming for reduced levels).

On November 17, 2020, a press release was issued describing the initial data from the phase 3 clinical trial. The trial did not meet statistical significance in any of the reported data; notably in the primary measurement of disease progression using the ALSFRS-R. A pre-specified subgroup of those with early disease was highlighted in the press release as showing clinically meaningful slowing of ALS progression, however these results were also not statistically significant. Further, it was reported that that NurOwn treatment resulted in an increase of neurotrophic biomarkers and reduction in neurodegenerative and neuroinflammatory biomarkers when compared to the placebo group, which is aligned with what the trial hoped to achieve. Follow up analysis will investigate whether these biomarker results, in addition to further analysis of the pre-specified subgroup of those with early disease, can reveal any additional information.

## Recommendation

**Based on the data released by BrainStorm, the SAC recommends that there is no conclusive evidence at this time to suggest NurOwn provides benefit to people with ALS. When additional trial data becomes available and further analysis is performed, the SAC will continue to provide updates as to what the scientific and medical community learns that can support development of effective treatments for ALS/MND.**