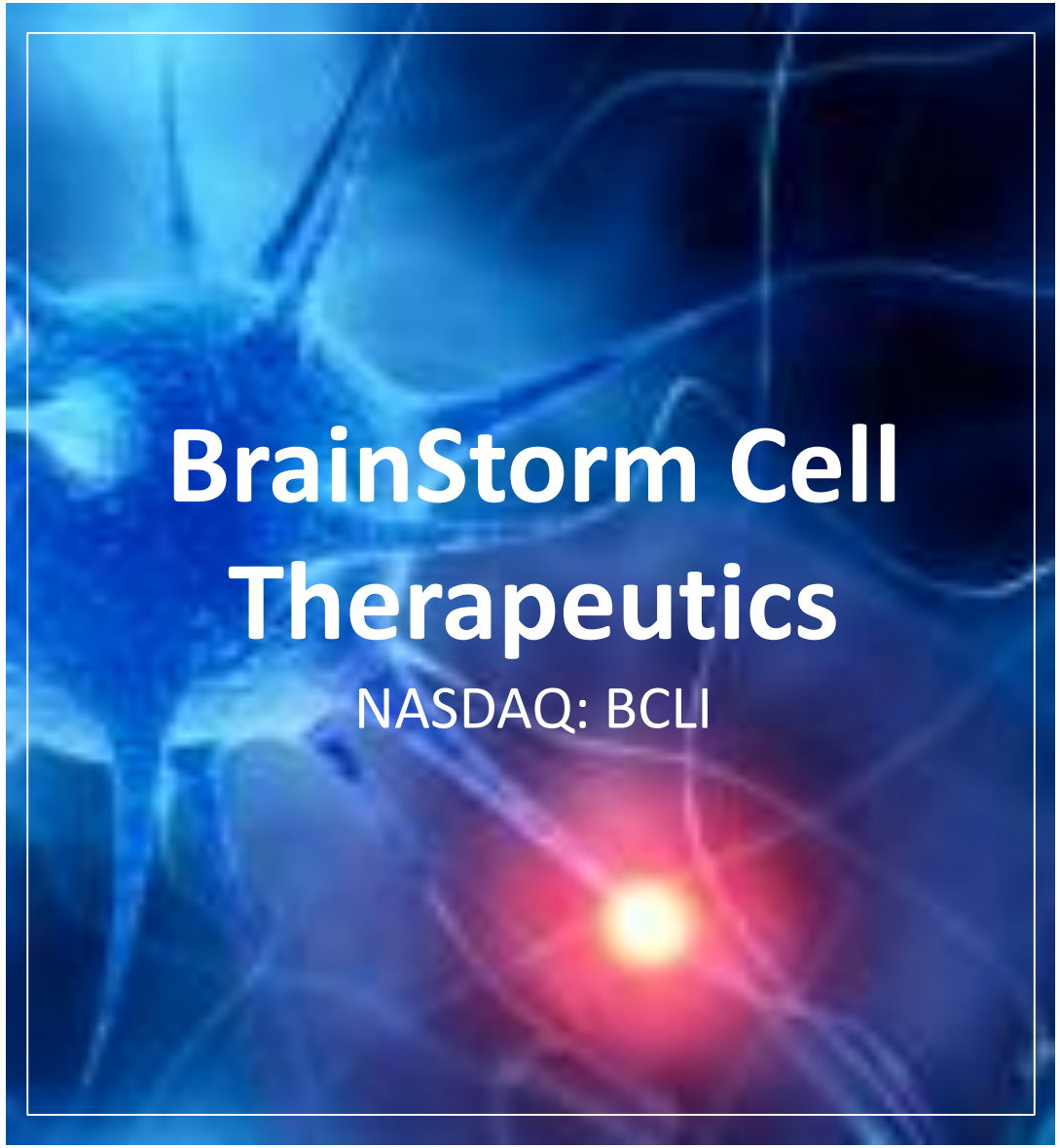


Stem Cell Therapeutic Approaches For ALS

Chaim Lebovits
CEO & President
BrainStorm Cell Therapeutics

Forward Looking 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.

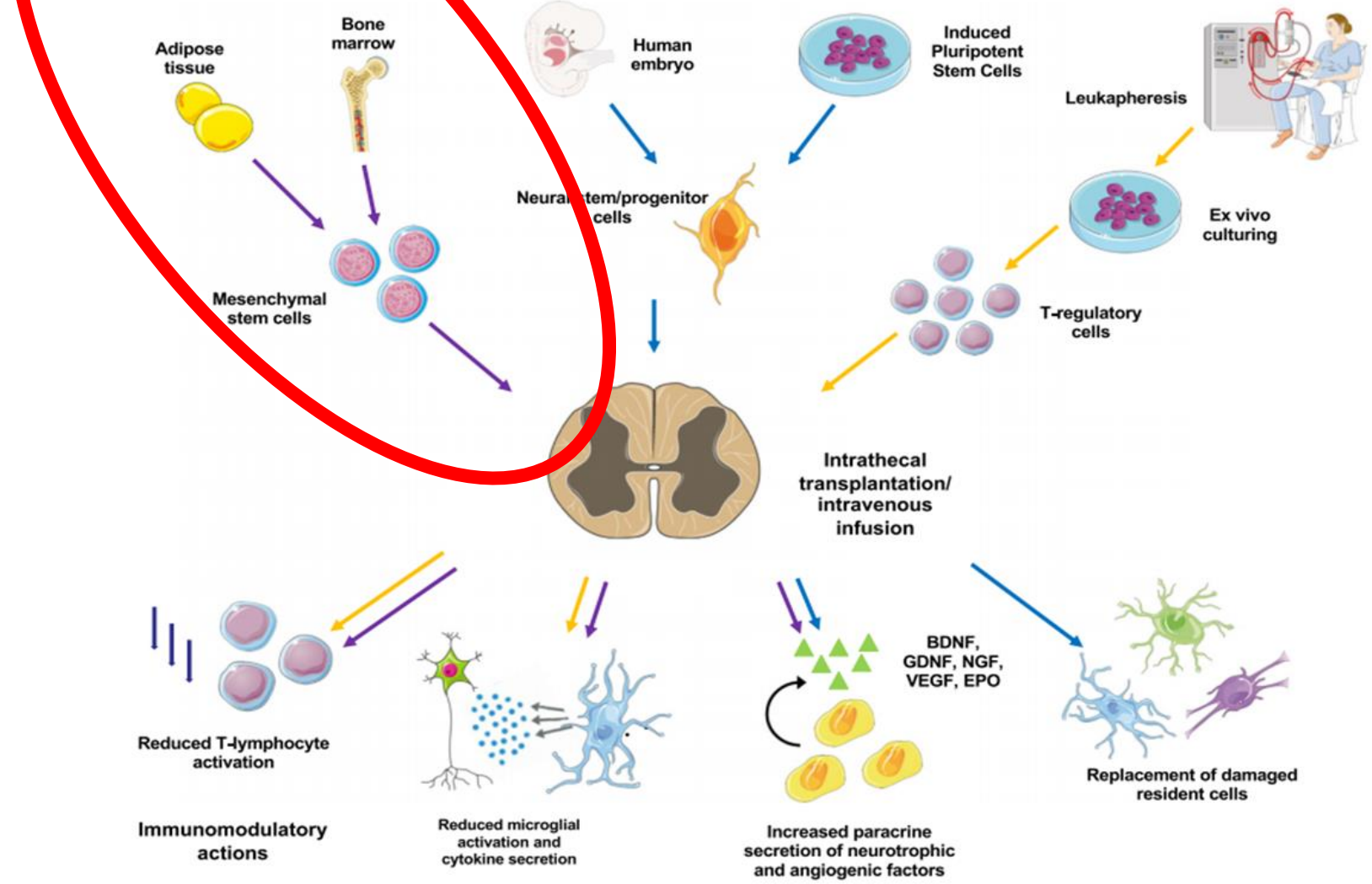
Stem cells therapy for ALS

brainstorm cell therapeutics

Mesenchymal stem cells

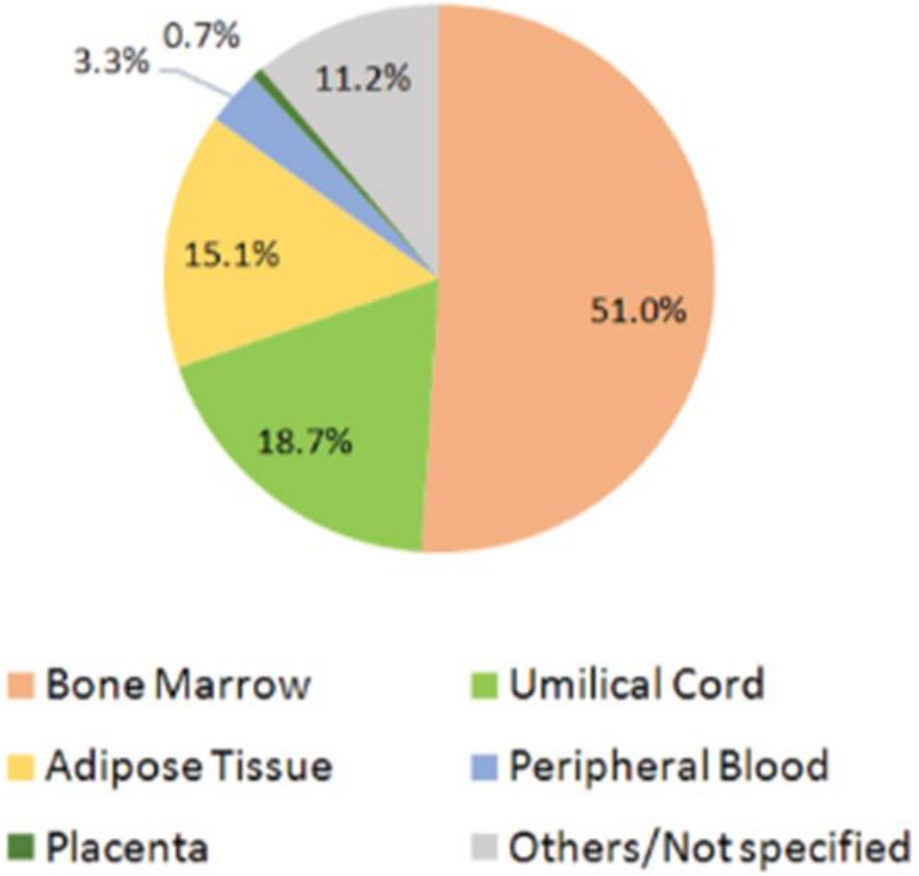
Neural stem cells

Immune cells



Abati et al Molecular Neurobiology (2019)

MSC sources used in clinical trials

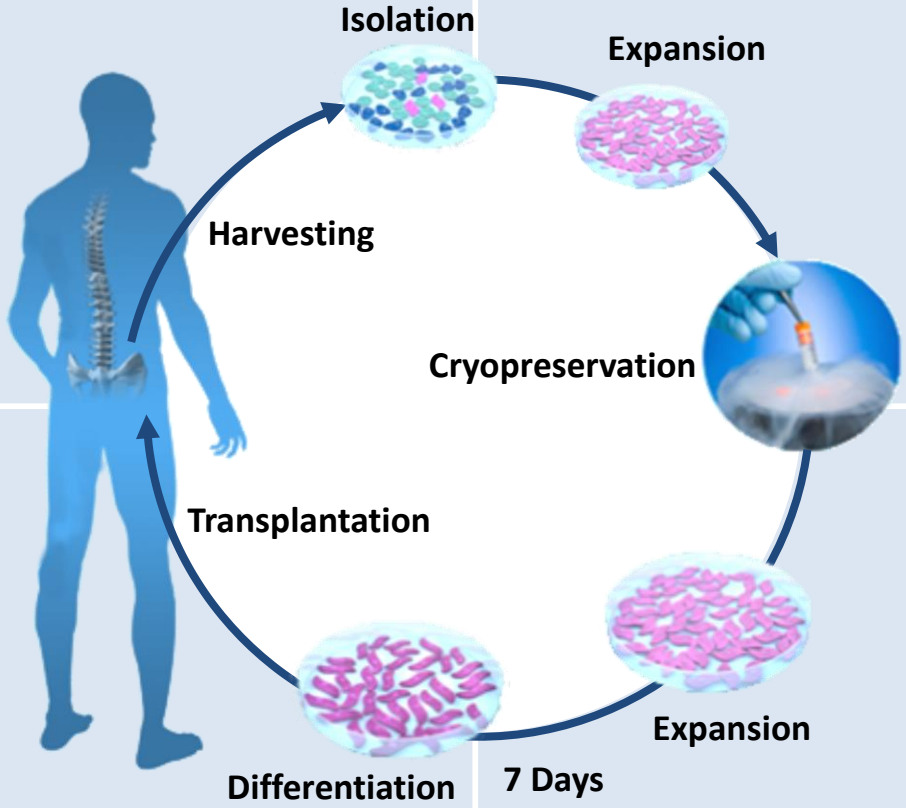


Taken from www.clinicaltrials.gov (2015)

NurOwn® Process

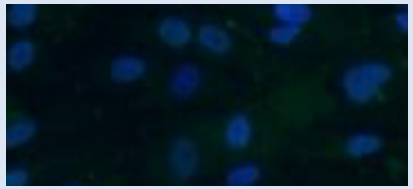
1

Manufacturing process begins with a bone marrow aspiration to harvest adult MSCs from the patient



2

Intermediate MSC product is cryopreserved

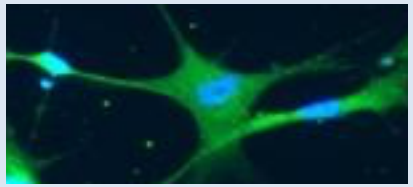


3

The proprietary culture medium induces the cells to secrete additional key neurotrophic factors (MSC-NTF cells)

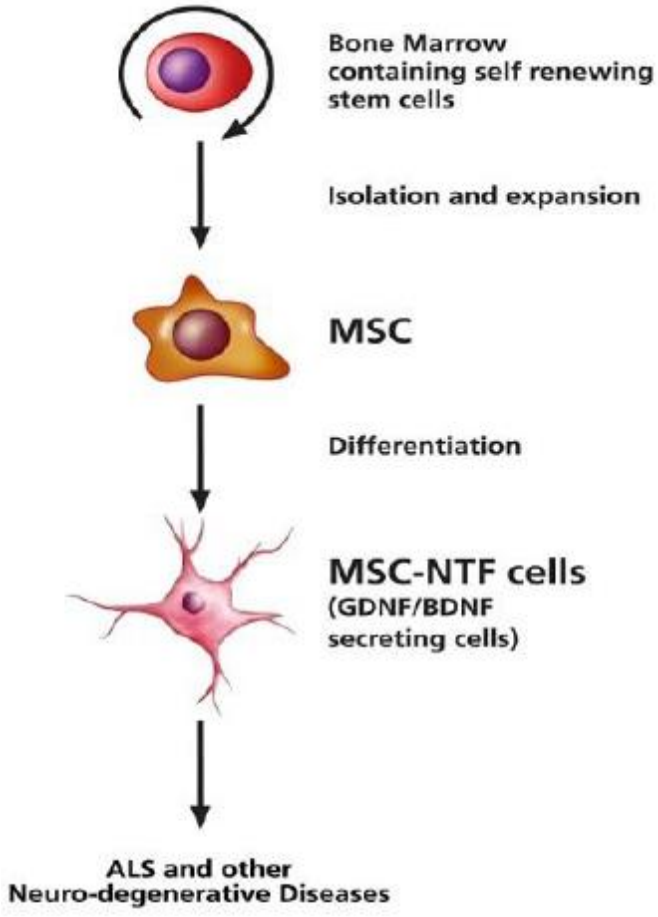
4

The cells are injected into the cerebrospinal fluid (CSF) of patients



NurOwn® Technology Advantages

- Autologous MSCs derived from bone marrow prevent risk of immune reaction to MHC class II antigens
- Intermediate cryopreserved product allows for 3 years of treatment from a single bone marrow aspiration
- Multiple mechanism of action including immunomodulation and neuroprotection through secreted NTFs and anti-inflammatory cytokines



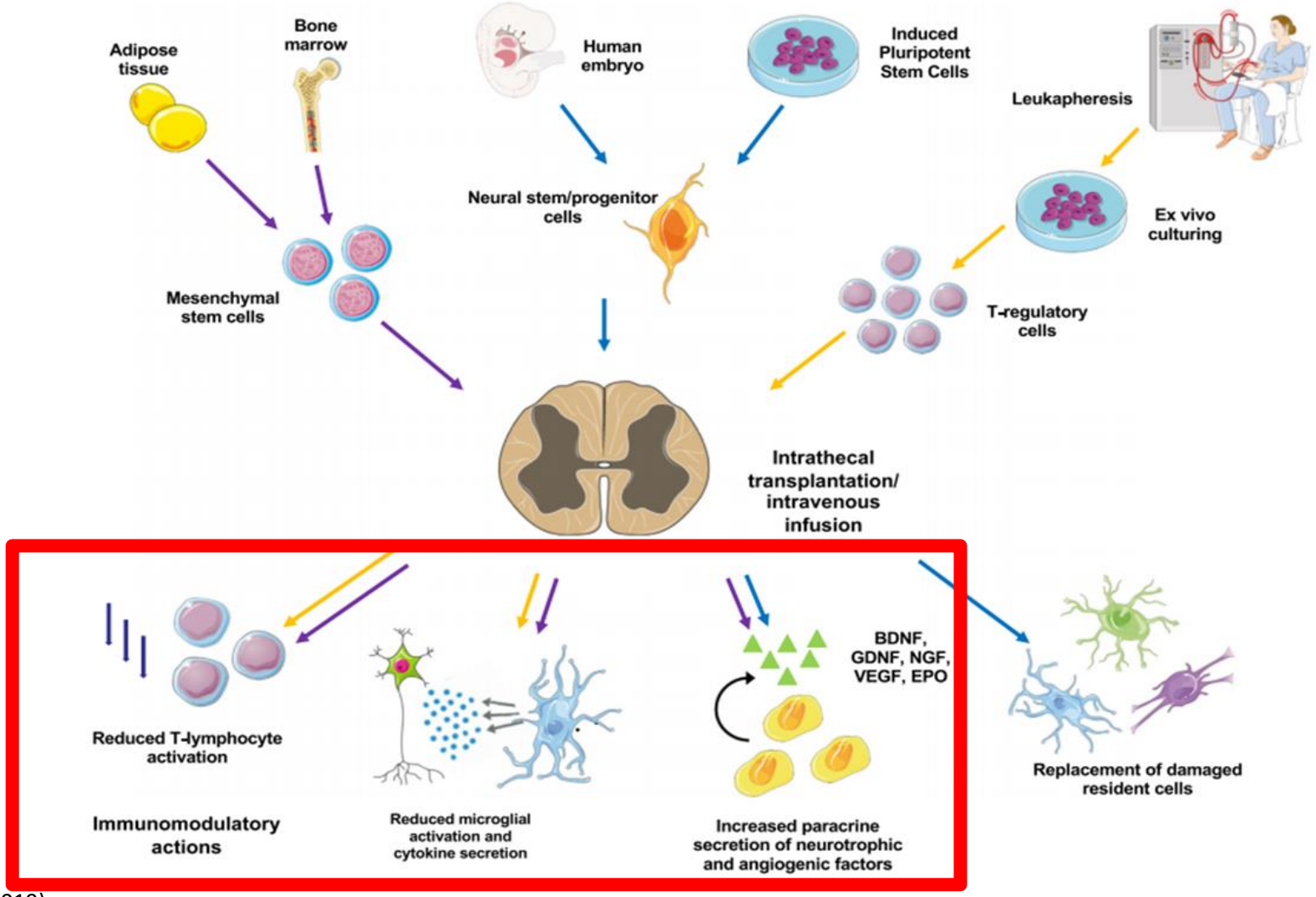
Stem cells therapy for ALS

brainstorm cell therapeutics

Mesenchymal stem cells

Neural stem cells

Immune cells

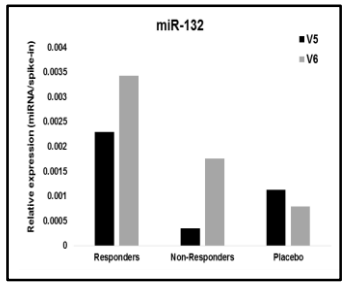


Abati et al Molecular Neurobiology (2019)

NurOwn MOA- Focus on Neuroprotection and Immunomodulation

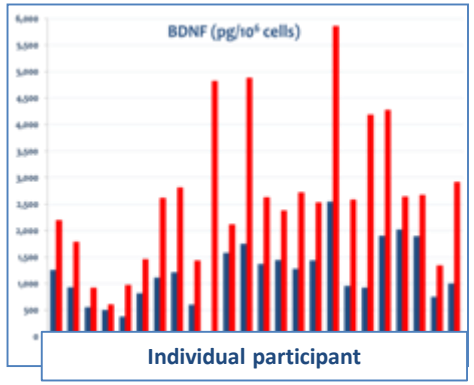
brainstorm cell therapeutics

NurOwn® ↑miR 132



miR-132

NurOwn® ↑NTFs



Neuroprotection

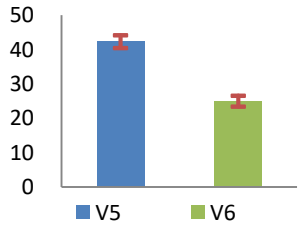
Increased T regulatory Cells

Decreased secretion of inflammatory cytokines

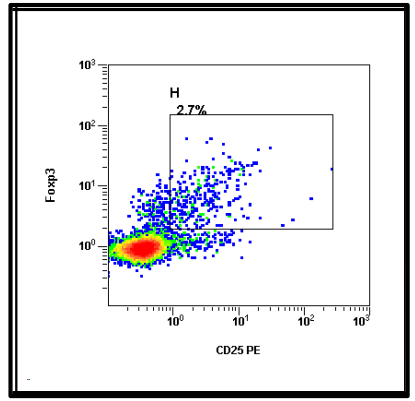
NurOwn® ↓ cytokines

	Activated PBMC (%)	Activated PBMC co-cultured with MSC-NTF cells (%)	% reduction
IFN-γ secretion	100	6.2 ± 2.24	93.8%
CD4+ T cells proliferation	100	45 ± 8.22	55%

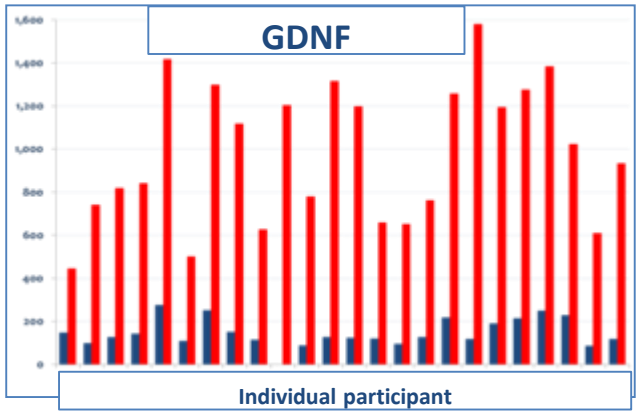
NurOwn® ↓ MCP-1

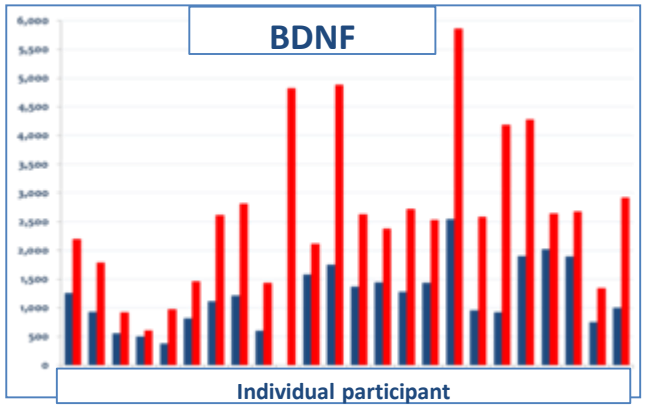


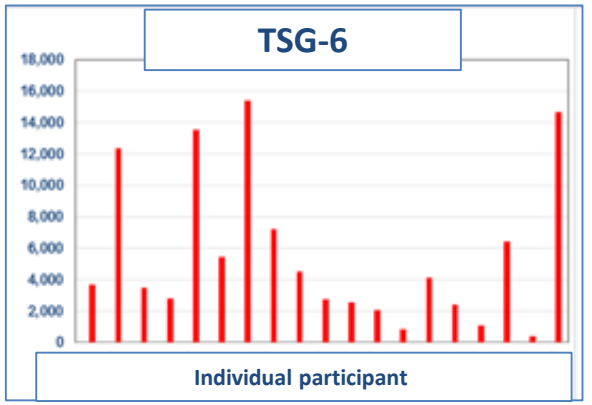
NurOwn® ↑Treg cells

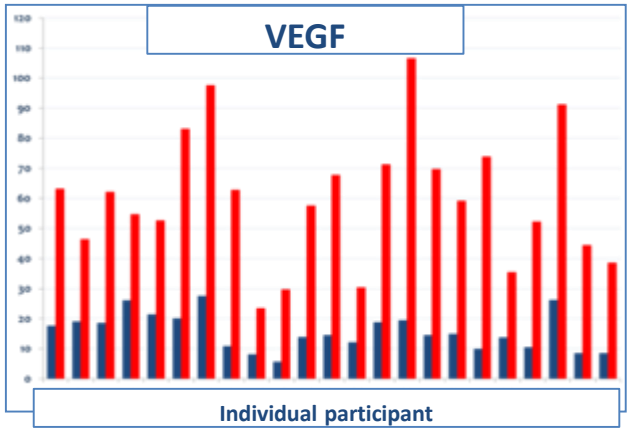


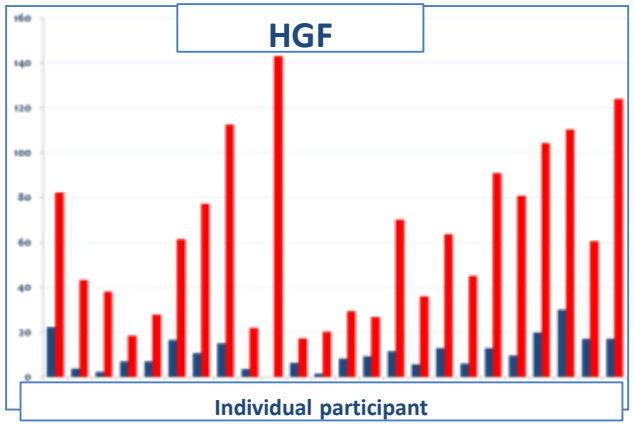
NurOwn® Enhanced Neurotrophic Factor Secretion Paired Comparisons Pre-Post Differentiation*

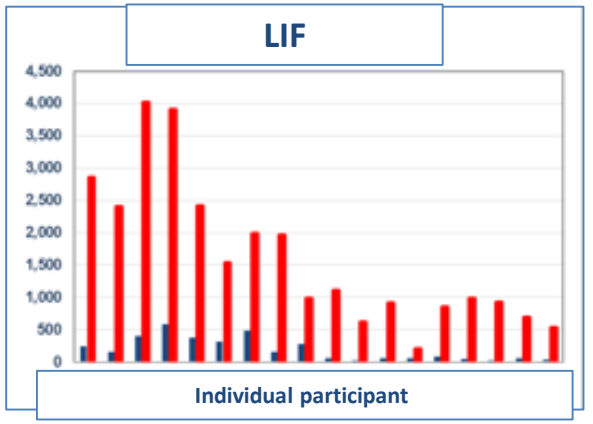








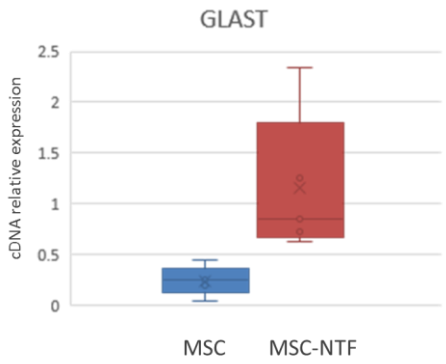




in vitro data from ALS patients, on file

NurOwn® MSC

NurOwn Mechanism of Action- Overview



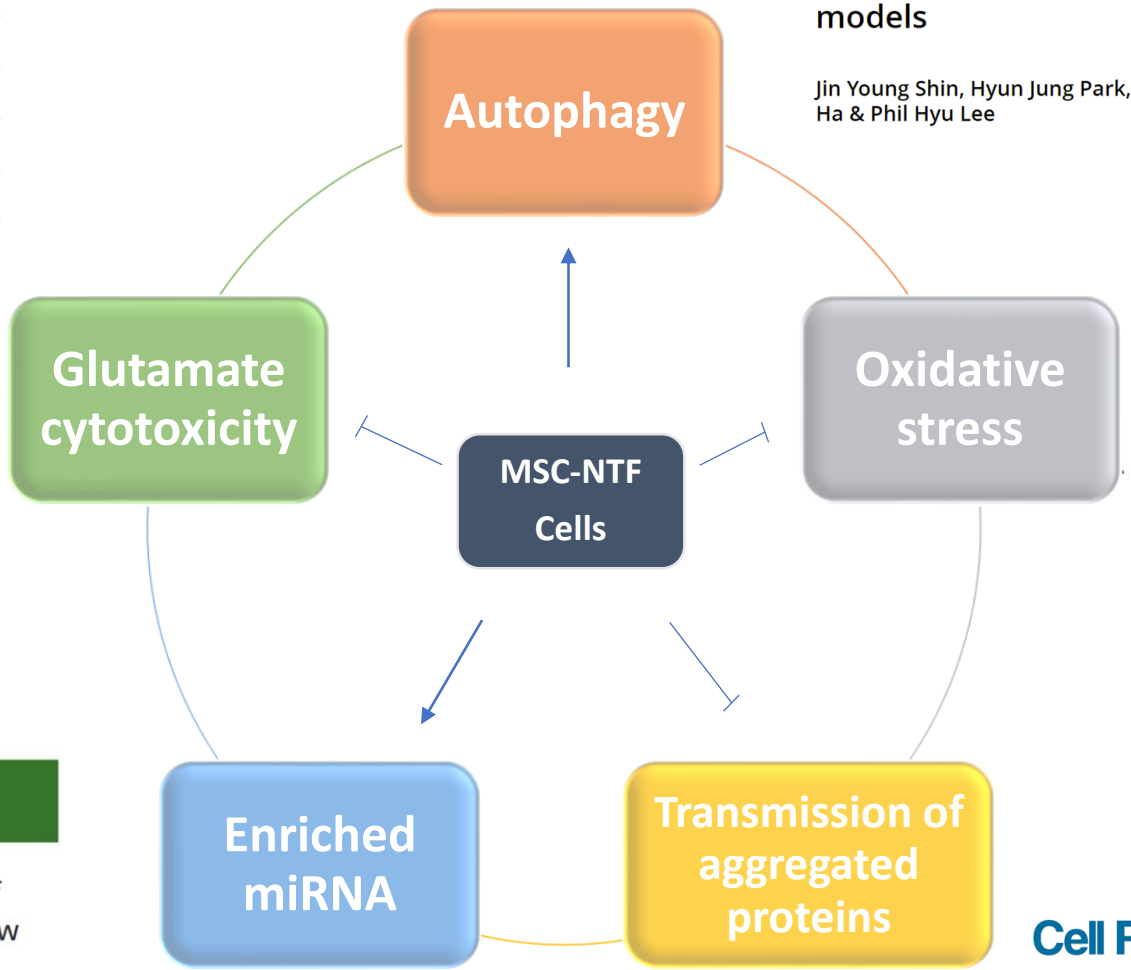
Mesenchymal stem cells protect CNS neurons against glutamate excitotoxicity by inhibiting glutamate receptor expression and function

April 2012 · Experimental Neurology 236(1):161-70
DOI: 10.1016/j.expneurol.2012.04.011
Source · PubMed

Androniki Voulgari-Kokota · R Fairless · Maria Karamita · Show all 10 authors · Lesley Probert

Mesenchymal stem cells enhance autophagy and increase β-amyloid clearance in Alzheimer disease models

Jin Young Shin, Hyun Jung Park, Ha Na Kim, Se Hee Oh, Jae-Sung Bae, Hee-Jin Ha & Phil Hyu Lee



Original Contribution

Transplantation of bone marrow mesenchymal stem cells decreases oxidative stress, apoptosis, and hippocampal damage in brain of a spontaneous stroke model

Michele Longoni Calió [a], Darci Sousa Marinho [b], Gui Mi Ko [b], Renata Rodrigues Ribeiro [a], Adriana Ferraz Carbonel [c], Lila Missae Oyama [d], Milene Ormanji [b], Tatiana Pinoti Guirao [b], Pedro Luiz Calió [e], Luciana Aparecida Reis [f], Manuel de Jesus Simões [c], Telma Lisbôa-Nascimento [a], Alice Teixeira Ferreira [a], Clélia Rejane Antônio Bertoncini [b]

Published online: September 1, 2015

Article

THE EMBO JOURNAL

Dysregulated miRNA biogenesis downstream of cellular stress and ALS-causing mutations: a new mechanism for ALS

Anna Emde[1], Chen Eitan[1], Lee-Loung Liou[2], Ryan T Libby[3], Natali Rivkin[1], Iddo Magen[1], Irit Reichenstein[1], Hagar Oppenheim[1], Raya Eilam[4], Aurelio Silvestroni[2], Betty Alajajian[2], Iddo Z Ben-Dov[5], Julianne Aebischer[6], Alon Savidor[7], Yishai Levin[7], Robert Sons[8], Scott M Hammond[8], John M Ravits[3,9,*], Thomas Möller[2,†] & Eran Hornstein[1,**,†]

Article

Cell Reports

Mesenchymal Stem Cells Inhibit Transmission of α-Synuclein by Modulating Clathrin-Mediated Endocytosis in a Parkinsonian Model

Brainstorm at a Glance

Clinical stage biotechnology company developing innovative autologous cellular therapies for neurodegenerative disease

Fully enrolled Phase 3 clinical trial in ALS, an orphan disease with no existing cure and limited treatment options. Phase 2 progressive MS trial actively enrolling; FDA granted IND in Dec' 18

Large addressable markets – progressive MS (500K US) and ALS (30K US)

Proven technology platform and strong manufacturing capabilities

Robust IP portfolio

Clinical-Stage and Preclinical Programs

– Source: Company filings, equity research, company website.

ALS

ALS Incidence

brainstorm cell therapeutics

What is ALS?

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease [(1)], is a progressive neurodegenerative disease that affects the function of nerves and muscles. This debilitating condition usually affects people aged 40 to 70, however, individuals in their 20s and 30s have also been known to develop ALS.

Future Predictions

Researchers have predicted that the number of worldwide ALS cases will increase by 69% in 2040, compared to 2015. The main cause of this projected increase is due to an ageing population, particularly in developing nations.

*It is estimated that **450,000** people worldwide are living with ALS, with over **30,000** people in the U.S. suffering from this neurodegenerative condition at any given time.*

Someone is diagnosed with ALS every

90

minutes

New US cases per year

6,000

$6B

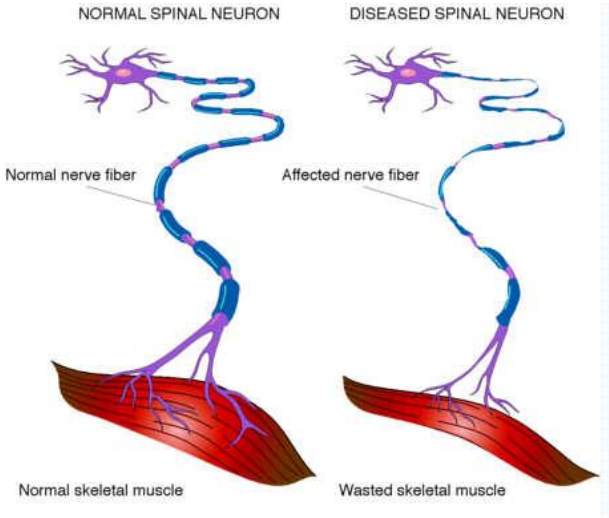
annual health care cost

30

months

Life expectancy from diagnosis

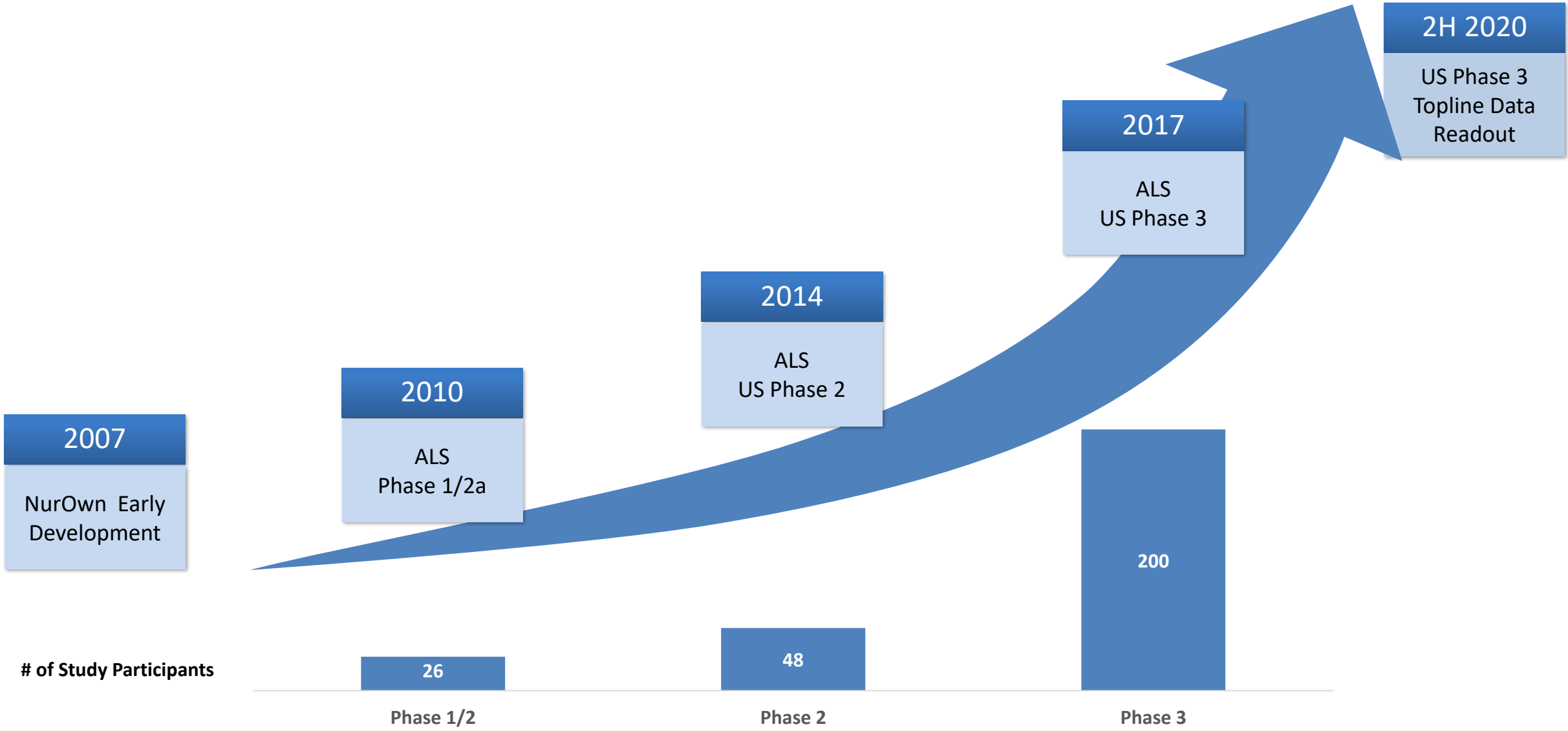
(1) Lou Gehrig was a famous American baseball player diagnosed with ALS in 1939.



Amyotrophic Lateral Sclerosis (ALS)

- A rapidly progressive disease that leads to degeneration of upper and lower motor neurons
- Clinically, the effect is progressive muscle weakness leading to death, usually from respiratory failure
- There is no known cause and no effective treatments
- Familial ALS (a hereditary form) occurs in 5%–10% of cases
- Average life expectancy: 2-5 years from the time of diagnosis

NurOwn® ALS Development



ALS Phase 2 Trial Design and Safety Outcomes

Safety Design

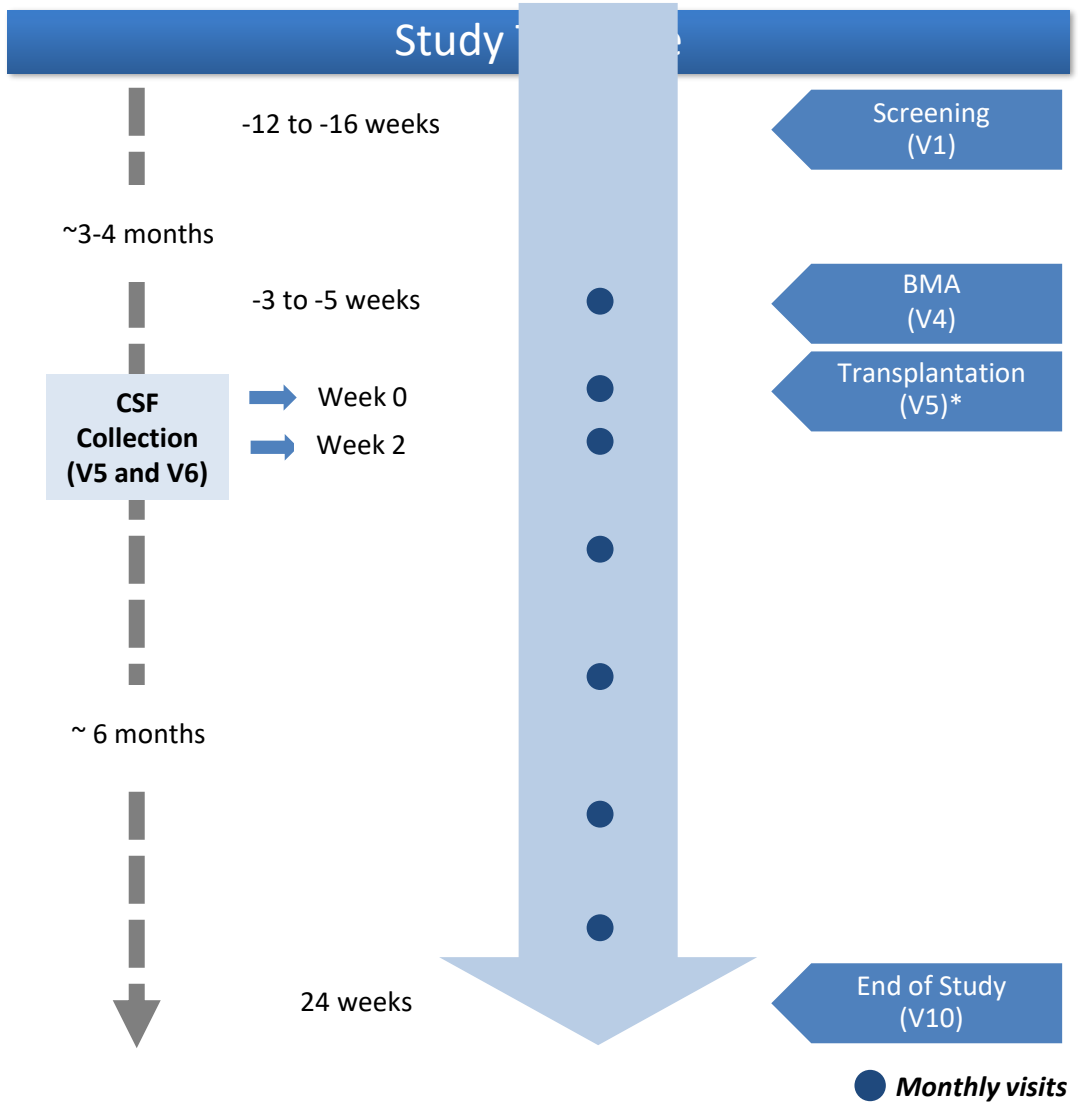
- 48 participants (16 per site)
- Randomized 3:1
- Blinded to allocation

Primary Outcomes

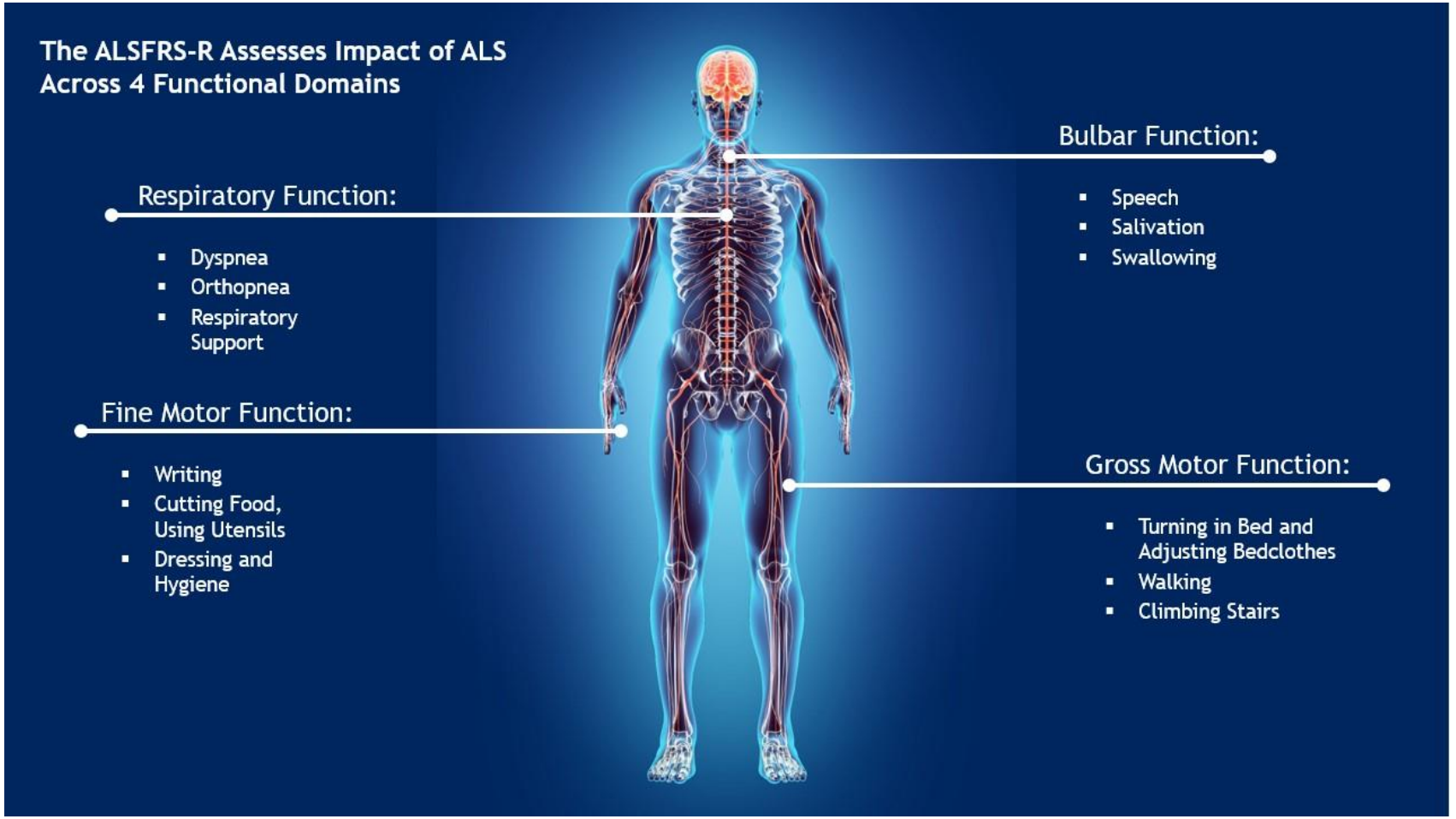
- No deaths or treatment related SAEs
- No drop outs related to SAEs
- Most common adverse events transient and mild/moderate severity and procedure related

Efficacy

- ALSFRS-R
- SVC



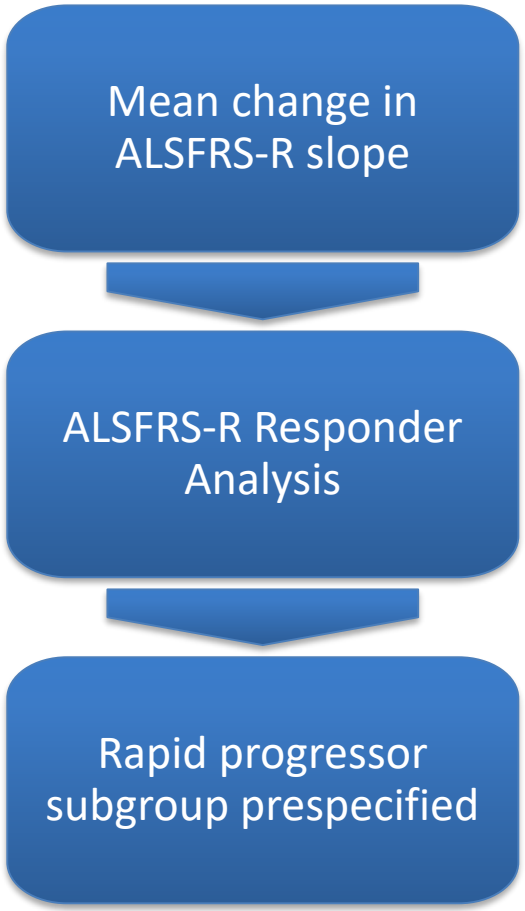
ALS Functional Rating Scale–Revised (ALSFRS-R)



Cedarbaum, JM. et al. *J Neurol Sci*. 1999;169:13-21.

Phase 2 Trial – Approach to Data Analysis

Phase 2 Trial: 3 Types of Efficacy Analysis



ALS Rapid Progressor Subgroup Has Different Characteristics

- ✓ Decline in ALS function in rapid progressors better predicts survival and quality of life
- ✓ Higher response rate in rapid progressors
- ✓ Rapid progressors have higher levels of neuroinflammatory biomarkers

NurOwn® Phase 2: ALSFRS-R slope improvement (mean slope change/month)

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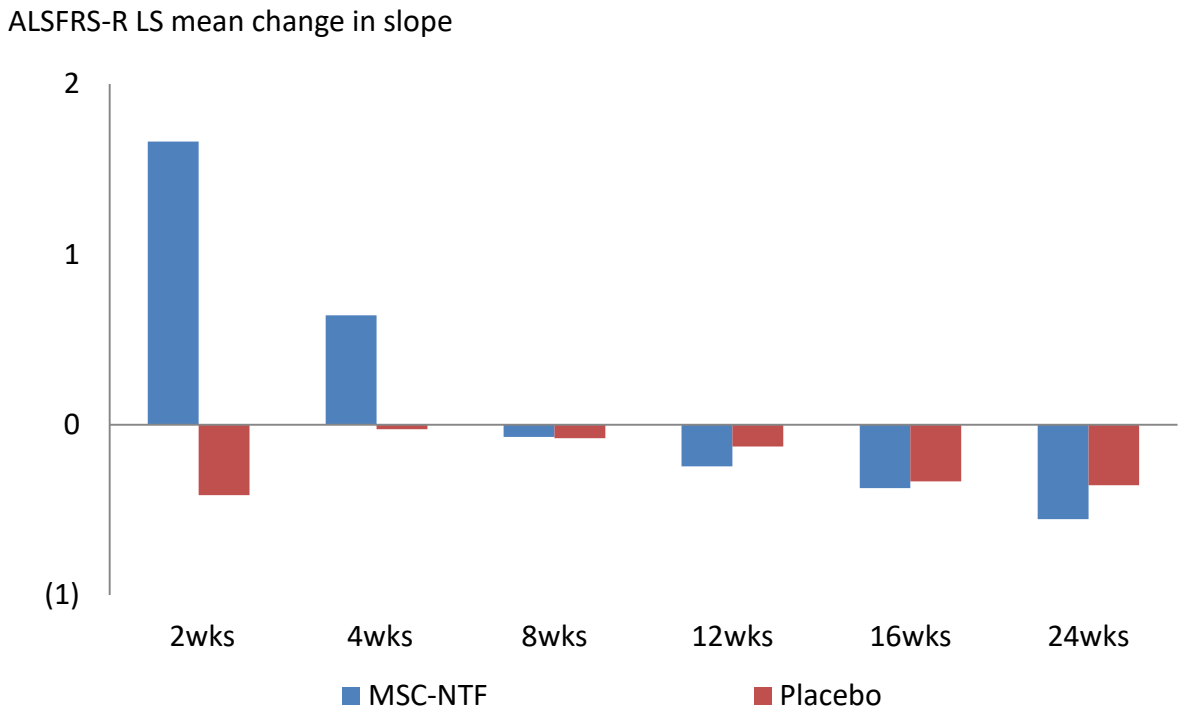
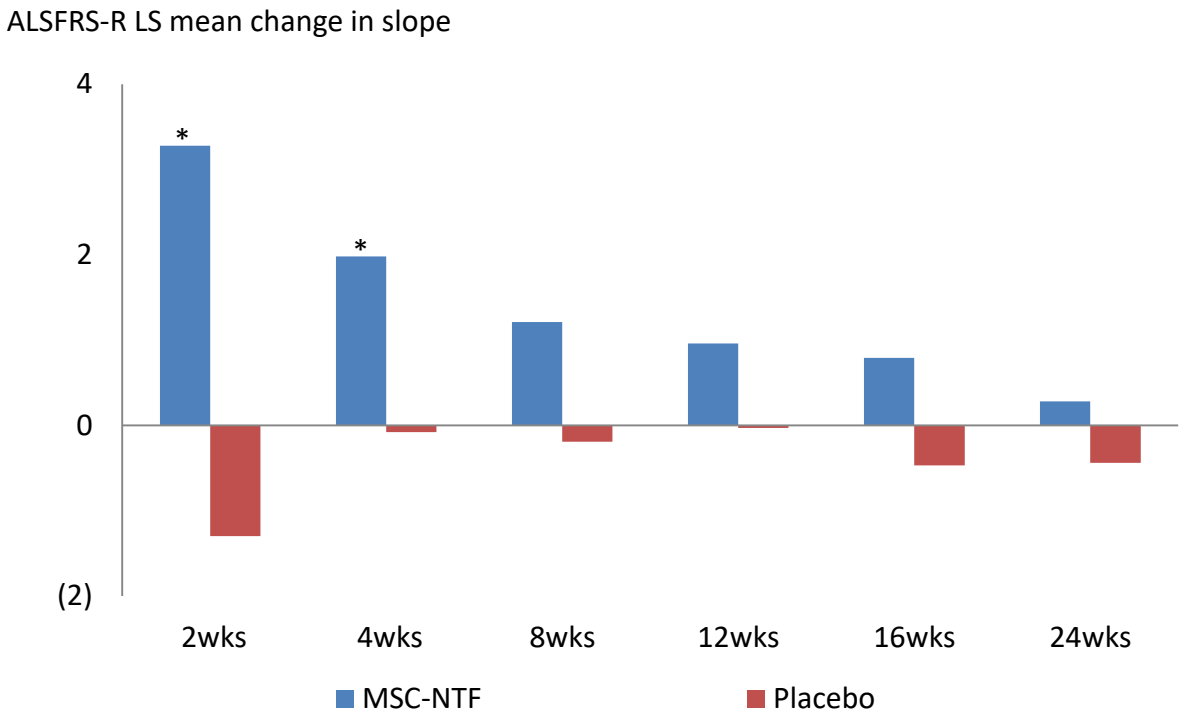
All participants (n=46)

Post-treatment - pre treatment slope



Rapid progressors (n=21)

Post treatment – pre treatment slope



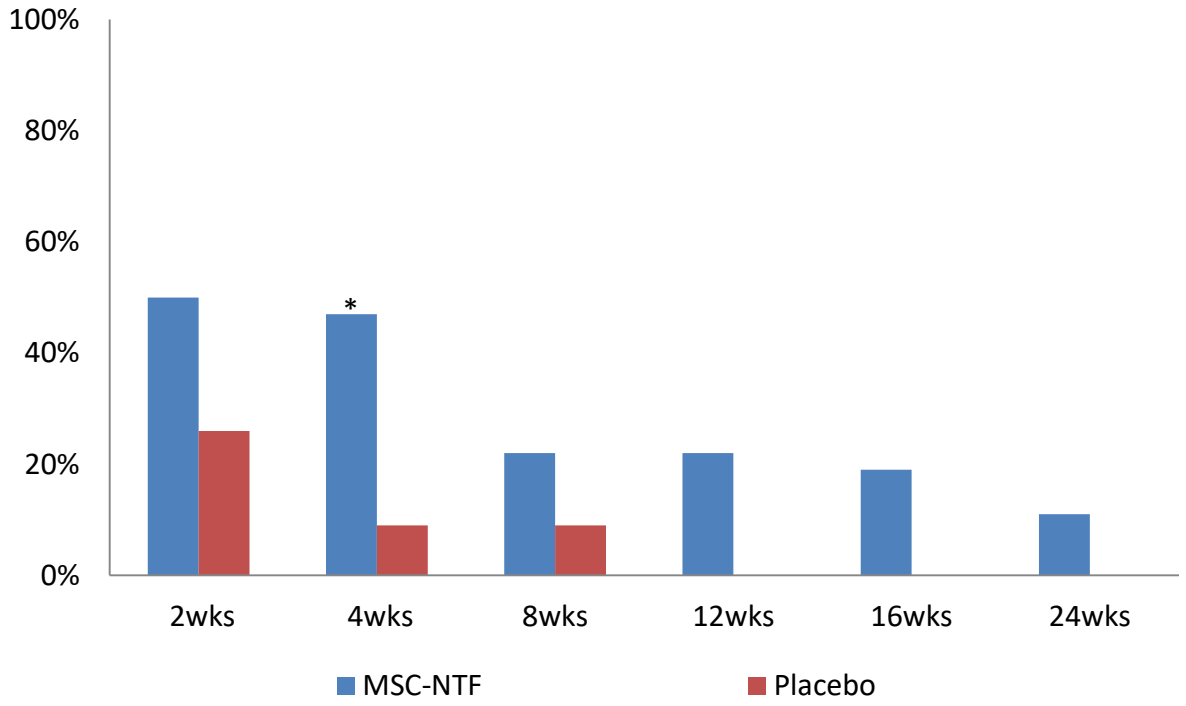
** p<0.05 (two-sided Fisher's exact test)*

NurOwn® Phase 2: Responder Analysis: ≥1.5 points/month ALSFRS-R slope improvement

brainstorm cell therapeutics

All participants (n=46)

ALSFRS-R ≥ 1.5 points improvement/month in post-treatment slope compared to pre-treatment slope



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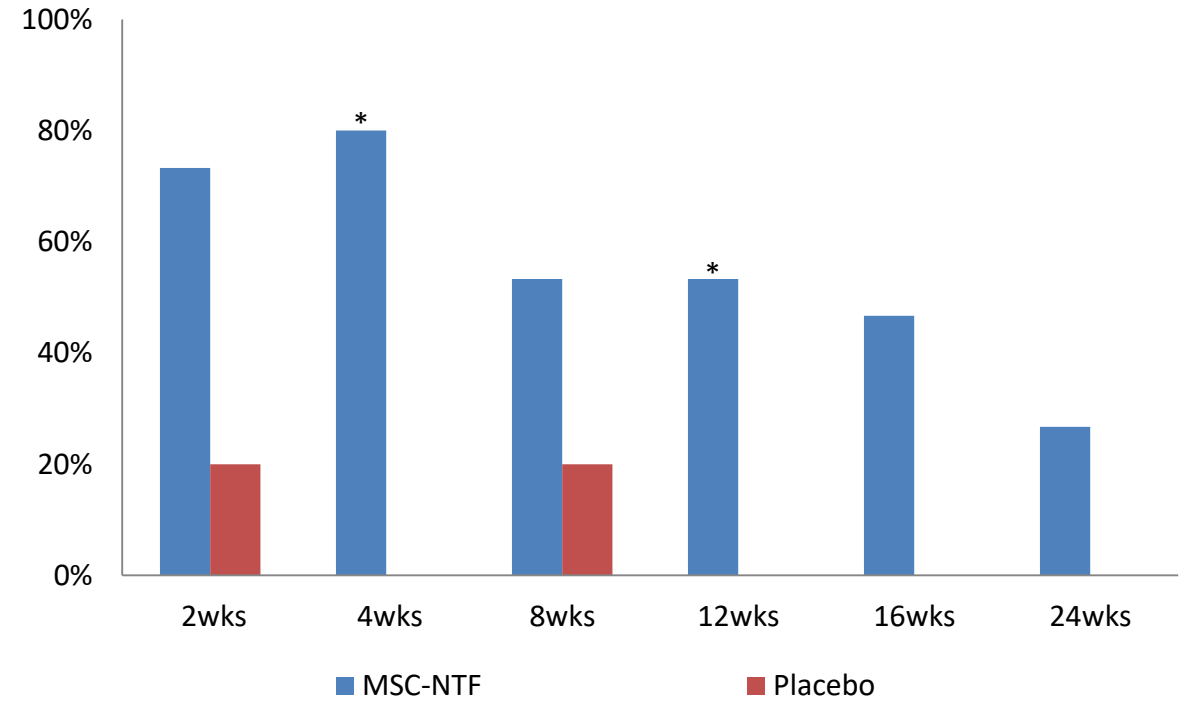
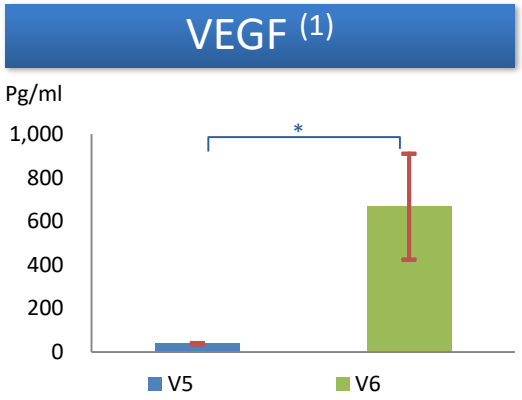
Rapid progressors (n=21)

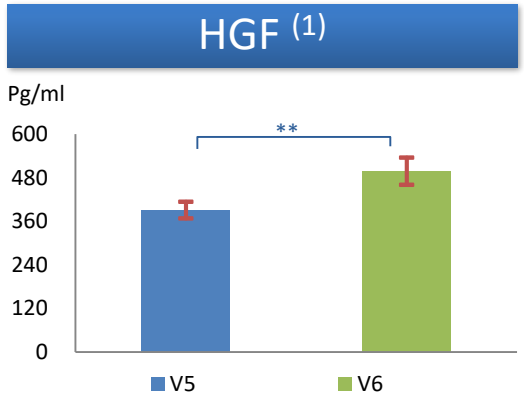
ALSFRS-R ≥ 1.5 points improvement in post-treatment slope compared to pre-treatment slope

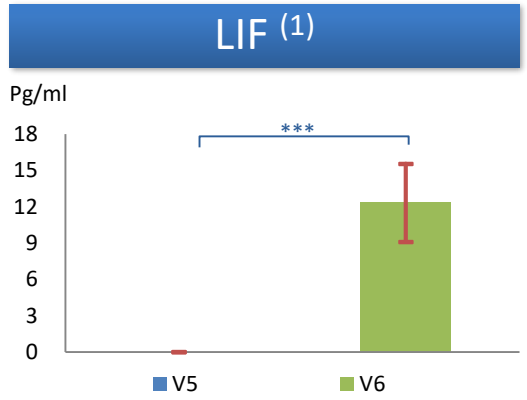


NurOwn® Phase 2 ALS Biomarkers: CSF NTFs Significantly Increased 2 Weeks Post-Treatment Compared to Baseline

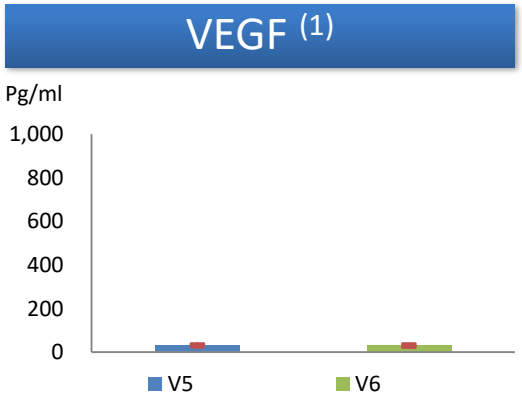
NurOwn®
(n = 26)

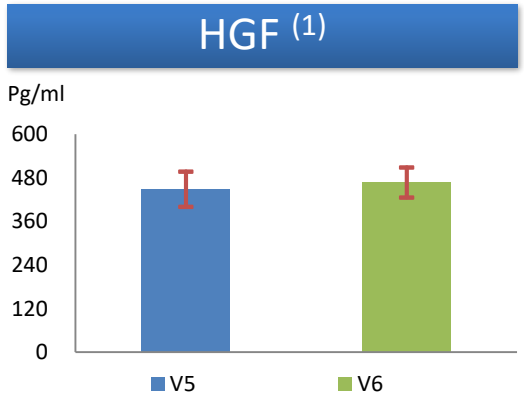


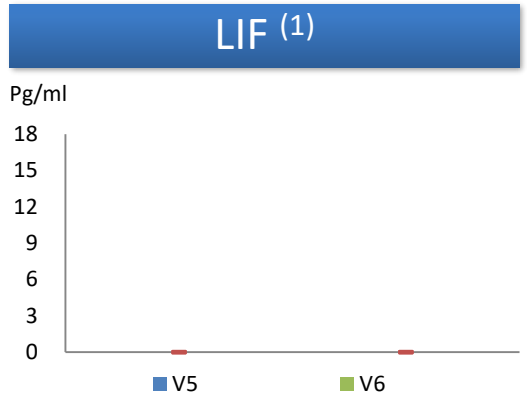




Placebo
(n = 9)







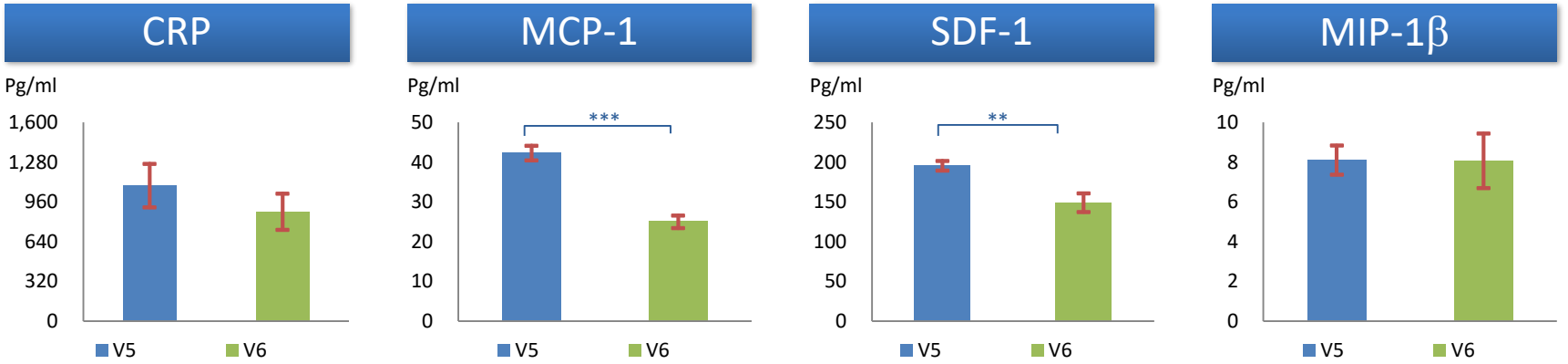
Pre transplantation

Post transplantation

1. *Mean ± SEM. p< 0.05, p<0.01, p< 0.001 for VEGF, HGF and LIF, respectively.*

NurOwn® Phase 2 ALS Biomarkers: CSF Inflammation Significantly Decreased 2 weeks Post-Treatment Compared to Baseline

NurOwn®
(n = 26)



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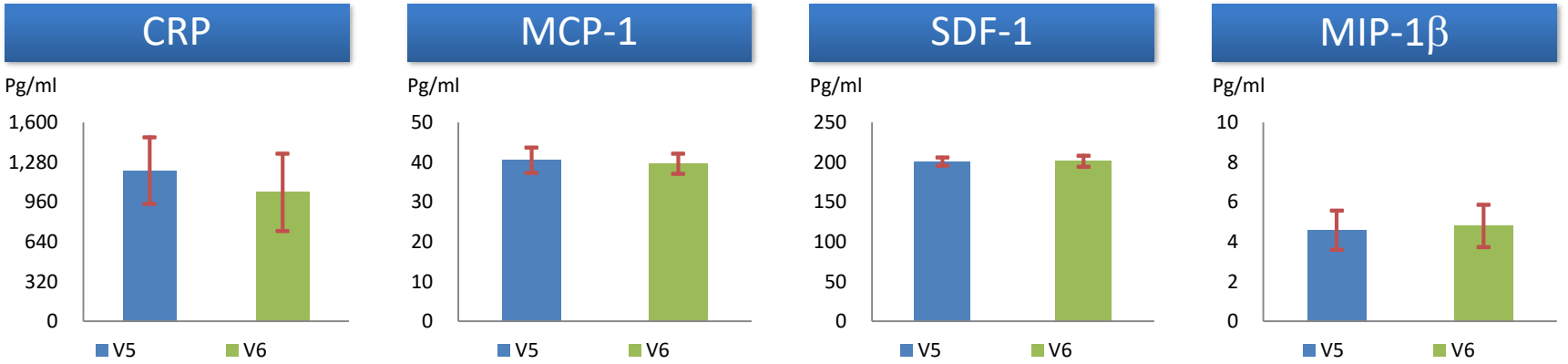


Pre transplantation

Post transplantation

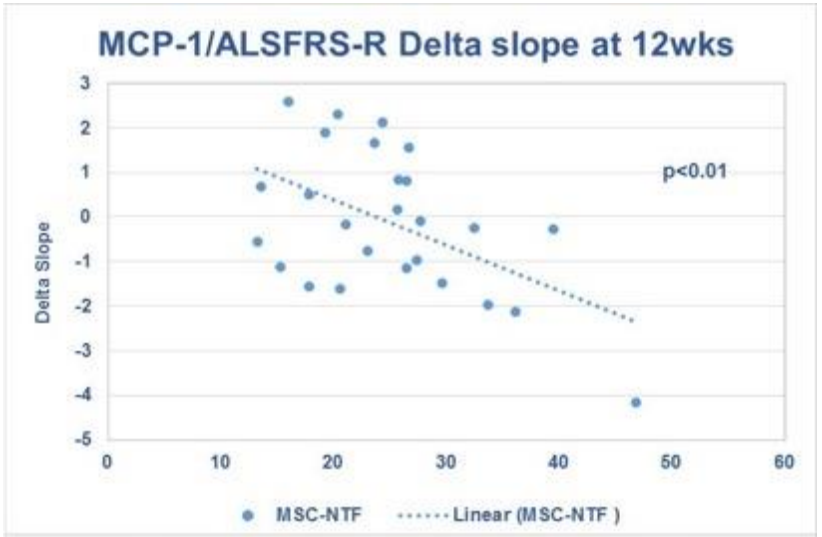
1. *Mean ± SEM. p<0.01, p< 0.001 for [], respectively.*

Strong correlations between post-treatment NTF increase and inflammatory factor decrease

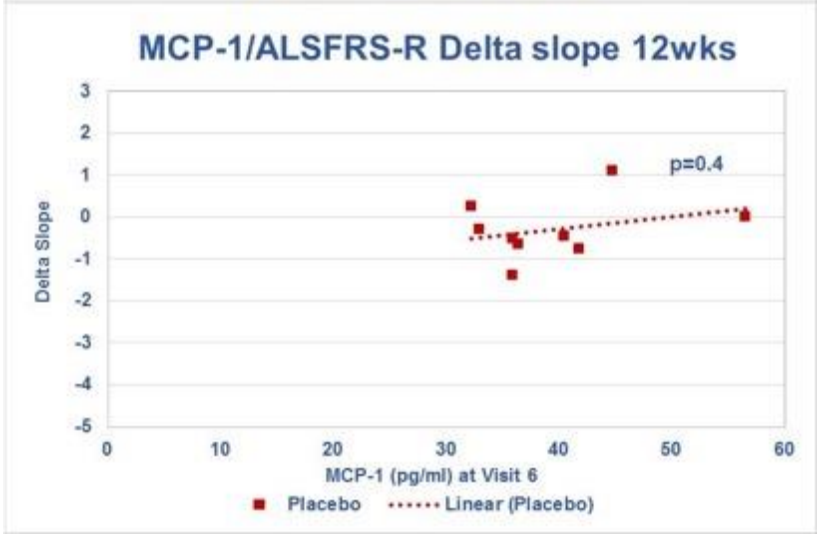
	Treated				Placebo			
	Pre-transplant		Post-transplant		Pre-transplant		Post-transplant	
	Correlation	p value	Correlation	p value	Correlation	p value	Correlation	p value
VEGF/MCP-1	-0.017	0.9326	-0.564	0.0027	-0.005	0.9904	0.214	0.5804
VEGF/SDF-1	0.236	0.2463	-0.765	<0.0001	-0.098	0.8025	-0.209	0.5886
HGF/SDF-1	0.119	0.5614	-0.412	0.0363	-0.388	0.3025	-0.140	0.7193
LIF/SDF-1	NA	NA	-0.534	0.0049	NA	NA	NA	NA
LIF/MCP-1	NA	NA	-0.422	0.0316	NA	NA	NA	NA

NurOwn® Phase 2: Strong correlation between reduction in MCP-1 (2 weeks) and clinical improvement (ALSFRS-R slope improvement at 12 weeks)

MSC-NTF cells



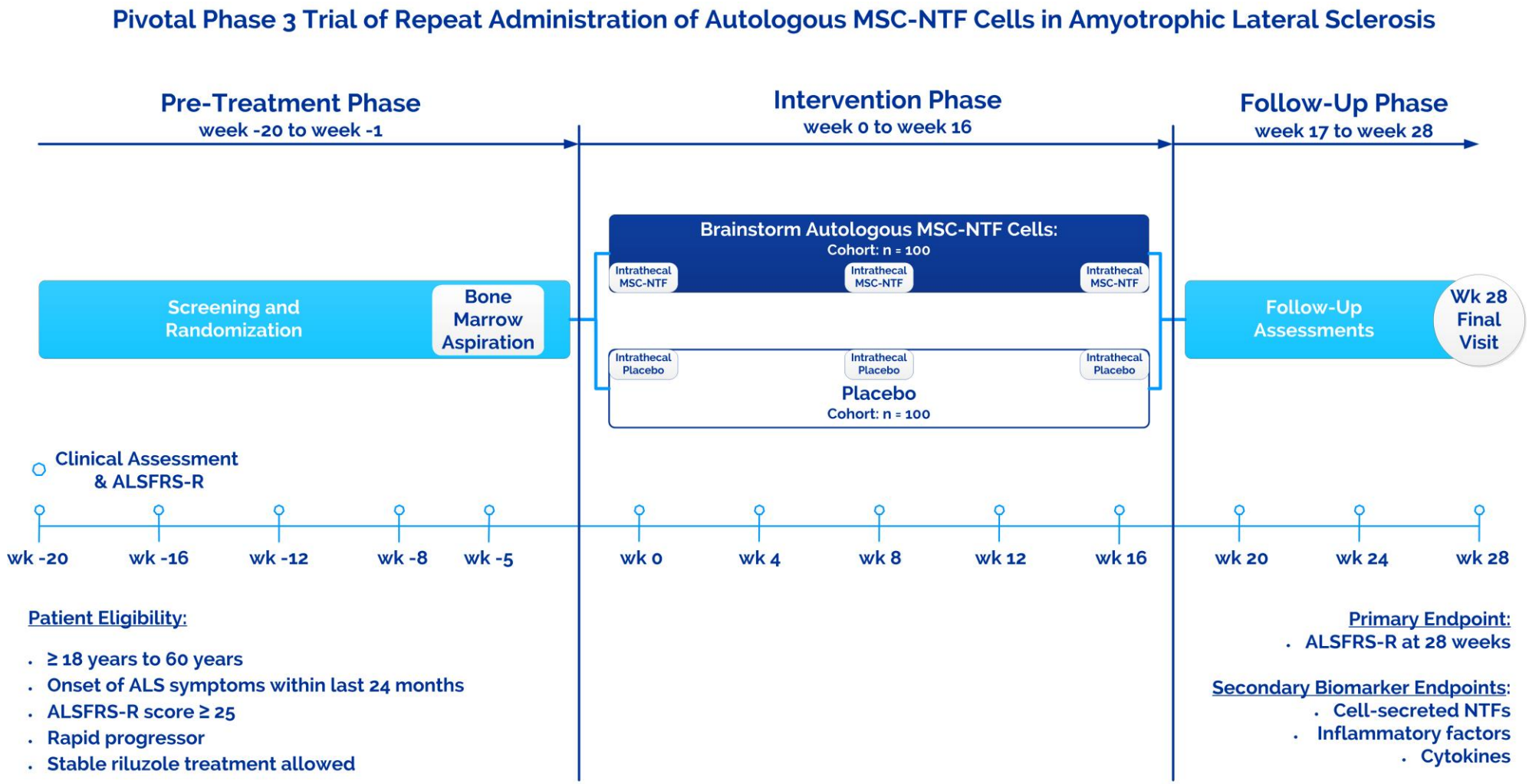
Placebo



Phase 2 ALS Trial Summary

- Intrathecal NurOwn treatment was safe and well tolerated
- Multiple doses will be needed to sustain efficacy
- Rapid progressor subgroup showed higher efficacy signal
- Responder analysis highlights clinically important response
- A significant increase in neurotrophic factors and decrease in inflammatory factors, was observed post-transplant in the treated group only, providing a biological mechanism supporting the observed clinical effect

ALS Phase 3 Trial Design & Assessments



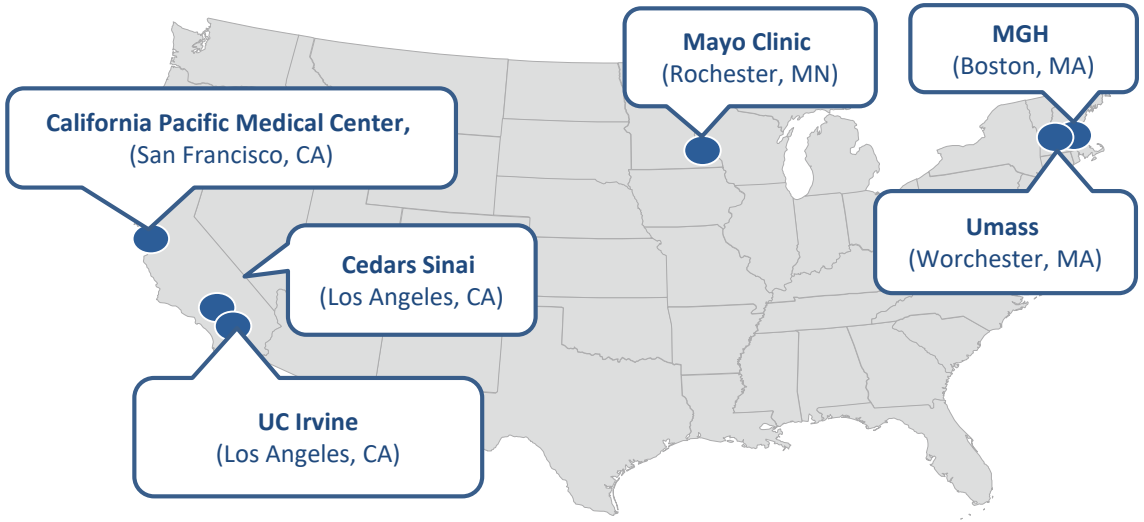
ClinicalTrials.gov Identifier: NCT03280056

NurOwn® ALS Phase 3 Clinical Trial

Study Timelines

- Enrollment completed October 2019
- Study duration:
  - 11.5 months total
  - Seven months post-first transplantation
- Top-line data expected Q4, 2020

Site Locations



BrainStorm Cell Therapeutics

NASDAQ: BCLI

brainstorm
cell therapeutics

Thank You