



# Brainstorm Cell Therapeutics

Nasdaq: BCLI

# Safe Harbor Statement

Statements in this announcement other than historical data and information 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, risks associated with Brainstorm's limited operating history, history of losses; minimal working capital, dependence on its license to Ramot's technology; ability to adequately protect the technology; dependence on key executives and on its scientific consultants; ability to obtain required regulatory approvals; 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.

# Brainstorm Cell Therapeutics: A Clinical Stage Biotechnology Company

## Our Mission

Brainstorm pioneers autologous cell therapies for neurological disorders, focusing on ALS and MS

## Flagship Product

NurOwn® - a cutting-edge autologous cell therapy platform

## Strong Pipeline

NurOwn® innovative therapy serves as a platform for treating neurodegenerative diseases

## Experienced Leadership

Decades of expertise in cell therapy and biopharma commercialization

# Pioneering Breakthrough: First-In-Class Therapy to Transform ALS Treatment



Promising data from our previous trials continues to support the therapeutic potential of NurOwn®, demonstrating meaningful improvements in key areas.



Robust biomarker data strongly supports NurOwn®'s mechanism of action.



Aligned with FDA on new clinical trial design through the Special Protocol Assessment (SPA), ensuring regulatory confidence and trial integrity.



Phase 3b plans: Comprehensive plan for Phase 3b trial, optimizing patient selection and dosing strategies.

# Innovating Cell Therapies for Neurodegenerative Diseases

| Indication                                | Preclinical | Phase 1 | Phase 2 | Phase 3  |
|-------------------------------------------|-------------|---------|---------|----------|
| <b>NeurOwn® MSC-NTF Cellular Platform</b> |             |         |         |          |
| <b>ALS*</b><br>NurOwn®                    |             |         |         | Phase 3B |
|                                           |             |         |         | Phase 3  |
| Progressive MS                            |             |         |         |          |
| Parkinson's Disease                       |             |         |         |          |
| <b>MSC-NTF Exosomes Platform</b>          |             |         |         |          |
| ARDS                                      |             |         |         |          |

# Experienced Team in Cell Therapy Development

## Proven Expertise

Decades of experience in developing innovative cell therapies across multiple therapeutic areas.

## Successful Track Record

Led the development of NurOwn®, producing over 470 GMP clinical batches for 190+ ALS trial. Extensive experience across all phases of clinical development, from preclinical to commercialization.

## Manufacturing Excellence

Expertise in scaling up complex cell therapy manufacturing processes to meet clinical and regulatory standards.

## Regulatory and Quality Leadership

Strong regulatory affairs team with a proven history of engaging with global health authorities, including the FDA and EMA.

## Innovation-Driven Approach

Focus on cutting-edge science and advancing new cell therapy technologies to improve patient outcomes.

# Proven Leadership with Deep Expertise in Biotechnology

Chaim Lebovits  
President and CEO

Haro Hartounian, PhD  
COO

Bob Dagher, MD  
CMO

Uri Yablonka  
CBO

Mary Kay Turner  
SVP, Advocacy and Government  
Affairs

Netta Blondheim-Sharga,  
PhD  
SVP, Research and Development

Yossef Levy, PhD  
VP. Cell Production

Leticia Tarilonte  
VP, Global Clinical Operations



# Looking Ahead: Key Upcoming Milestones

## Clinical Trial Agreements (CTA) Signed

Finalize agreements with leading clinical sites, setting the stage for a successful Phase 3b trial.

## 15 Clinical Sites Announced

Officially unveil our partnership with 15 premier clinical sites, ensuring broad geographic coverage and access to top-tier patient care.

## GMP Manufacturing in Full Swing

GMP manufacturing of clinical-grade products is ready to support upcoming trials, ensuring timely execution and quality.

## Engaging Top-Tier CRO

Signed an agreement with a leading CRO to manage patient recruitment, trial execution, and regulatory compliance, maximizing trial success.

## First Patient Enrollment by December

On track to enroll the first patient in December 2024, marking a significant milestone in advancing NurOwn®.



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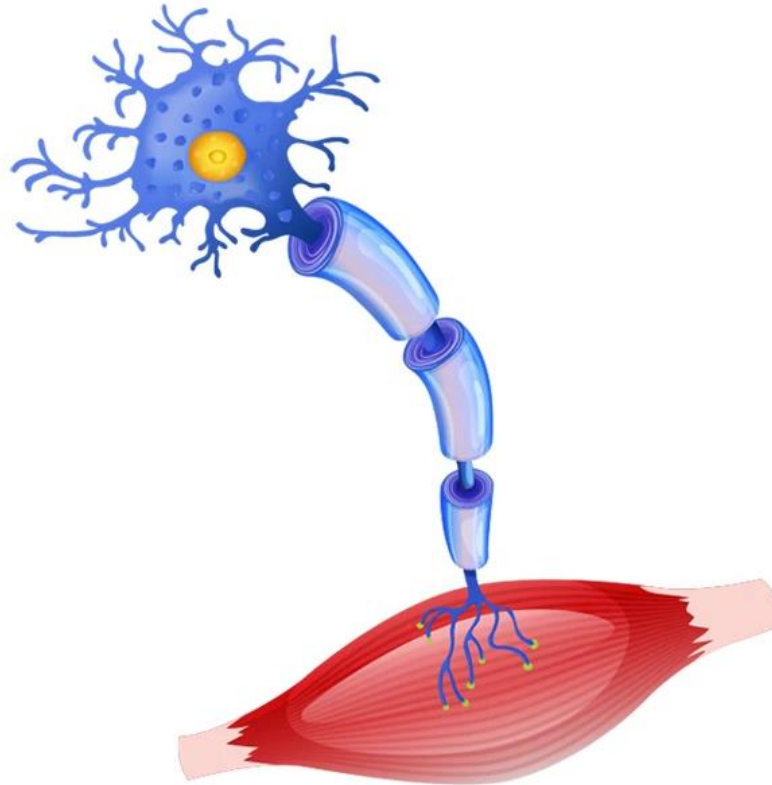
# Our Technology

Cutting-Edge Innovation: Advancing the Future of Cell Therapy

# Amyotrophic Lateral Sclerosis- ALS

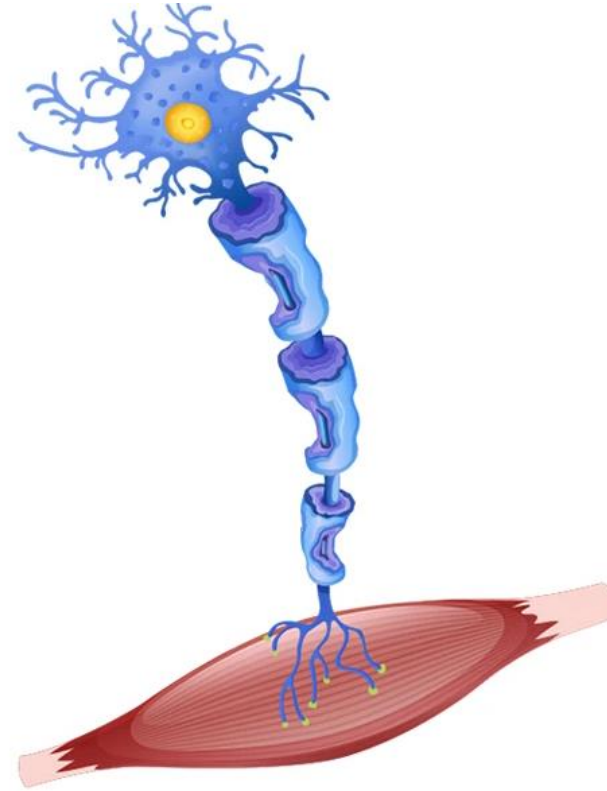
Devastating disease with hope on the horizon through Brainstorm's groundbreaking treatment

Normal motor neuron



muscle contracts

Motor neuron damaged in ALS



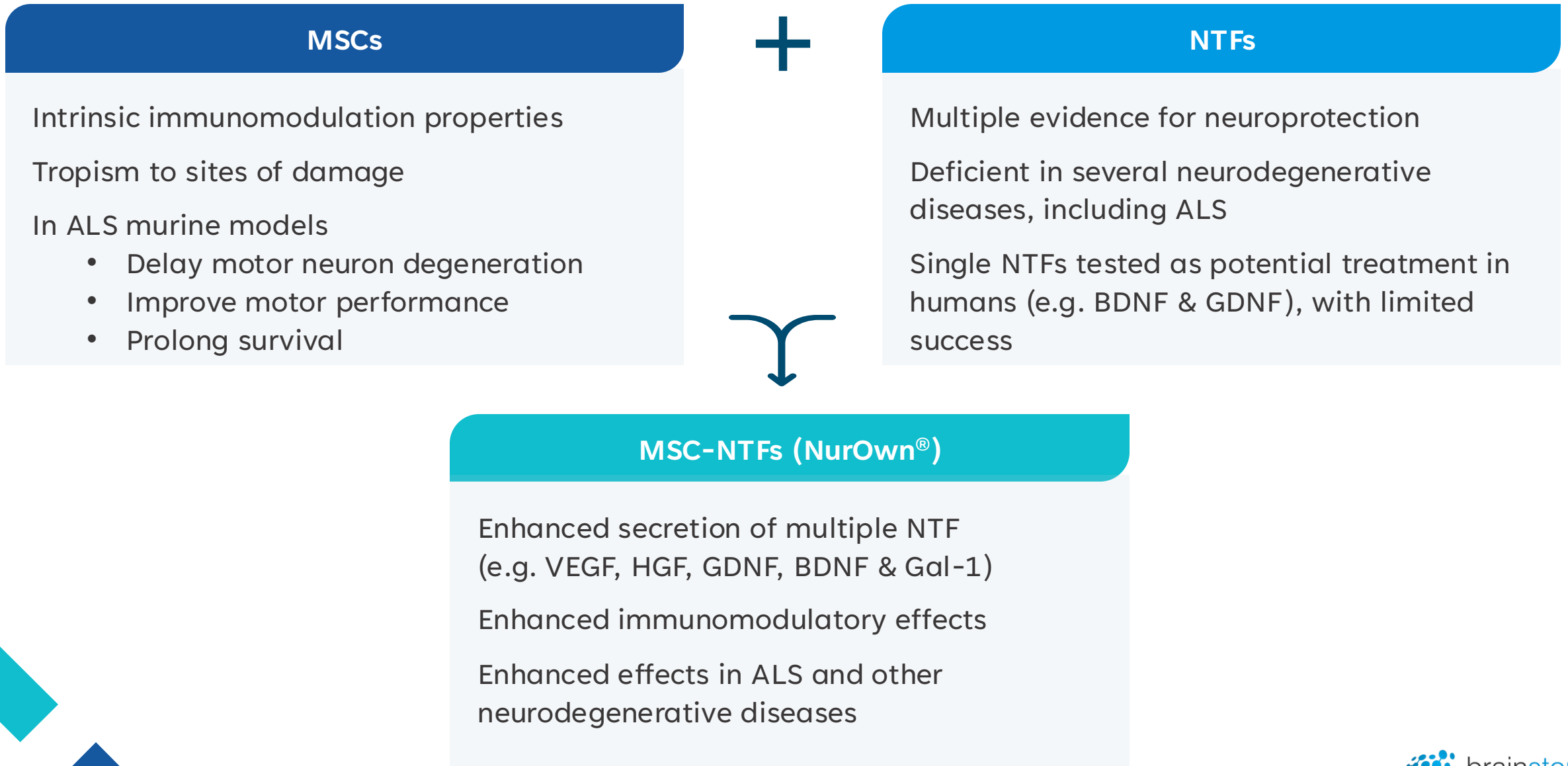
muscle unable to contract

# Developing NurOwn® as a Groundbreaking Platform to Treat ALS

ALS is a progressive neurodegenerative disease that impairs walking, talking, eating, and breathing, and is currently 100% fatal

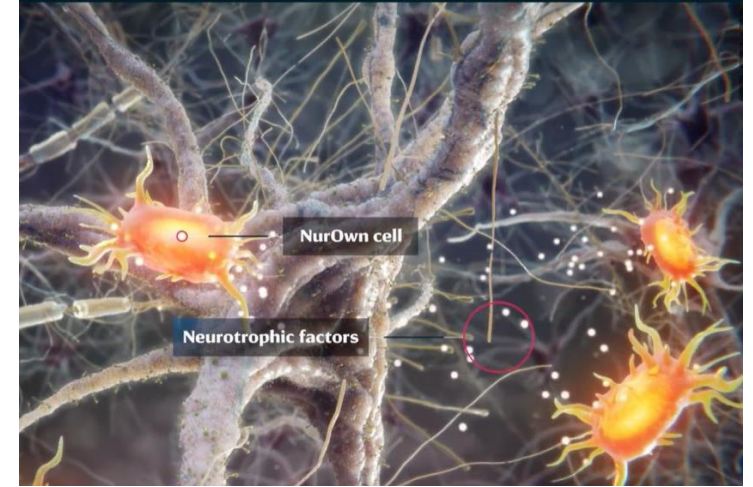
- Survival is 2 to 5 years from onset, with a lifetime risk of 1 in 300 people.
- ALS affects 1.6 per 100,000 people annually worldwide.
- 90% to 95% of ALS cases are sporadic, with no known family history.
- Projected market to grow significantly, driven by factors such as advancements in research, rising prevalence due to aging populations, and emerging therapeutic modalities like cell and gene therapy.
- Market valued at approximately \$669 million in 2023, is expected to surpass \$1.2 billion by 2034, growing at a compound annual growth rate (CAGR) of around 6.4% (Datam Intelligence (IMARC)).

# NurOwn®: Harnessing MSC Characteristics and NTF Production



# Our Technology: Transforming ALS Treatment with Advanced Cell Therapy

- NurOwn®: Uses the patient's own cells, reducing immune rejection risks, contributes to the high tolerance and good safety profile, and enhancing natural neurorepair.
- Introduced to the spinal cord CSF, MSC-NTF cells secrete bioactive molecules like NTFs, microRNA, and cytokines, activating neuroprotective and immunomodulatory pathways after intrathecal administration.
- FDA-Approved Therapies: Riluzole and Edaravone offer limited benefits, targeting glutamate toxicity and oxidative stress, respectively.
- NurOwn® Platform: Explored for use in other neurodegenerative diseases like MS and Parkinson's, showing broad potential.



# NurOwn®: Tipping the Balance to Favor Neuroprotection

Biomarkers in CSF from ALS patients demonstrate pathological hallmarks of active neurodegenerative and neuroinflammatory processes

CSF biomarker changes following NurOwn treatment suggest a favorable disruption of pathological processes:

- Reduction in CSF neuroinflammatory and neurodegenerative biomarkers
- Increase observed in CSF anti-inflammatory and neuroprotective biomarkers



# Robust biomarker data strongly supports NurOwn®'s mechanism of action

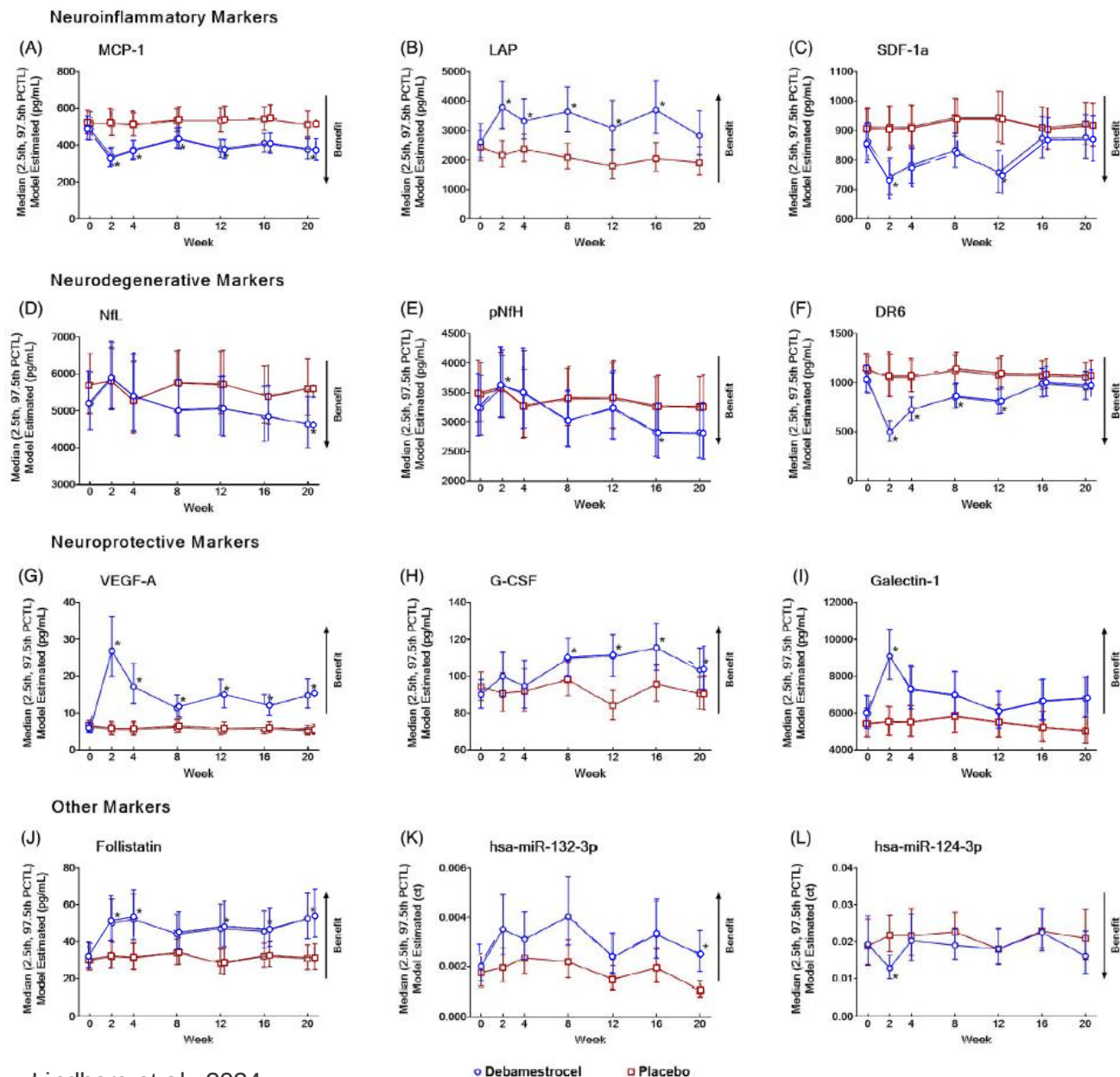
## Changes in biomarkers across main-pathways following NurOwn treatment

|                                                                                                                                                                                                                                            |                                                                                                                                                                                                                  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  <b>Inflammatory pathway</b><br>MCP-1<br>OPG<br><b>S100B</b><br><b>SDF-1α</b><br>CHI3L1/YKL-40<br>Chitotriosidase-1<br>GFAP<br>ICAM-1<br>IP-10*<br>TREM-2 | <b>Anti-Inflammatory pathway</b> <br>Fetuin-A<br>IL-37<br>LAP (TGF-β1)<br>MSR1<br>hsa-miR-146a-5p<br>hsa-miR-146b-5p          |
|  <b>Neurodegeneration pathway</b><br>pNfH<br>DR6<br>NfL<br>TWEAK<br>Tau<br>UCH-L1<br>hsa-miR-142-5p*<br>Caspase-3                                         | <b>Neuroprotection pathway</b> <br>VEGF-A<br>BDNF<br>G-CSF<br>GDF-15<br>Galectin-1<br>HGF<br>NMNAT1<br>Clusterin/ ApoJ<br>LIF |

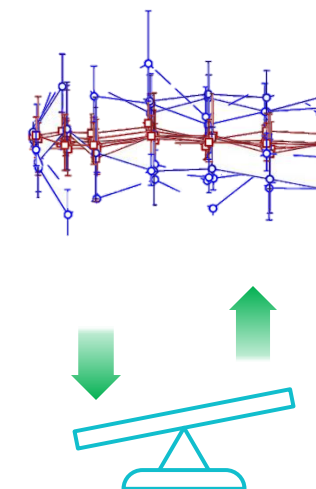
**Bold** = significant change from baseline detected during the study; p<0.05

\*= non-significant trend in other direction

# Biomarkers Change Following NurOwn Treatment



Illustrative approach to demonstrate the cumulative biomarker changes over time following NurOwn treatment, compared to placebo:



Change from placebo, neuroprotective markers

Change from placebo, neurodegenerative and neuroinflammatory markers

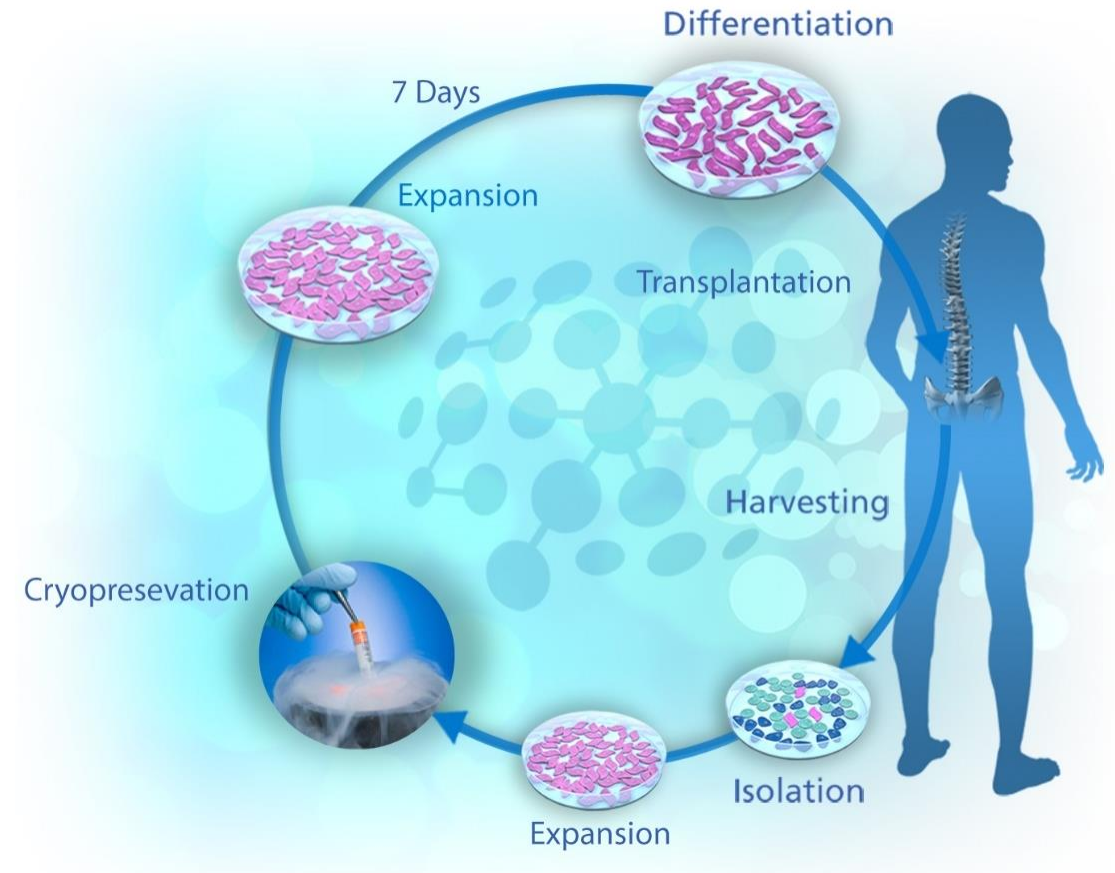
# The NurOwn® Process: Step by Step

The patient's bone marrow is harvested and Mesenchymal Stromal Cells (MSCs) are isolated from the total bone marrow population.

The MSCs are expanded ex-vivo and cryopreserved.

Cryopreserved MSCs are thawed, expanded and induced to differentiate into MSC-NTF cells (MSC cells that secrete Neurotrophic Factors).

The MSC-NTF cells are then injected back into the patient at or near the site of damage (the spinal cord).



# Manufacturing Expertise: Delivering Quality and Scale for NurOwn®

- 470+ GMP Batches Produced: Proven ability to deliver clinical-grade materials at scale, dosing over 190 patients in multiple trials.
- Successfully executed technology transfer across multiple clinical sites for the production of NurOwn®, ensuring consistency and quality in manufacturing.
- State-of-the-Art Facilities: Advanced manufacturing in the US and Israel with cutting-edge technology for precision and efficiency.
- cGMP Compliance: Fully compliant with cGMP, ensuring consistent product quality and safety through rigorous quality controls.
- Global Manufacturing Footprint: Supporting global clinical and commercial needs with best-in-class facilities.





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**NurOwn®**

**A Breakthrough in ALS Treatment  
with Promising Clinical Data**

# Our Milestones: NurOwn® Development Program in ALS



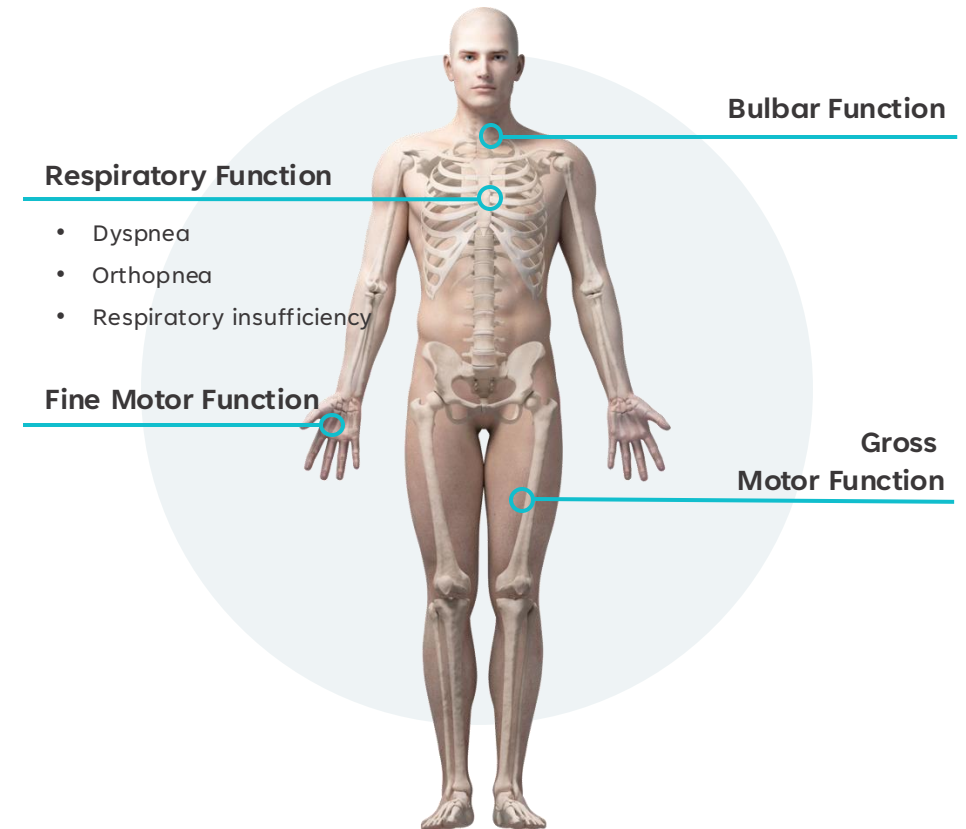
# Primary Endpoint ALS Functional Rating Scale- Revised (ALSFRS-R)

Change in ALSFRS-R slope (rate of disease progression) >20-25% is clinically meaningful<sup>2</sup>

Validated approvable questionnaire-based tool

Used as basis for approval of Radicava in 2017 with mean score change at 24 weeks as primary endpoint

Data from the PRO-ACT database shows the average rate of ALSFRS-R decline is 1.02 points/month



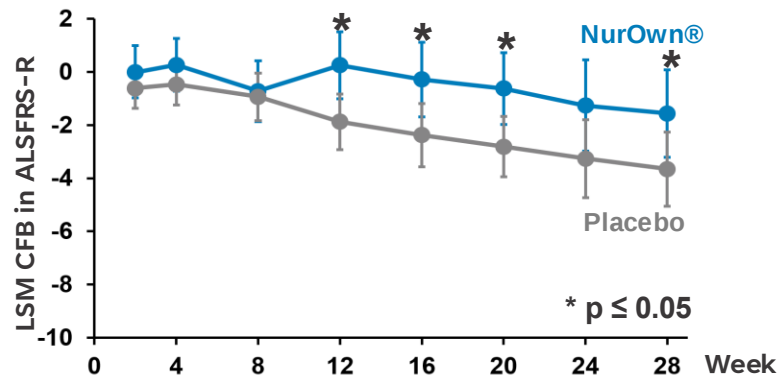
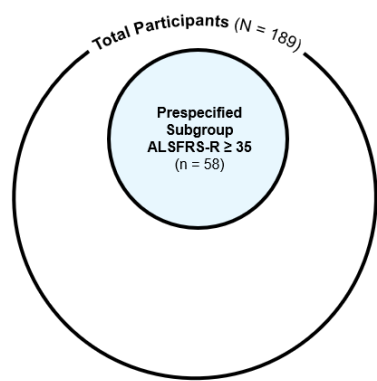
48-point scale with 4 domains

# NurOwn®: Phase 3 Clinical Trial in ALS (BCT-002-US)

## Subgroup analysis: positive results in early disease population

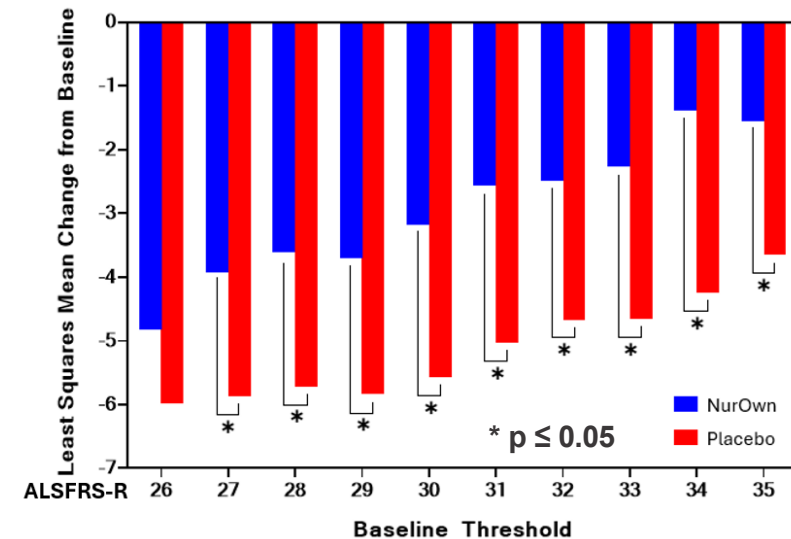
### Pre-specified subgroup with baseline ALSFRS-R $\geq 35$ (N=58)

- Change from baseline in ALSFRS-R to week-28: over 2 points benefit in function
- Consistent and nominally significant treatment effect over time, starting at week-12



### Sensitivity analyses across different cutoffs: Baseline ALSFRS-R Threshold from $\geq 26$ to $\geq 35$

- Nominally significant and robust treatment effect in early disease, based on baseline cutoffs of ALSFRS-R



# Clinical Data Summary



NurOwn® demonstrated a significant treatment effect in subgroup of patient with less advanced disease.



More advanced ALS patients did not show a treatment benefit, likely due to a floor effect.



Data reinforces the safety of repeat intrathecal administration.



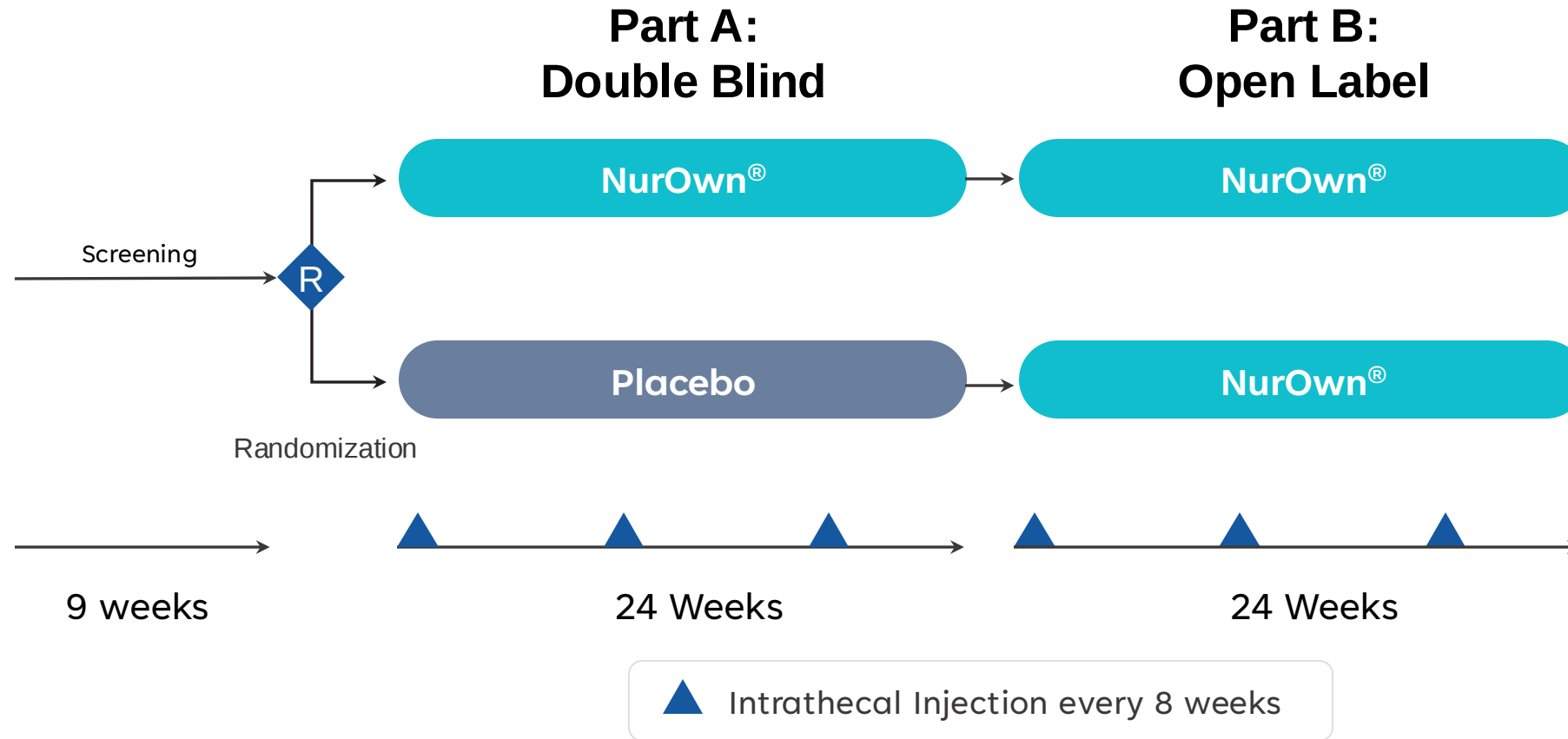
The next trial will focus on enrolling less advanced patients and measuring the delta between the baseline and week 24 to maximize the statistical power.



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# **NurOwn®: Optimized Phase 3b Trial in Early ALS Disease**

# NurOwn®: Phase 3 Clinical Trial in ALS (BCT-006-US)



Upon successful completion of our double-blind Phase 3b study, we will be positioned to submit our Biologics License Application (BLA) for regulatory approval, potentially accelerating our path to market.

# NurOwn<sup>®</sup> Phase 3b (BCT-006): Key Design Criteria

Significant changes made to upcoming Phase 3b clinical trial

## Phase 3 (BCT-002-US)

## Phase 3b (BCT-006)

### Patient population

≥25, followed by 20-week “run-in” period, allowing the possibility to enroll advanced-disease participants

Early-disease participants: ALSFRS-R criteria targeting less advanced levels of functional decline ( $\geq 2$  points on each item of the ALSFRS-R)

### Primary endpoint

Responder: proportion with  $\geq 1.25$  points/month improvement in the post-treatment slope vs. pre-treatment slope in ALSFRS-R at week 28

Use of “gold standard” in recent registrational trials (change from baseline to Week 24 in ALSFRS-R total score)

- p-value derived from inference model of Combined Assessment of Function and Survival (CAFS)

### Study duration

28-week double blind period

24-week double blind (Part-A) to be followed by 24-week open label extension (Part B)

- Extended to evaluate long-term effects on survival and neurodegenerative biomarkers

### Screening period

20 weeks screening, including 3-months “run-in” period to evaluate pre-treatment disease progression via ALSFRS-R

Elimination of “run-in” and shortening of screening period to minimize changes between screening and baseline

### Regulatory

Filing at week-28: Responder analysis in overall population, including advanced disease

Filing at week-24: Special Protocol Assessment (SPA) agreement with FDA

# NurOwn®: Positioned for Success

## Proven Expertise

Our team has extensive experience in conducting clinical trials, including Phase 1, 2, and 3 studies.

## Regulatory Alignment

Strong alignment from the FDA with Special Protocol Assessment (SPA) approval, ensuring trial design meets regulatory standards and de-risking regulatory aspects of the program.

## Data-Driven Approach

Lessons from prior Phase 3 trials have refined patient selection, endpoints, and trial protocols, increasing the probability of success.

## Robust Manufacturing Process

Securing partnerships with leading CDMOs for reliable production of clinical-grade materials, ensuring smooth execution.

## Operational Excellence

A dedicated team, resources, and a clear execution plan are in place to manage and monitor the trial effectively.

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# Thank you

Chaim Lebovits  
President & CEO

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