

Brainstorm Cell Therapeutics

August 2020 | NASDAQ: BCLI

Forward-Looking Statements

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 At-a-Glance

A leader in developing innovative autologous cellular therapies for highly debilitating neurodegenerative diseases

NASDAQ	BCLI
HEADQUARTERS	New York, NY
R&D CENTER	Israel
MANUFACTURING SITES	Dana Farber Cancer Institute, City of Hope
NUMBER OF EMPLOYEES	42
SHARES OUSTANDING	31,527,937 (as of July 31, 2020)
MARKET CAP	~\$427.2 million (as of July 31, 2020)
CASH & LIQUIDITY	~\$38 million (as of July 31, 2020)

Brainstorm Senior Leadership Team

Chaim Lebovits
Chief Executive Officer

Ralph Kern, MD, MHSc
President & Chief Medical Officer

Arturo Araya, MBA
Chief Commercial Officer

David Setboun, PharmD, MBA
EVP & Operating Officer

Preetam Shah, PhD, MBA
EVP & Chief Financial Officer

Uri Yablonka
EVP & Chief Business Officer

Stacy Lindborg, PhD
EVP & Head of Global Clinical Research

Revital Aricha, PhD
VP Research & Development

Yael Gothelf, PhD
VP Scientific & Regulatory Affairs

Yossef Levy, PhD
VP Cell Production

Mary Kay Turner
VP Patient Advocacy & Gov. Affairs

Susan Ward, PhD
Head of Clinical Operations

SANOFI GENZYME 

 NOVARTIS

 Biogen



AstraZeneca 

 Bristol-Myers Squibb

ALS Hope
Foundation 
Hope is on the horizon

 Mitsubishi Tanabe Pharma

 InterPharm

 TEL AVIV UNIVERSITY

AMERICAN COMMITTEE FOR THE
WEIZMANN
INSTITUTE OF SCIENCE 





 CLINQUEST

NurOwn®

A unique cell therapy product

Autologous and convenient

NurOwn® autologous cell therapy uses the patient's own cells

- Safety and cell persistence

Cryopreservation creates an 'off-the-shelf' product for each patient

A single bone marrow harvest creates several years of therapy

Short cycle time, 7 days from thawing to injection in the clinic

Consistent and reliable

No animal proteins, antibiotics, genetic modifications or viral vectors are used in the manufacturing process

NurOwn® is culture-rescued creating very high cell viability and consistent performance characteristics

Cell potency release criteria

Platform technology

Consistent biology observed in-vitro and in-vivo

- Neurodegenerative disease animal models
- Human biomarker studies

Neuroprotection, neurotrophic support and immunomodulation confirmed in phase 2 ALS trial

Safety experience is growing across indications

One Platform, Multiple Indications

NurOwn® autologous cell therapy platform is broadly applicable

ALS, Progressive MS, Alzheimer's Disease

Robust IP

Strong global presence with experienced executive team

Flagship Program in ALS

Phase 3 fully enrolled

- Top-line data expected in Q4 2020

Phase 2 provides clinical proof of concept in ALS

Agreement with FDA supporting regulatory pathway to approval

Diversified Clinical Pipeline

Phase 2 progressive MS ongoing

- Top-line data expected Q4 2020
- No DSMB safety concerns or protocol changes

Phase 2 in prodromal to mild AD planned for 2H 2020

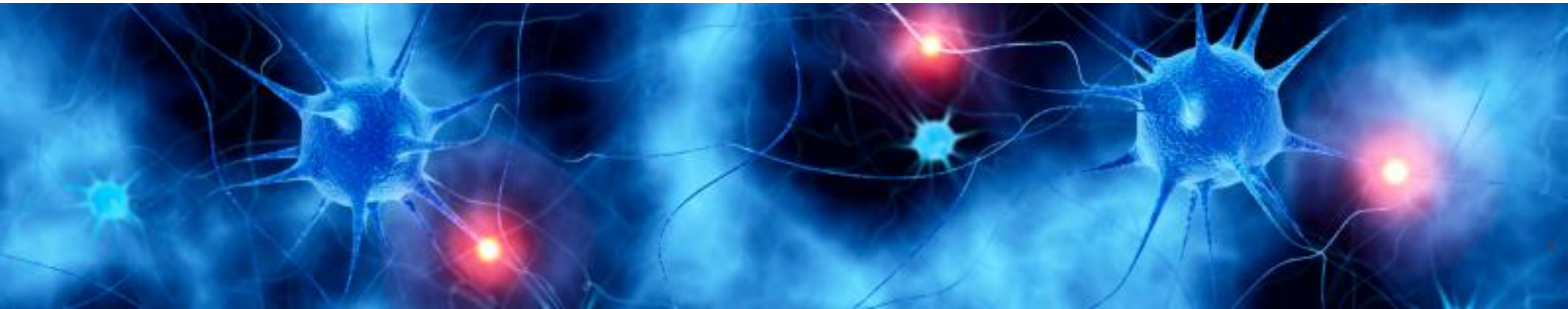
- Protocol submitted for EU regulatory approval in Q2 2020

Brainstorm's Growing Pipeline

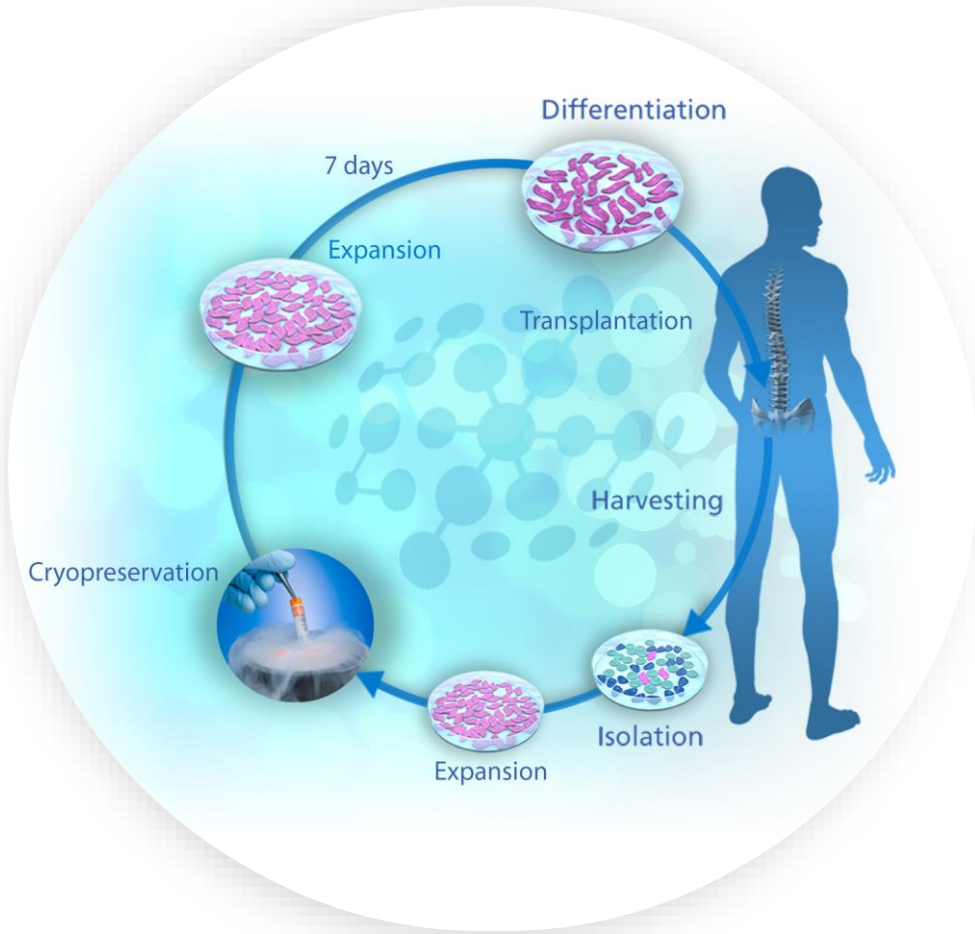
Indication	Preclinical	IND Enabling	Phase 1	Phase 2	Phase 3	Next Milestones
NurOwn® MSC-NTF Cells Platform						
ALS						Q4'20E Top-line data
Progressive MS						Q4'20E Top-line data
Alzheimer's Disease						CTA: Q2'20E Phase 2: 2H'20E
Parkinson's Disease						
Huntington's Disease						
Autism Spectrum Disorder						
Peripheral Nerve Injury						
MSC-NTF Cell Exosome Platform						
ARDS						

NurOwn[®] Technology Platform

Best-in-class autologous cell therapy



NurOwn[®] Manufacturing: Fast, Consistent and Reproducible

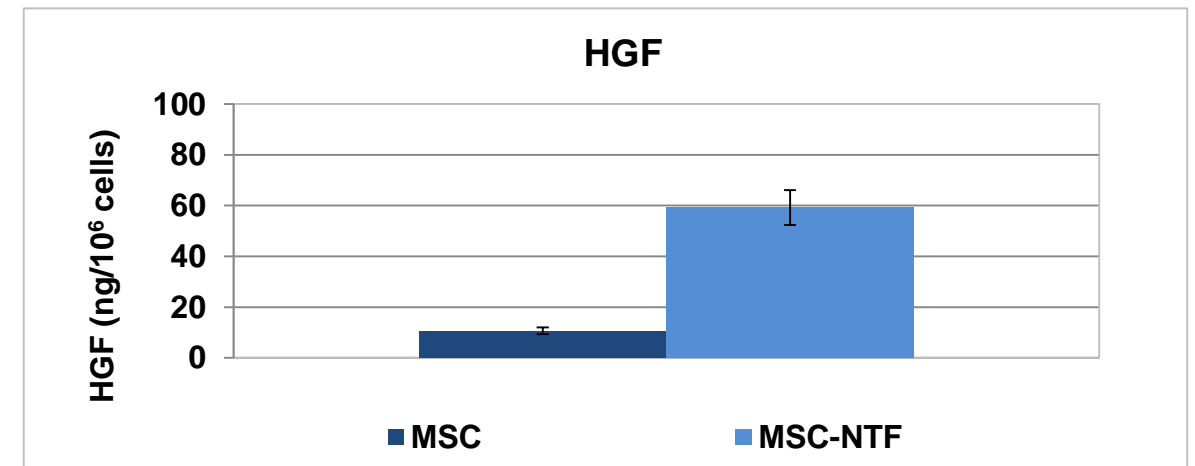
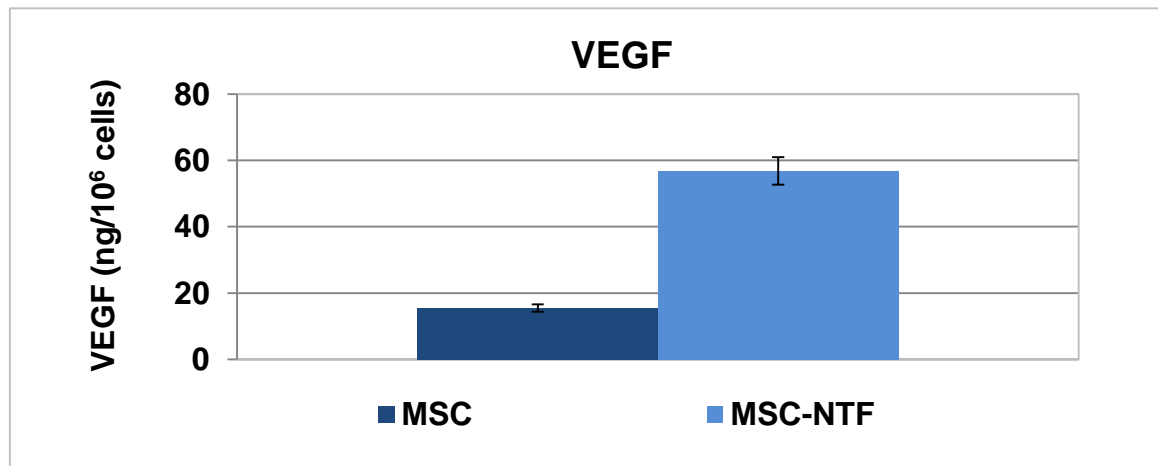
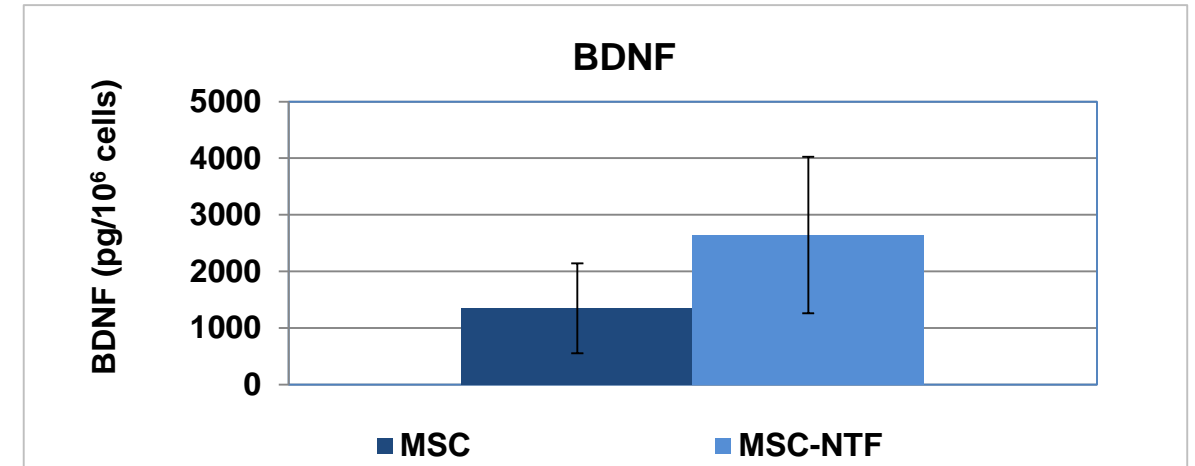
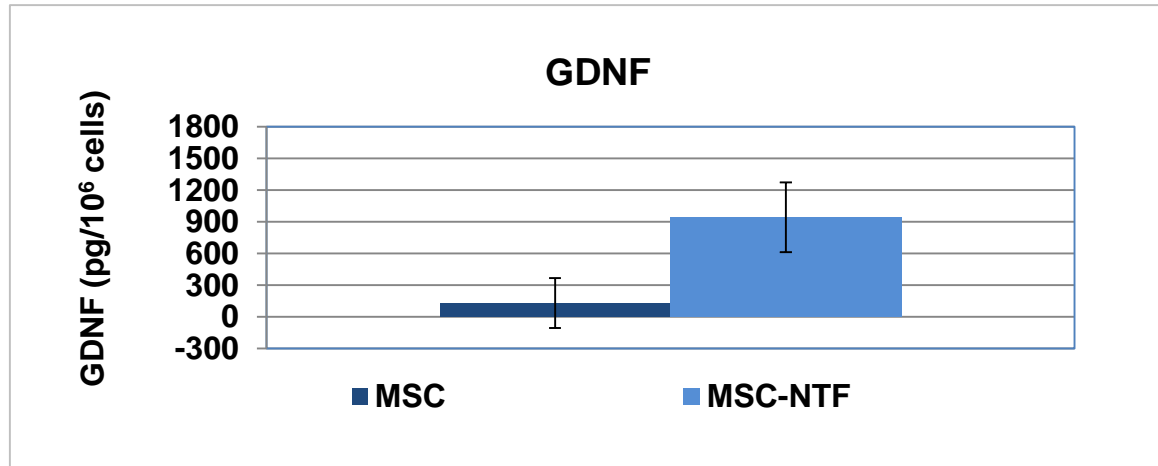


1. **Harvesting:** Outpatient procedure for **collection** of patient's bone marrow sample
2. **Isolation & Expansion:** Mesenchymal **stem cells** (MSCs) isolated from the total bone marrow sample and MSCs expanded ex-vivo (**12 days**)
3. **Cryopreservation:** Creates an off the shelf product for each patient, enabling **retreatment** for up to 3 years.
4. **NurOwn Production:** MSCs are thawed, expanded, and **induced** to differentiate into MSC-NTF cells optimized to secrete neurotrophic factors. (**7 days**)
5. **NurOwn Administration:** MSC-NTF cells are CSF delivered back into patient at or near the site of damage

Total time from harvest to treatment is **19 days**

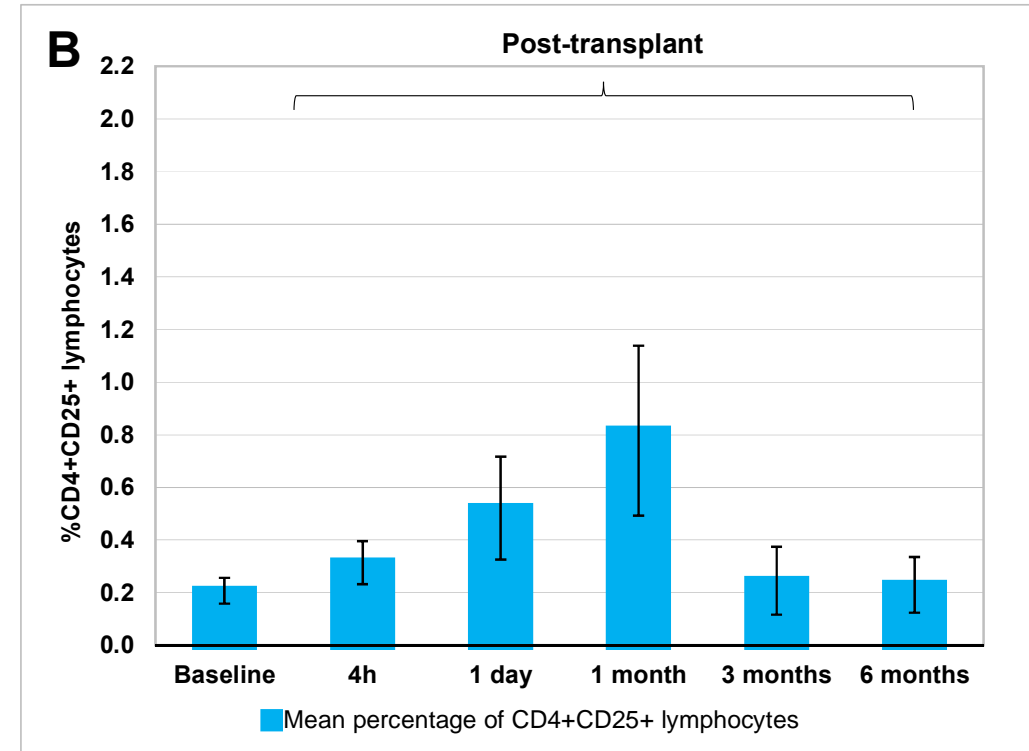
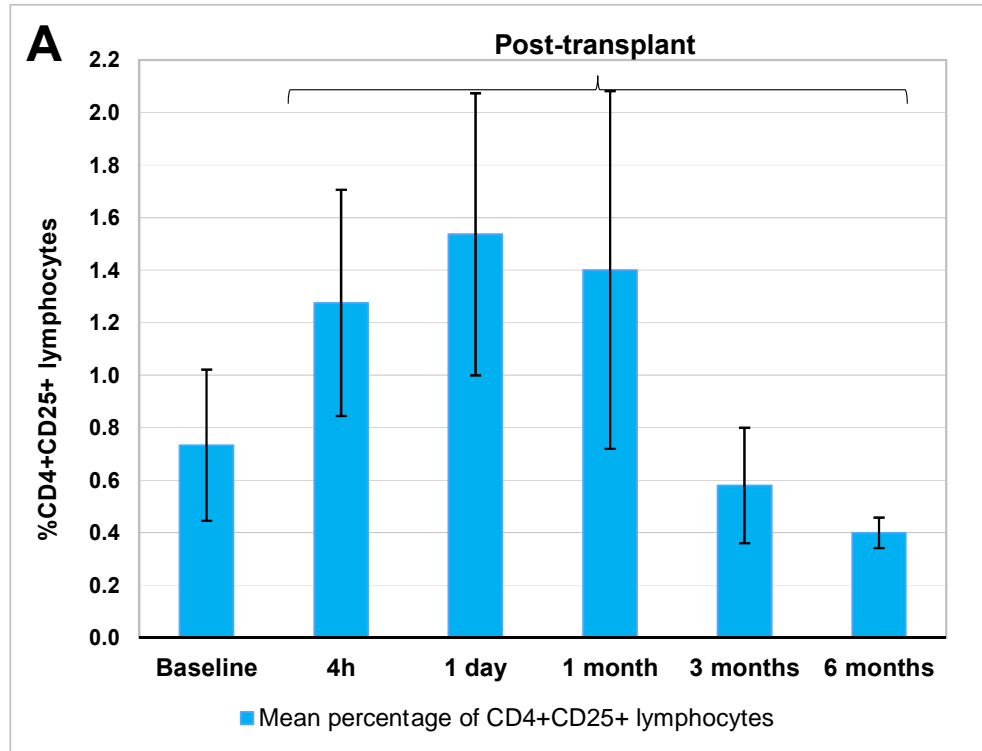
NurOwn[®] Effect on MSC-NTF Neurotrophic Factors

n=28 ALS Patients



GDNF: Glial cell line derived neurotrophic factor; BDNF: Brain-derived neurotrophic factor; VEGF: Vascular Endothelial Growth Factor; HGF: Hepatocyte growth factor.
Data from ALS Phase 1/2 and Phase 2a studies.

NurOwn[®] Promotes Expansion of Anti-inflammatory Treg Cells

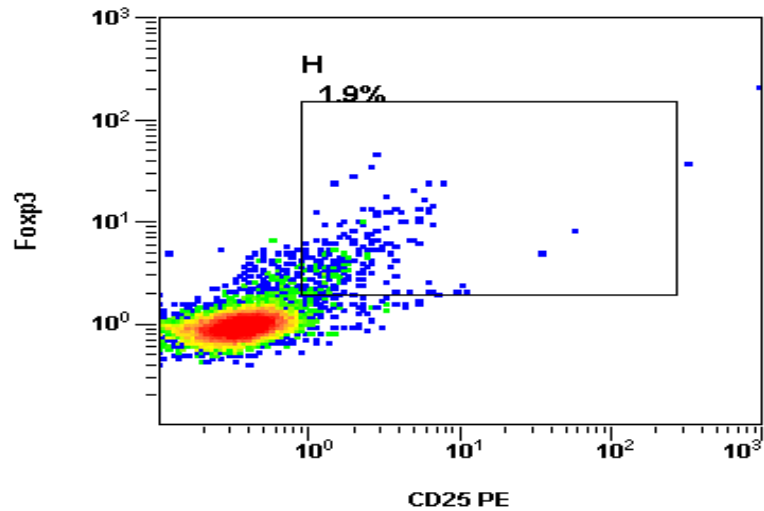


T Regulatory Cells Increased in Phase 1/2a

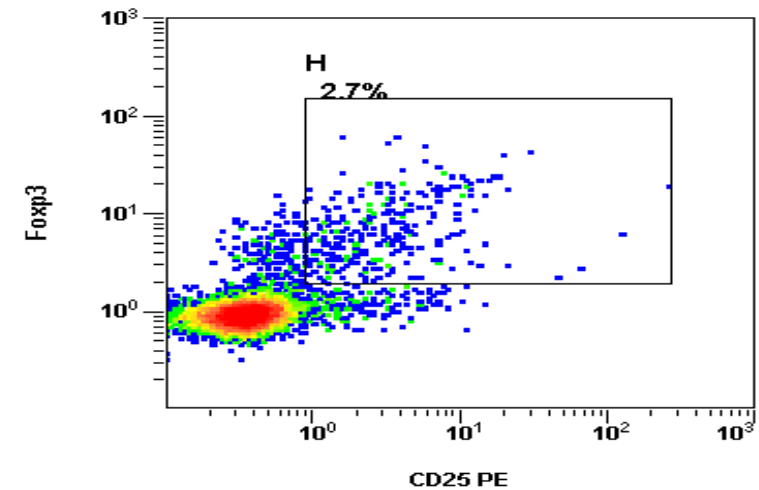
Mean percentage \pm SEM of peripheral blood lymphocytes stained positive for CD4 and CD25 surface markers (double staining) using FACS analysis, in ALS patients treated with MSC-NTF cells, in the Phase 1/2 trial (A) and in the Phase 2a (B) study at the indicated pre- (baseline) and post-treatment time-points.

NurOwn[®] *in vitro* Induction of Regulatory T cells

PBMC only



PBMC co-cultured with MSC-NTF



T Regulatory Cells Increased In-vitro

Representative FACS analysis of double positive FoxP3 and CD25 cells in a gate of CD4+ cells showing an increase of regulatory T cells (CD4+ CD25+FoxP3+), after co-culture of Peripheral Blood Mononuclear Cells (PBMC) with MSC-NTF cells (right panel).

NurOwn® MOA: Broadly Applicable Across Neurodegenerative Diseases

Underlying pathologies of ALS, MS, and AD

Neuronal Degeneration

Astrocyte Dysfunction and Loss of Neurotrophic Support

Neuroinflammation and Microglial Activation



NurOwn MSC-NTF MOAs

Neuroprotection

Reduces CSF Caspase-3

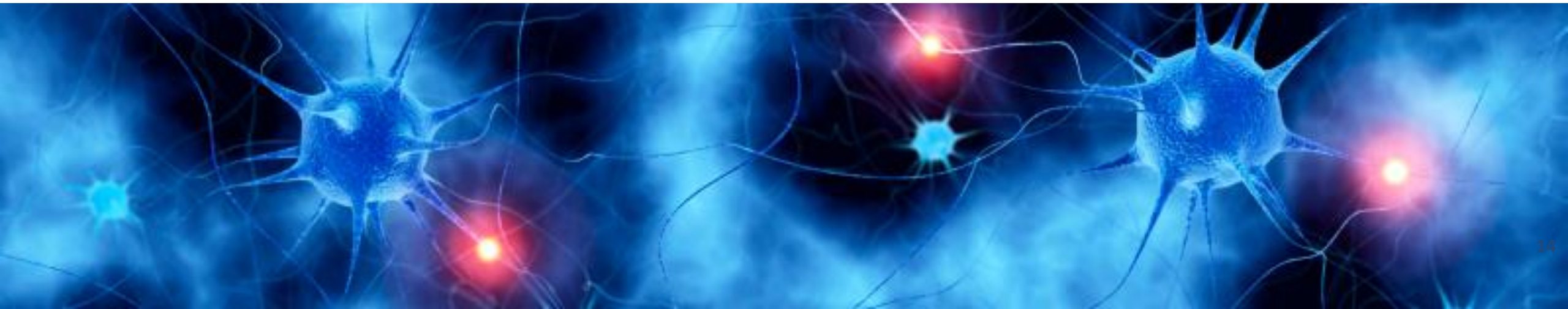
Enhanced delivery of NTFs

Increases CSF VEGF, HGF, LIF, BDNF, GDNF

Immunomodulation

Reduces CSF MCP-1, SDF-1, CHIT-1

NurOwn® for the Treatment of Amyotrophic Lateral Sclerosis (ALS)



ALS: High Unmet Medical Need



Disease and Symptoms

Progressive neurological disorder with many symptoms including progressive muscle weakness, difficulty breathing, and death. Severity of collective symptoms is measured via the ALSFRS-R functional score



Life Expectancy

3 - 5 years from diagnosis; median survival from diagnosis ~30 months



Prevalence

30,000 patients in the U.S.
450,000 patients globally
Most likely to effect males over 50+ years of age

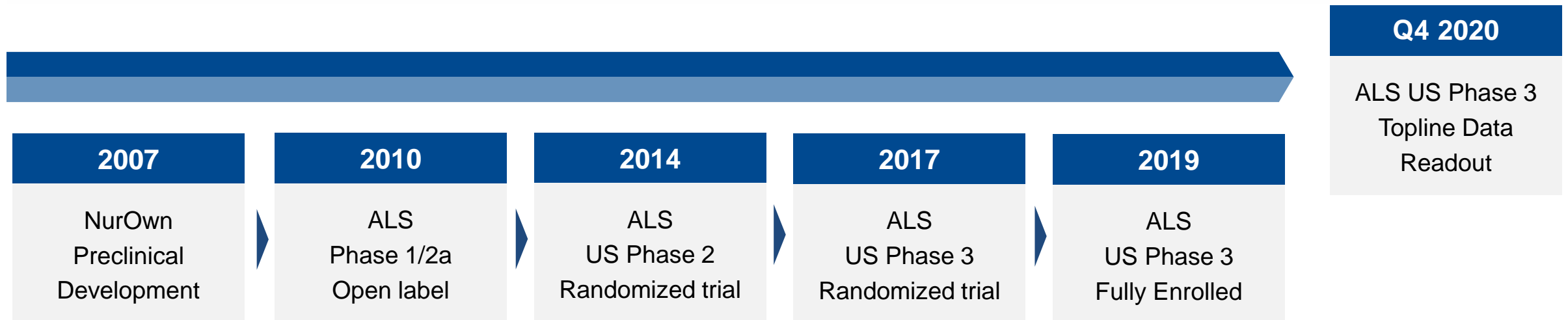
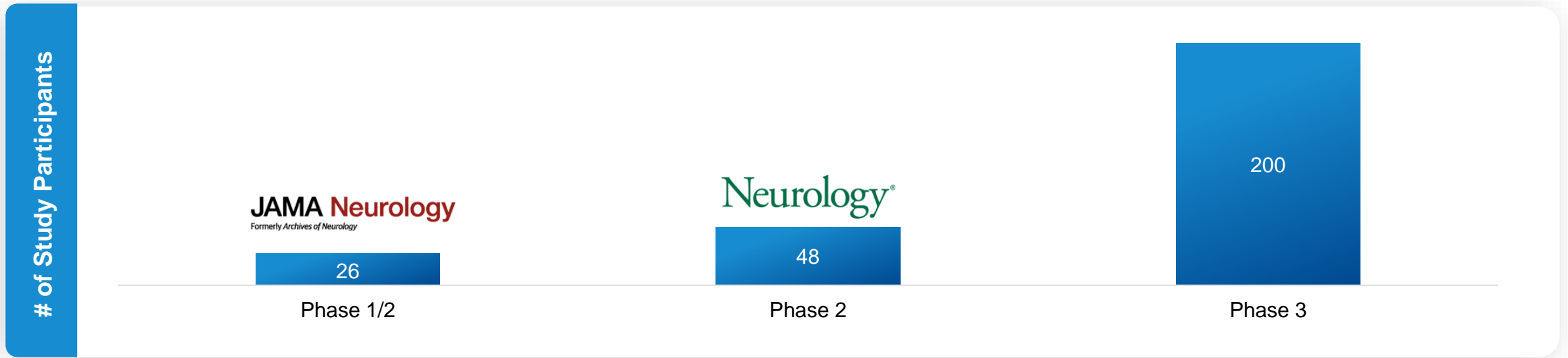


Current Standard of Care

Riluzole: No observed effect on function (ALSFRS-R score); Improves 18 month survival by ~3 months

Edaravone: Reduces rate of ALSFRS-R decline (~33%) over 6 months, approved by FDA in 2017

NurOwn® in ALS: 10+ Years Clinical Development



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

Validated and Regulatory Accepted Measure of ALS Function

48-point scale with 4 domains

- Respiratory, fine motor, bulbar, gross motor
- 12 different items (scored 0-4) - rate of disease progression over time

Validated approvable questionnaire-based tool

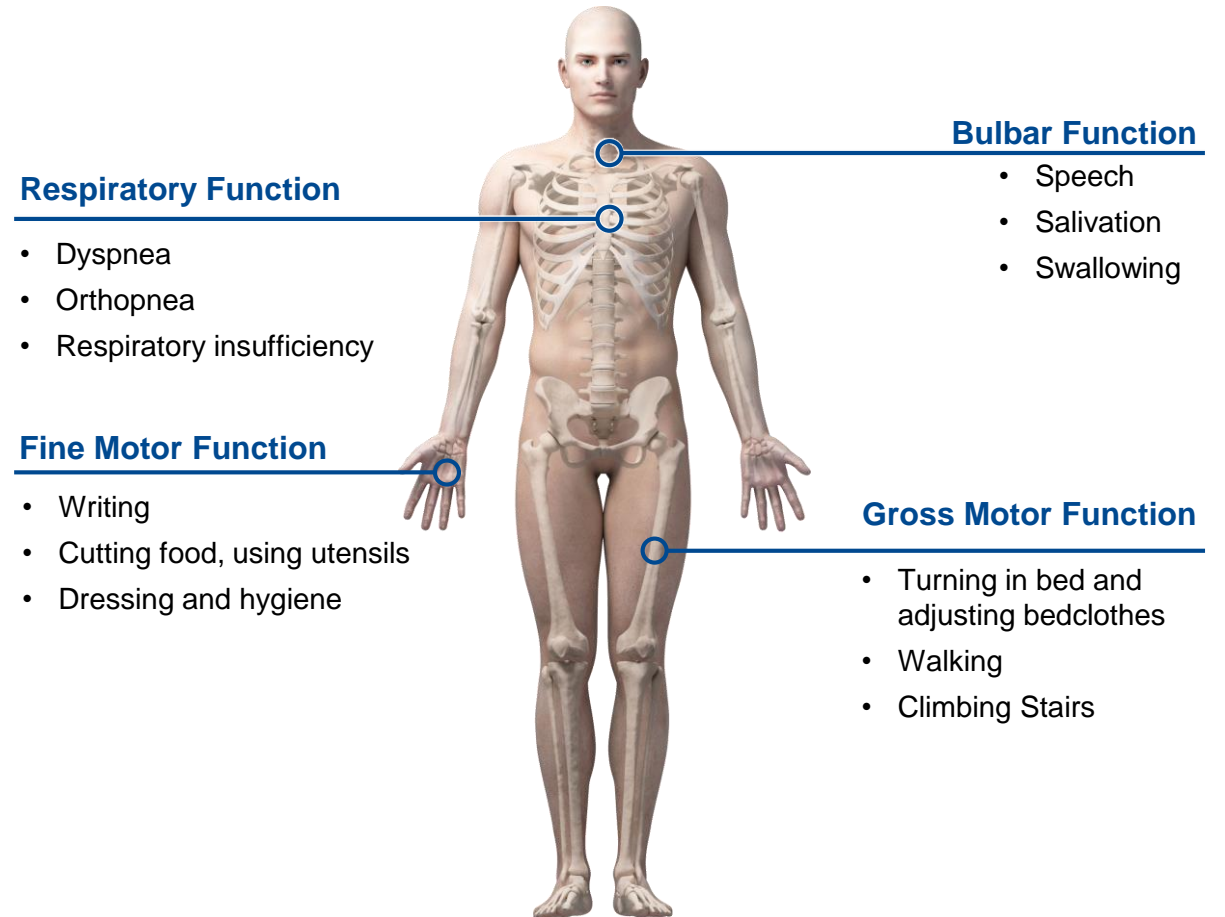
- Used as basis for approval of Radicava in [2017](#) with mean score change at 24 weeks as primary endpoint
- Data from the PRO-ACT database shows the average rate of ALSFRS-R decline is 1.02 points/month²
- Change in ALSFRS-R slope (rate of disease progression) >20-25% is clinically meaningful¹

Primary endpoint for Phase 2 and Phase 3

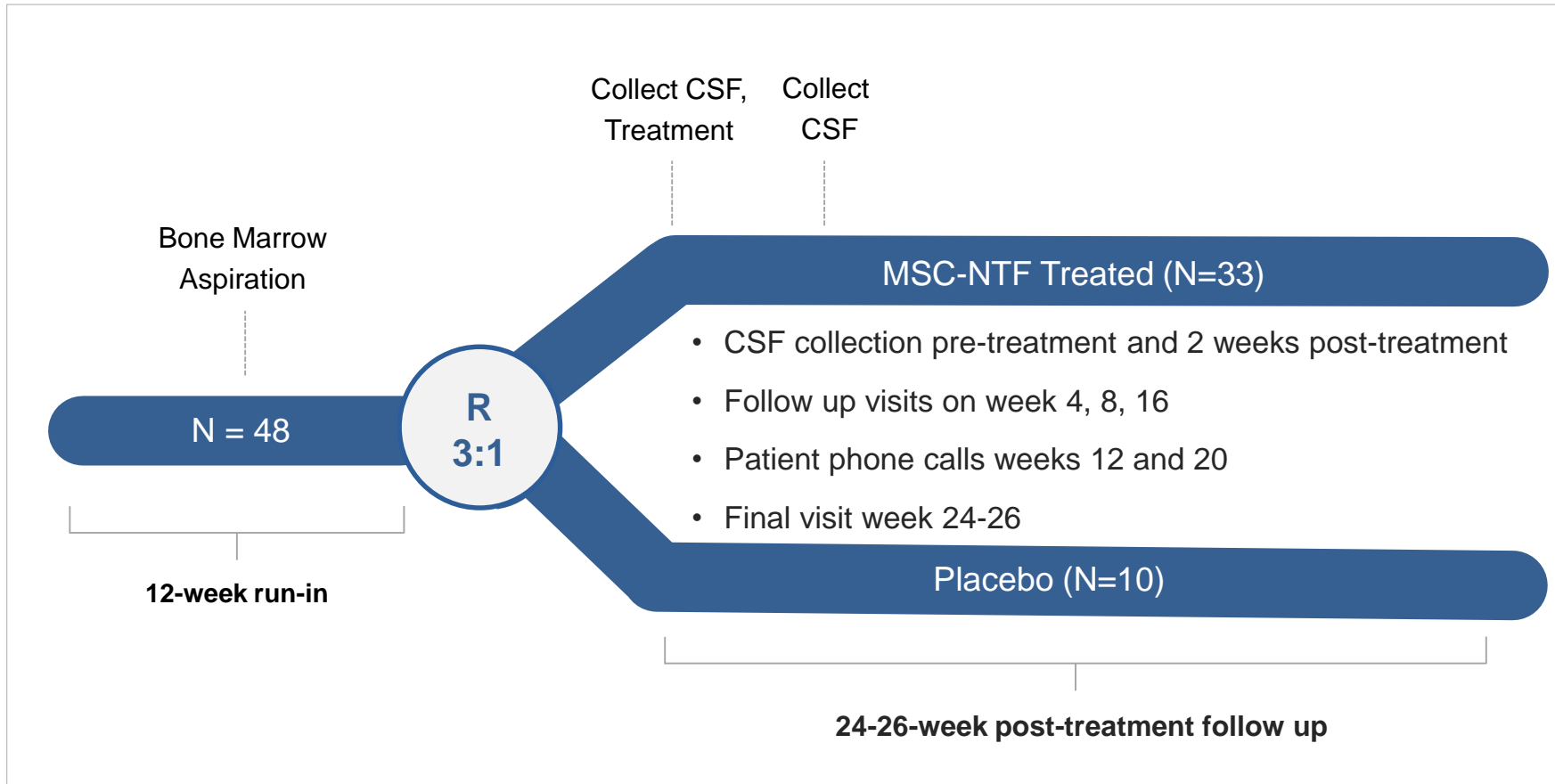
- **Phase 2:** change in rate of disease progression (ALSFRS-R slope) determined at 24-weeks.³
- **Phase 3:** Responder analysis – change in ALSFRS slope at 28-weeks.

[Link](#)

1. Castrillo-Viguera C, Grasso DL, Simpson E, et al. Clinical significance in the change of decline in ALSFRS-R. *Amyotroph Lateral Scler.* 2010;11(1-2):178-180
2. Atassi N, Berry J, Shui A, et al. The PRO-ACT database: design, initial analyses, and predictive futures. *Neurology.* 2014;83:1719-1725
3. NurOwn, phase 2, randomized, clinical trial in patients with ALS. Safety, clinical, and biomarker results James D. Berry, et.al. *Neurology* Dec 2019, 93 (24) e2294-e2305



NurOwn[®] ALS Phase 2 Trial Design



- No deaths or treatment related serious adverse events (SAEs)
- No dropouts related to SAEs
- Most common adverse events transient and mild/moderate severity and procedure related

Patients completing follow up

43

Primary Endpoint

Safety & Tolerability

Secondary Endpoint

Treatment vs. placebo changes in:

ALSFRS-R slope

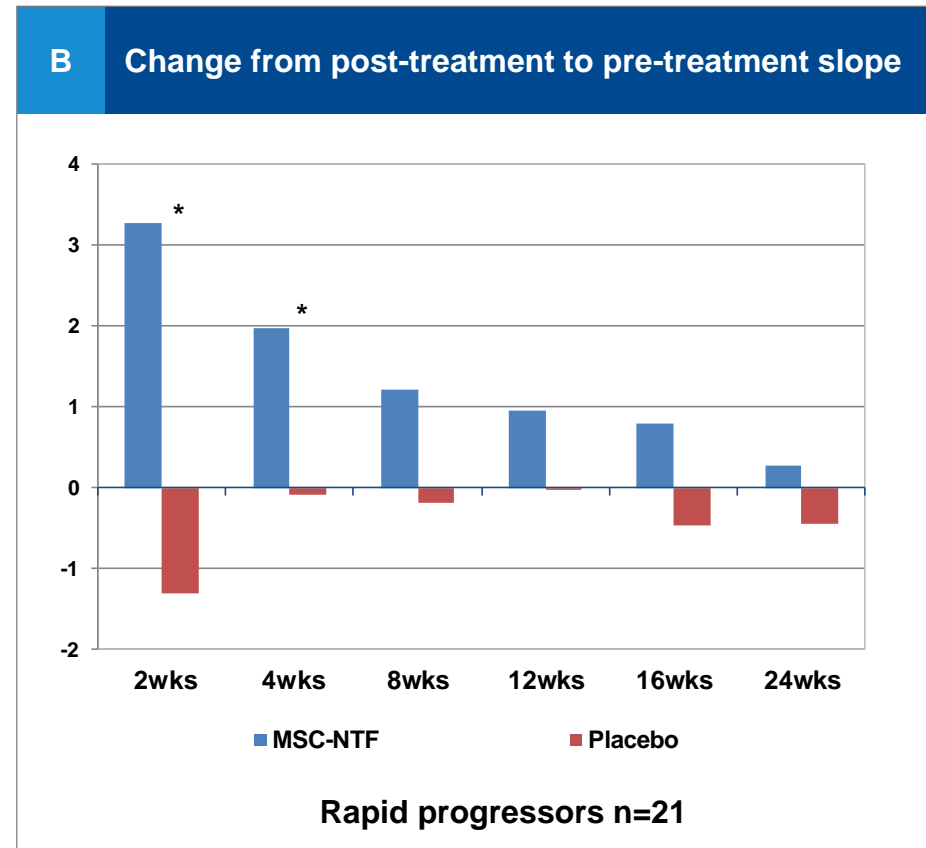
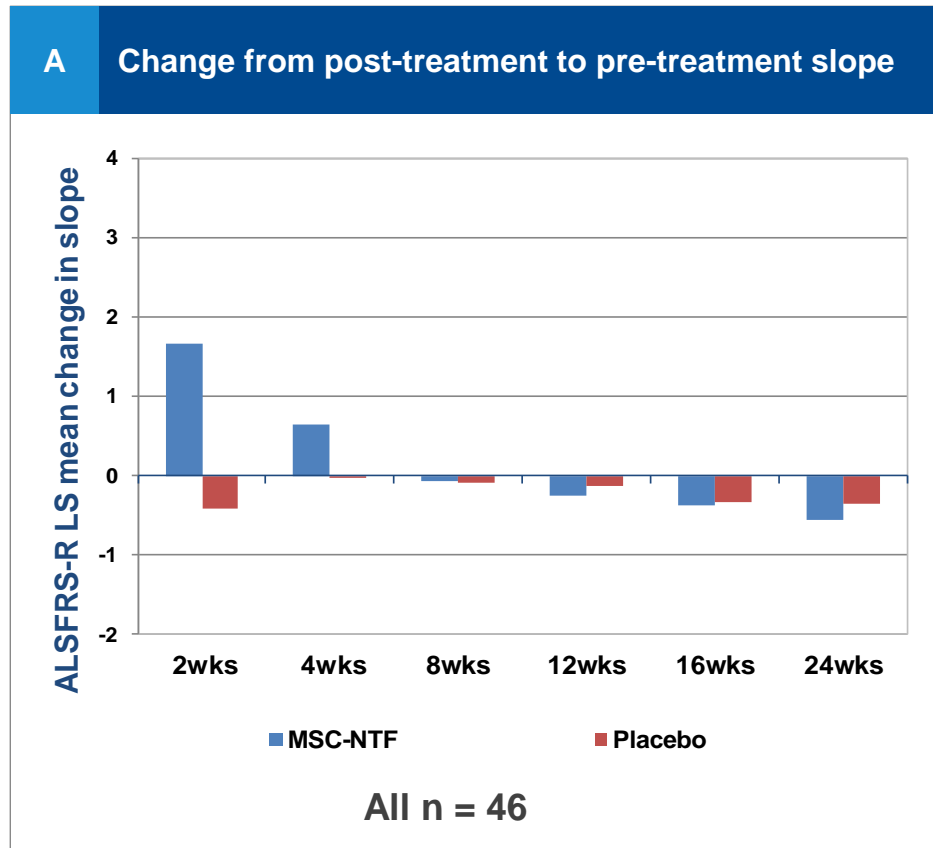
Slow Vital Capacity

Fast progressor criteria:
Pre-specified as participants with > 2-point decrease in the 3 months lead-in period

Phase 2 Outcomes: Greater Efficacy Observed in Rapid Progressors

Phase 3 has enrolled only rapidly progressing patients

Single dose NurOwn® slowed the rate of disease progression by improving the ALSFRS-R LS mean change in slope vs. pre-treatment slope

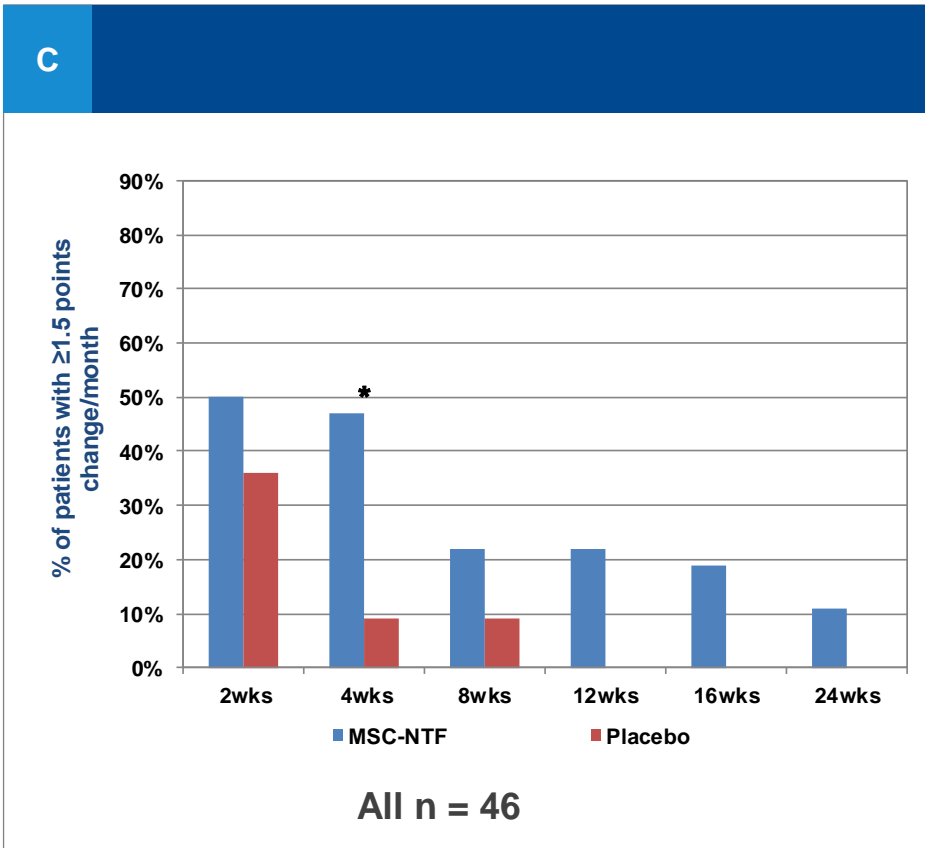


- Primary safety endpoint met
- Efficacy demonstrated in ALSFRS-R, a measure of ALS function
- Multiple doses will be needed

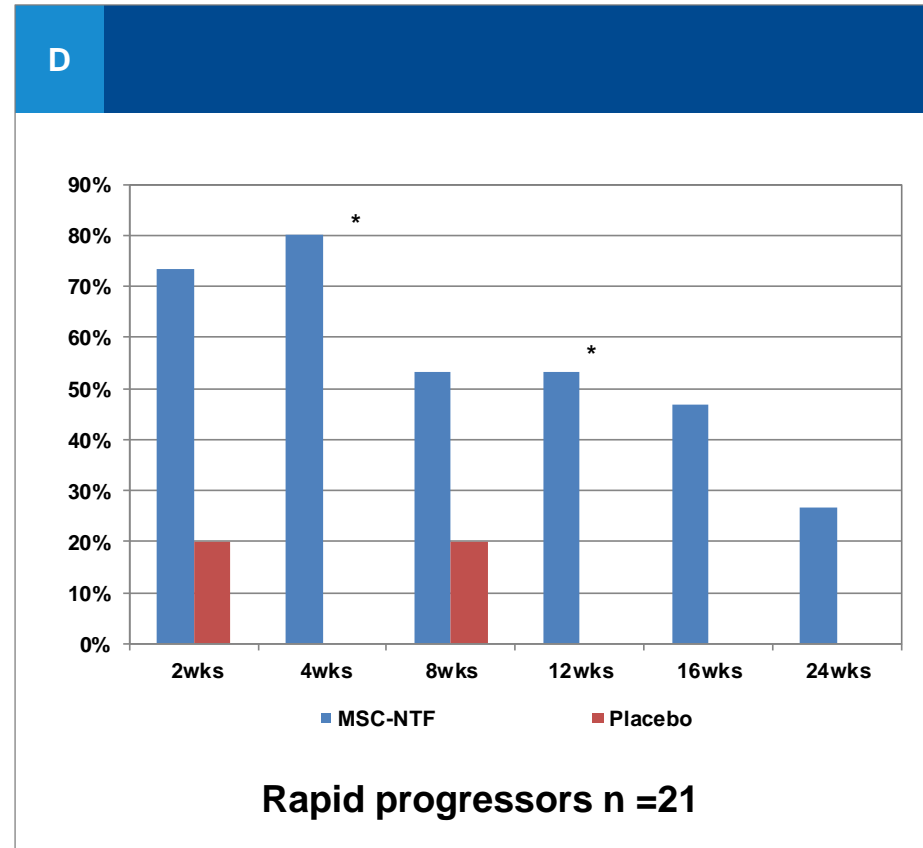
■ MSC-NTF ■ Placebo

Phase 2 Responder Analysis: Improved Outcomes in Rapid Progressors

Responder defined as ≥ 1.5 point/month ALSFRS-R slope improvement



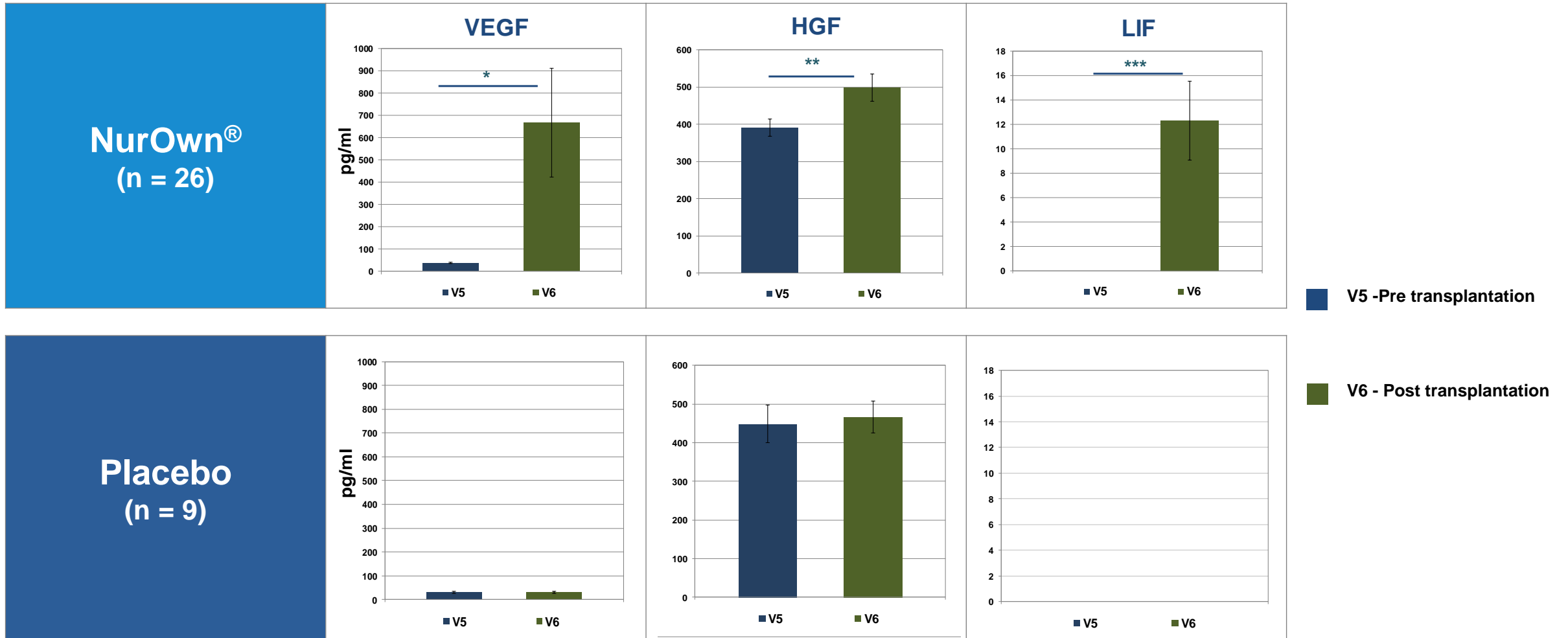
■ MSC-NTF ■ Placebo



- Prespecified responder analyses defined as a 20%–30% improvement in post-treatment slope compared to pretreatment
- A higher proportion of responders were observed in the MSC-NTF cells group compared to placebo at all time points
- In the rapid progressors subgroup, a higher proportion of responders (≥ 1.5 points/month ALSFRS-R slope improvement) were observed in the MSC-NTF group compared to the placebo group at all time points

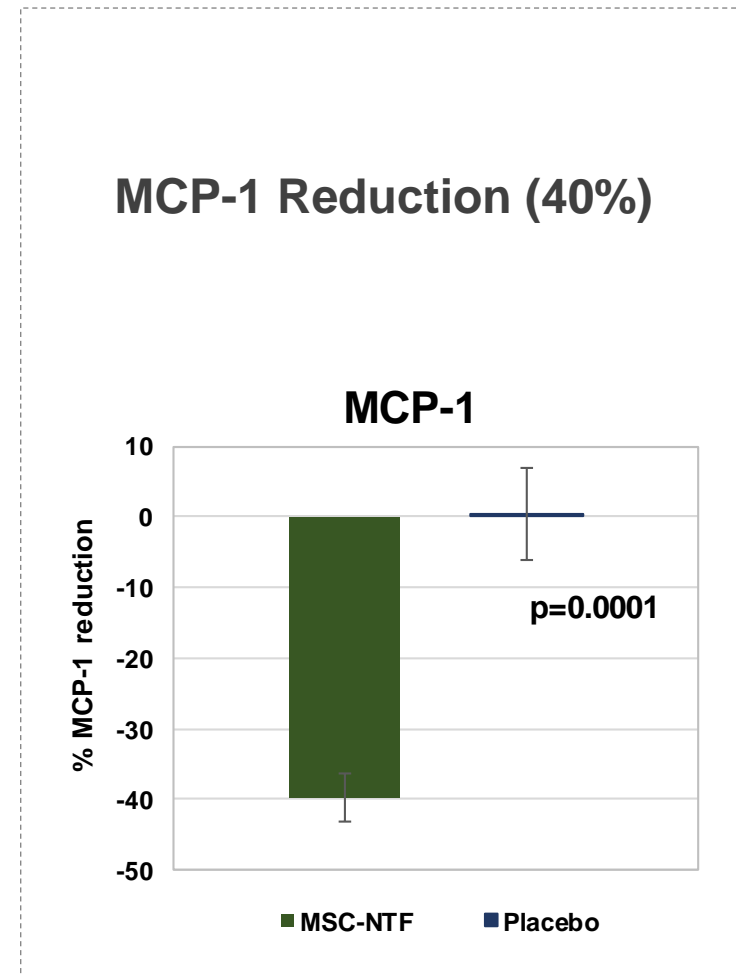
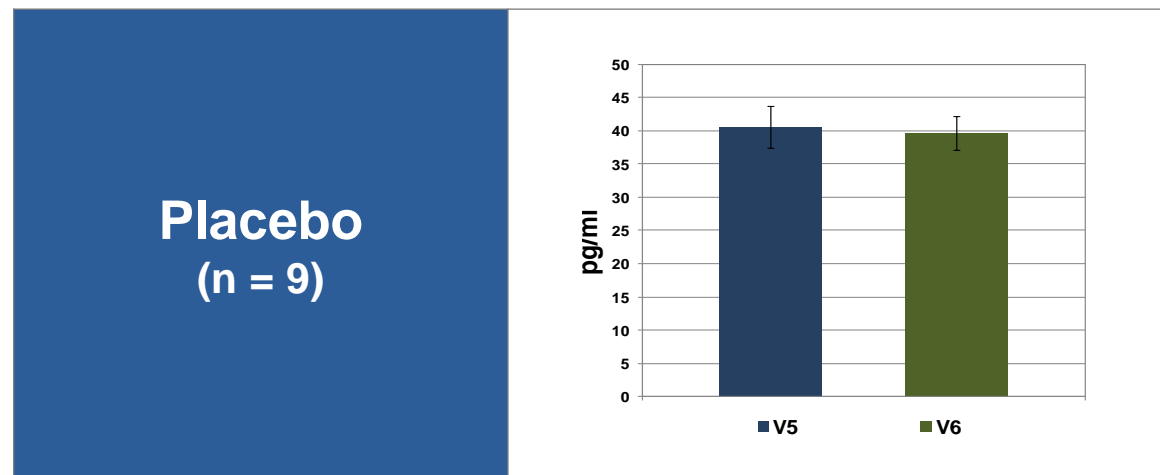
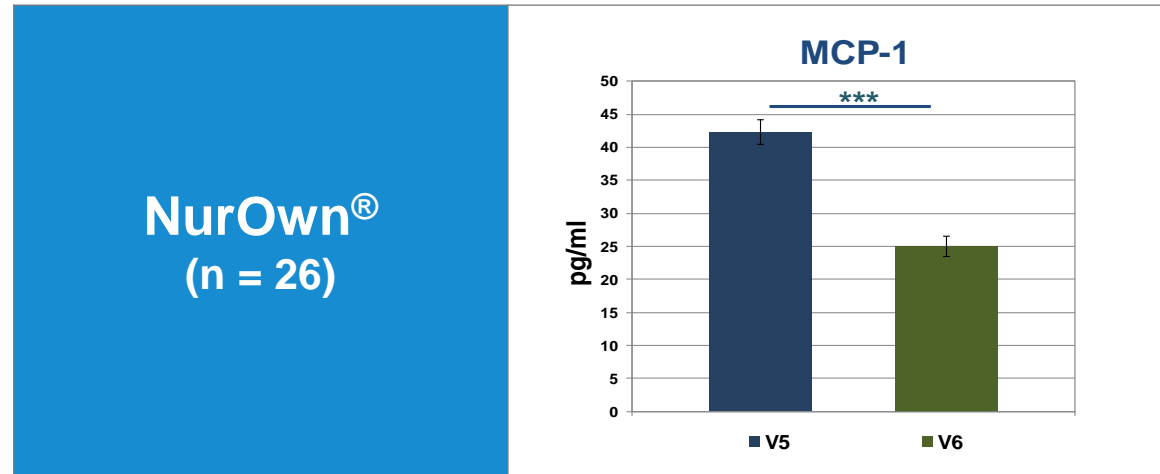
Phase 2 Biomarker Analysis

CSF Profile 2 Weeks Post Treatment Demonstrates Delivery of NTFs



Phase 2 Results in ALS

MCP-1 (an inflammatory mediator) is Significantly Reduced 2 Weeks Post-Treatment



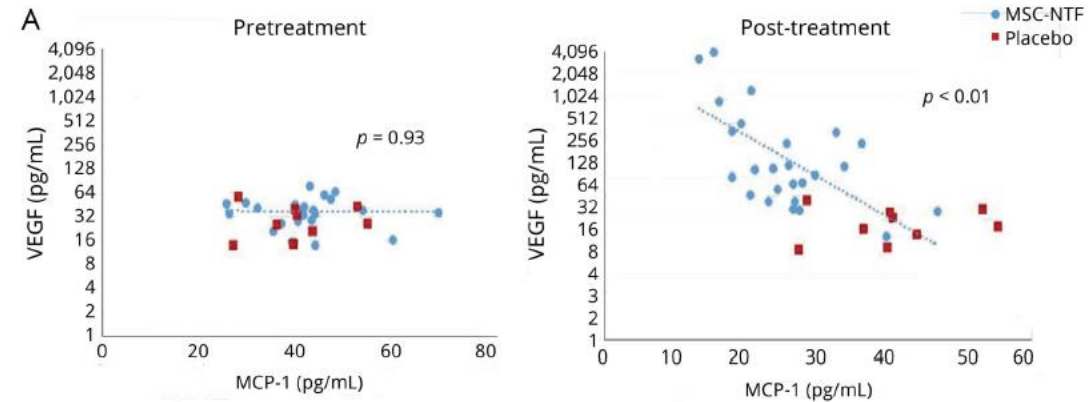
■ V5 - Pre transplantation
■ V6 - Post transplantation

*p<0.05, **p<0.01, ***p<0.001

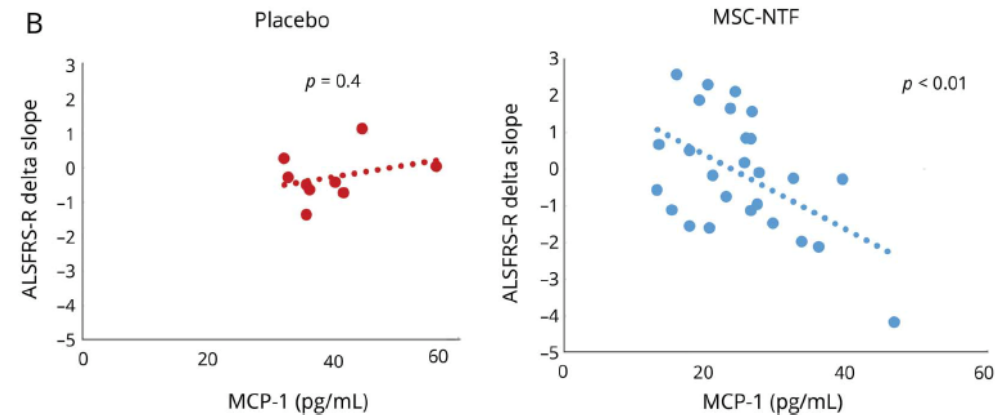
Phase 2 CSF Biomarker Results in ALS

Post-Treatment CSF MCP-1 Shows Inverse Correlation with CSF VEGF and with ALSFRS-R slope improvement

CSF MCP-1 inverse correlation with CSF VEGF



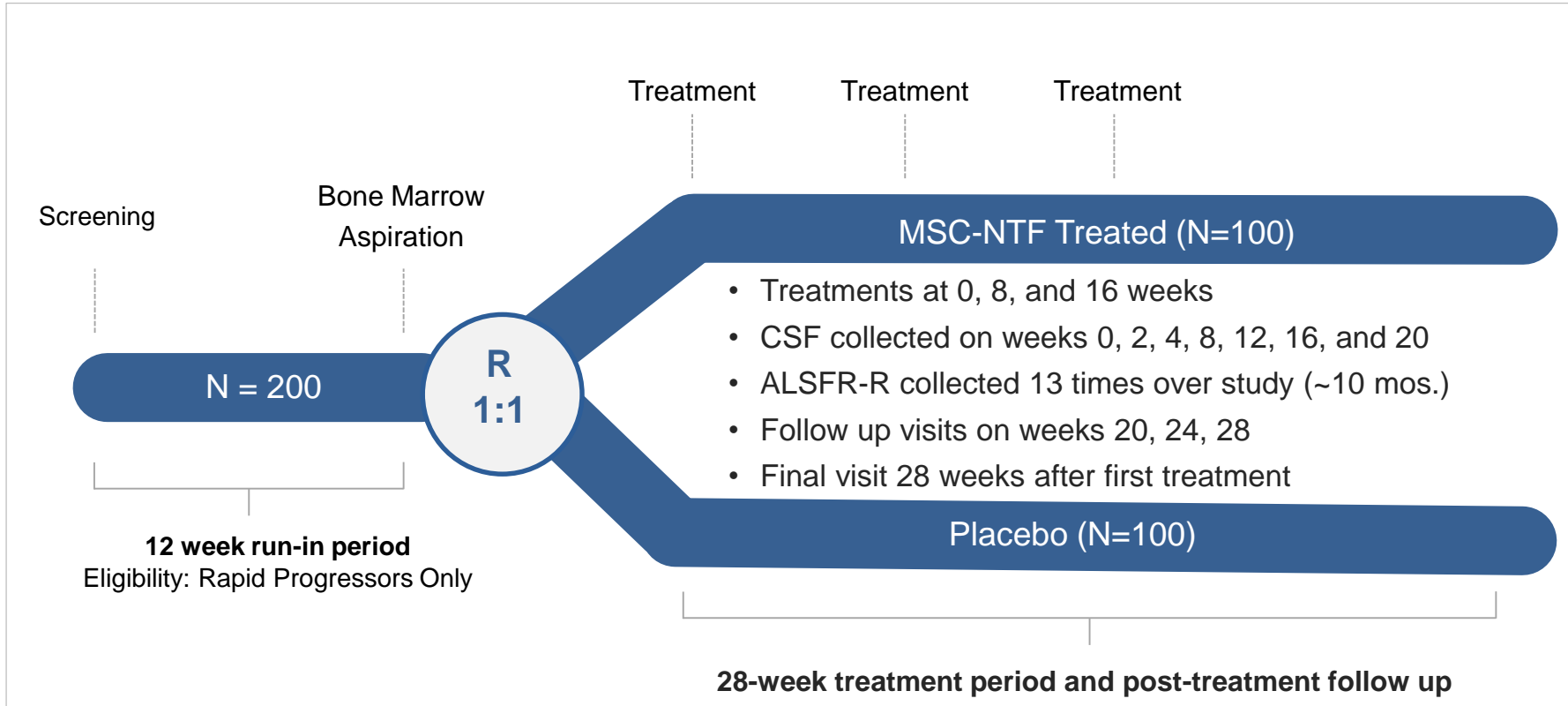
CSF MCP-1 inverse correlation with ALSFRS-R Slope Improvement



NurOwn[®] ALS Phase 3 Trial Design

Topline Data Expected Q4 2020

Phase 3 was designed based on safety, efficacy and durability data from Phase 2



Primary Endpoint

A responder analysis of the rate of decline as assessed by ALSFRS-R

Secondary Endpoints

Safety

ALSFRS-R change from baseline

Slow vital capacity

Tracheostomy-free survival

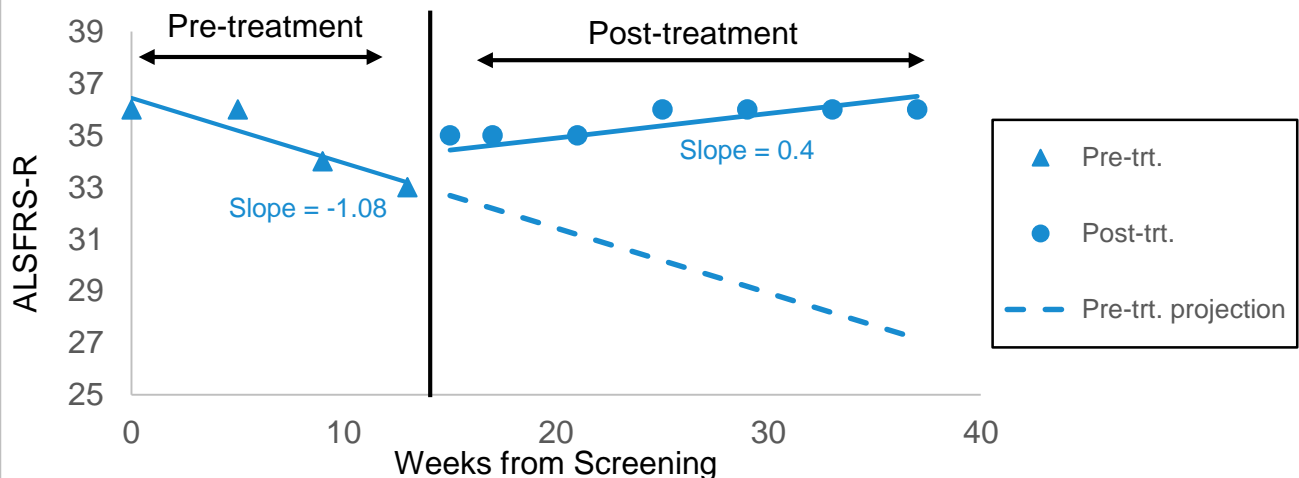
CSF/biomarkers

- Trial fully enrolled; dosing complete
- No COVID-19 related delays
- Adequately powered

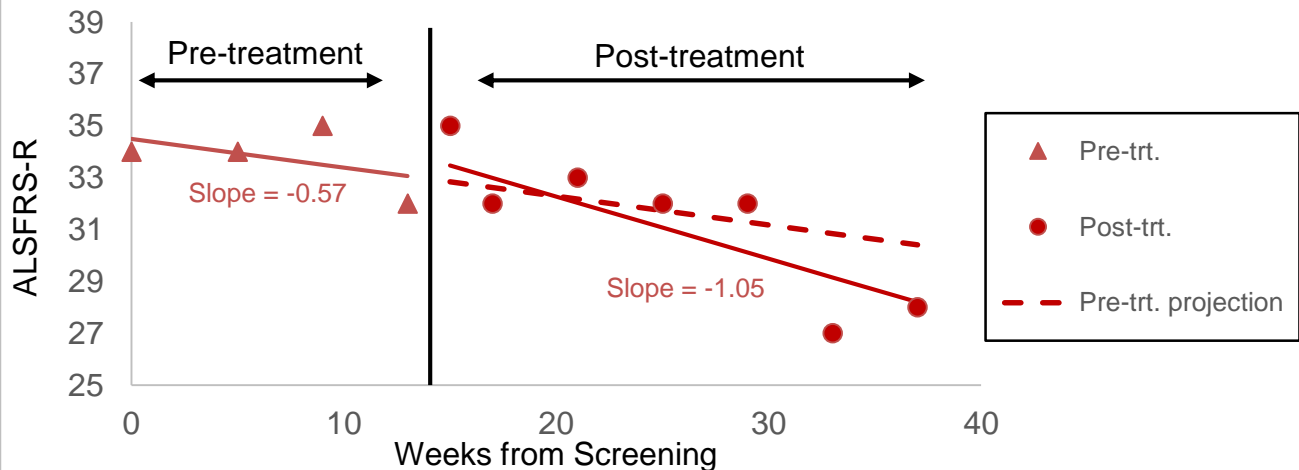
ALS Phase 3 Primary Endpoint Illustration – Responder Analysis

Slope represents the *rate* of functional decline per month for each patient

Patient 1 (NurOwn®)



Patient 2 (Placebo)



Patient	Treatment	Pre-trt Slope	Post-trt Slope	Diff. in Post vs. Pre-trt Slope	Responder (Diff. ≥ 1.25)
1	NurOwn	-1.08	0.4	1.48	Yes
2	Placebo	-0.57	-1.05	-0.48	No

Responder Analysis Using Logistic Regression

Regression Covariates from literature:

- Treatment
- Baseline ALSFRS-R
- Duration - onset of symptoms to first treatment
- Site of onset
- Riluzole use
- ALSFRS-R pre-treatment slope

Phase 3 ALS Trial: Two Manufacturing Sites, Six Treatment Centers

Manufacturing Sites



City of Hope Center for Biomedicine & Genetics

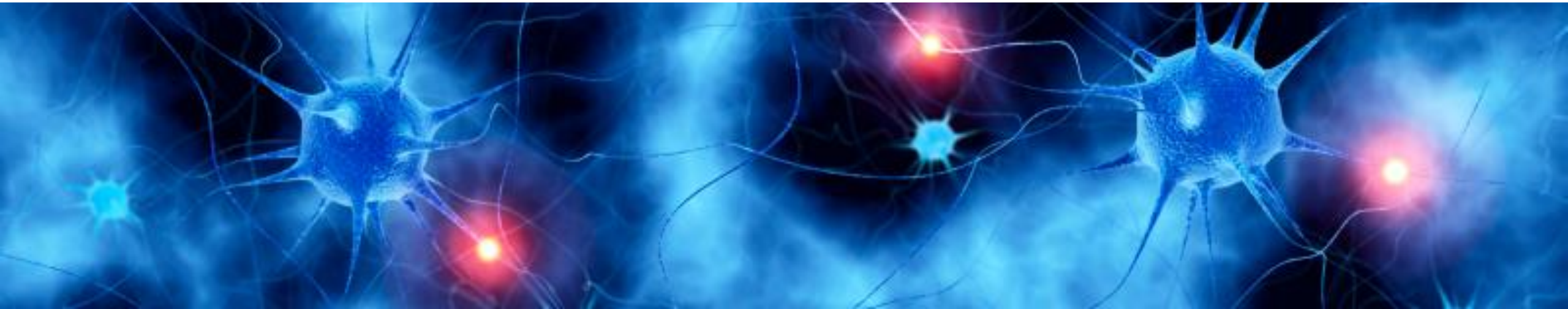


Dana-Farber Harvard Cancer Center
Cell Manipulation Core

Treatment Centers



NurOwn[®] for the Treatment of Progressive Multiple Sclerosis



Progressive MS: High Unmet Medical Need



Disease and Symptoms

Progressive neurological disorder with the brain's inability to control one's body. Symptoms include pain, electric shock sensations, muscle weakness, trouble walking, vision problems, numbness, dizziness, balance etc.



Life Expectancy

5-10 years lower than average; diagnosis with progressive MS sets you on a lifelong journey with one or more of the above listed symptoms



Prevalence

500,000 patients in the U.S.

1,250,000 patients globally

Women are more likely to be diagnosed with MS than men



Current Treatment

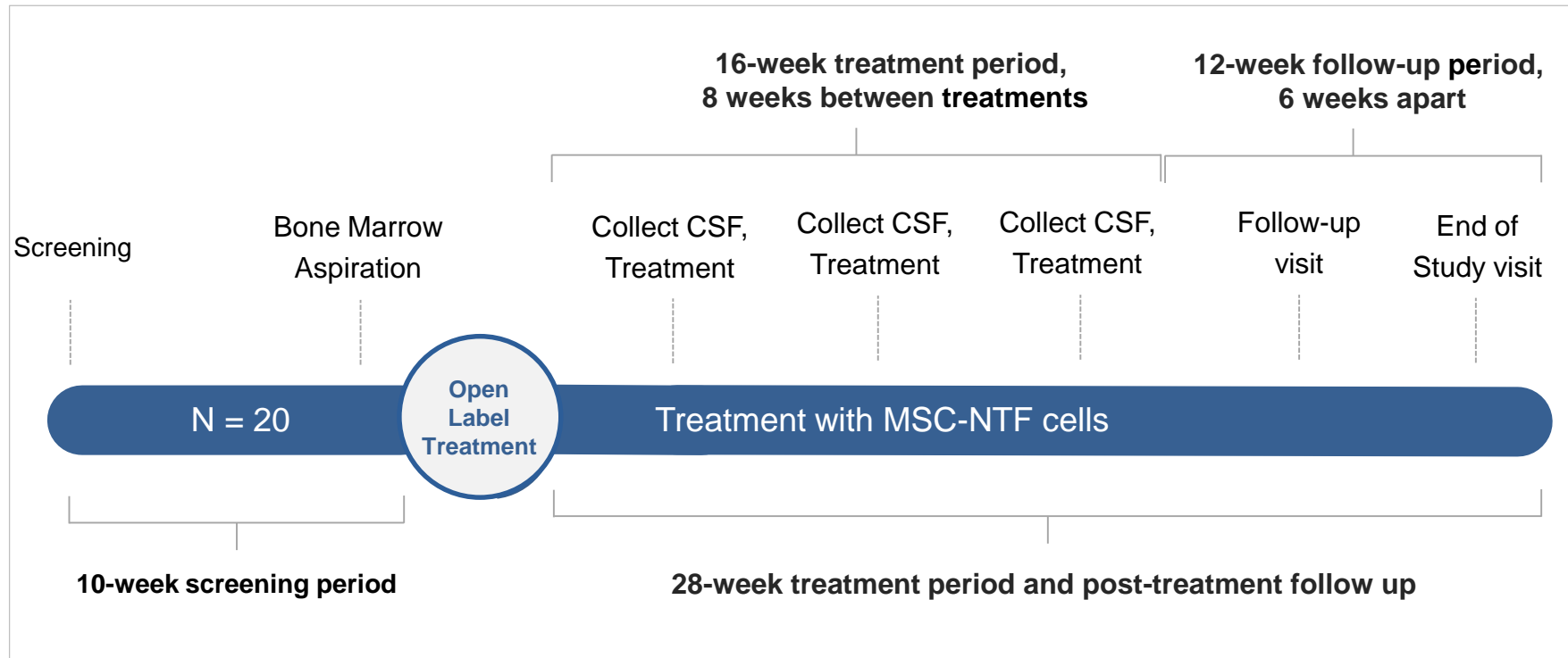
Progressive MS is less studied with only one approved drug - **Ocrelizumab (Ocrevus)**

- Ocrevus reduces disability from getting worse on average by 25% vs placebo which shows the remaining high unmet need and need for additional treatments
- Ocrevus is an immunosuppressor: Increases the risk of infection and increases risk of cancer in a smaller proportion of patients
- Several other chemotherapeutic agents available, but have significant toxic side-effects

NurOwn[®] Progressive MS Phase 2 Trial Design

Topline Data Expected Q4 2020

Phase 2 study to evaluate the safety and efficacy of NurOwn[®] in Progressive MS



Primary Outcome

Safety

Secondary Outcomes

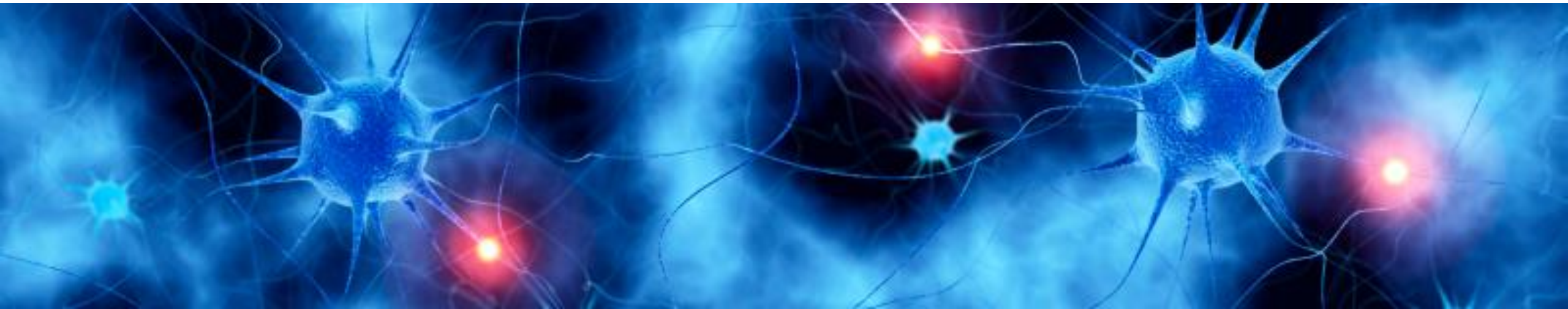
Biomarkers

Changes from baseline in

Timed 25 foot walking speed

9 hole peg test

NurOwn[®] for the Treatment of Prodromal to Mild Alzheimer's Disease



Alzheimer's Disease: High Unmet Medical Need



Disease and Symptoms

Progressive central nervous system disorder. Symptoms include difficulty learning new information, mood changes, severe disorientation, memory loss, behavior changes, and difficulty speaking, swallowing and walking



Life Expectancy

On average 3-11 years following diagnosis, with the above symptoms progressing over time



Prevalence

>5M patients in the U.S.; >7.5M in EU

US: Projected to grow to 13.8M by 2050; EU: Projected to grow to 13.1M by 2040



Current Treatment

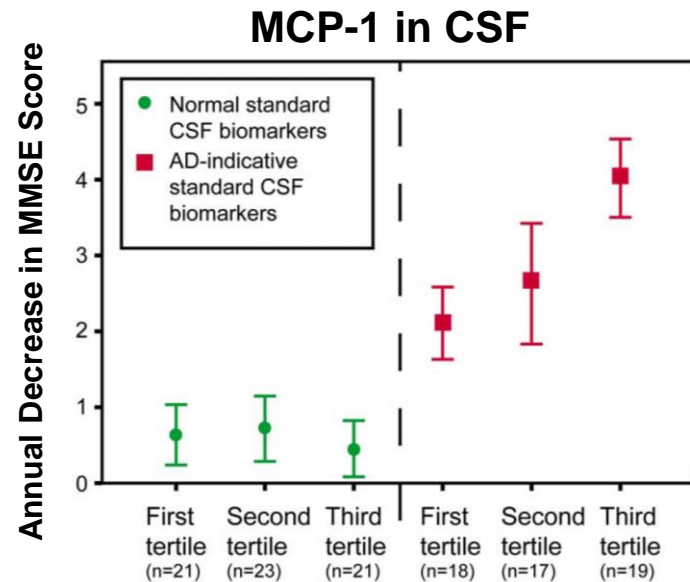
Currently no FDA approved therapies to stop or slow the progression of Alzheimer's Disease

Approved therapies for Alzheimer's patients that only treat symptoms include Aricept[®], Razadyne[®], Exelon[®], Namenda[®], and Namzaric[®]

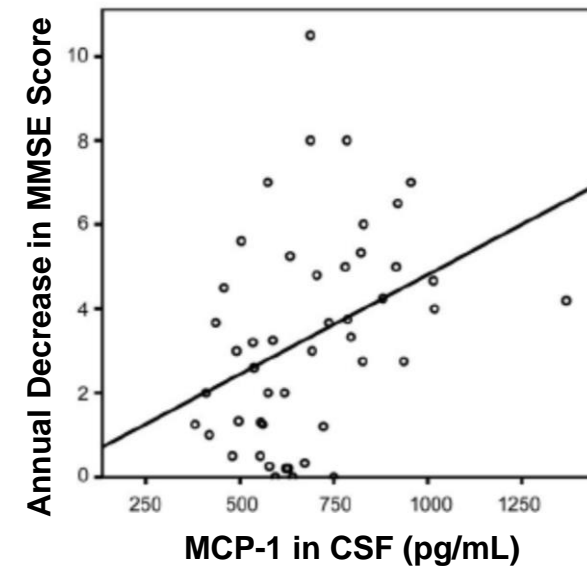
NurOwn[®] induced decrease in MCP-1 may address AD pathology

NurOwn[®] treatment decreases CSF MCP-1, which increases with disease severity in AD patients

CSF MCP-1 is increased in AD¹



Increased CSF MCP-1 correlates with cognitive decline

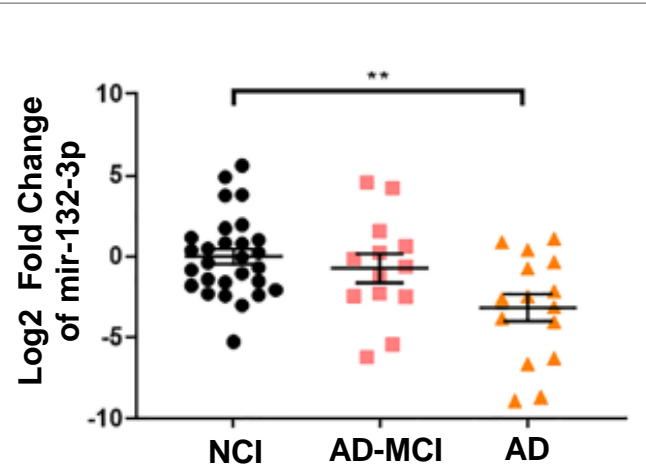


Single NurOwn treatment decreased CSF MCP-1 by 40% in Phase 2 ALS study

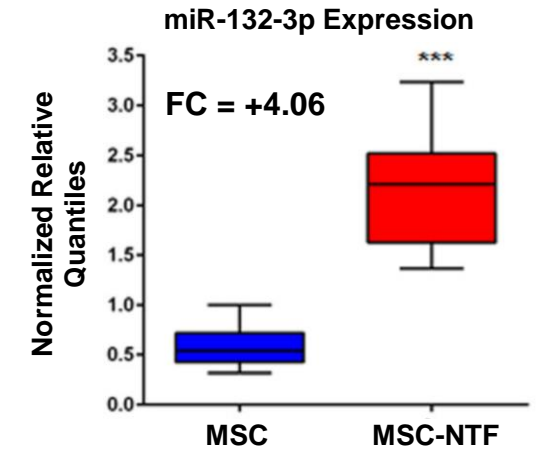
NurOwn[®] delivery of miR-132 may address the pathology of AD

NurOwn MSC-NTF cells express and deliver miR-132, which is downregulated in AD

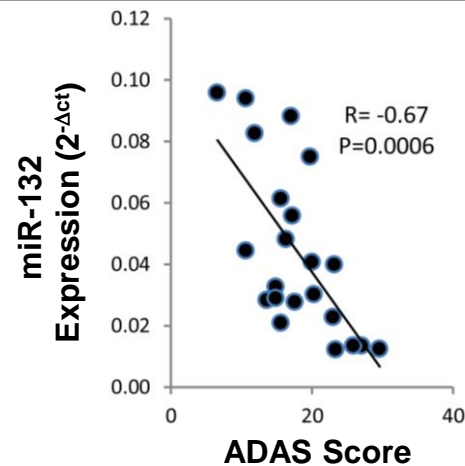
miR-132 is downregulated in AD¹



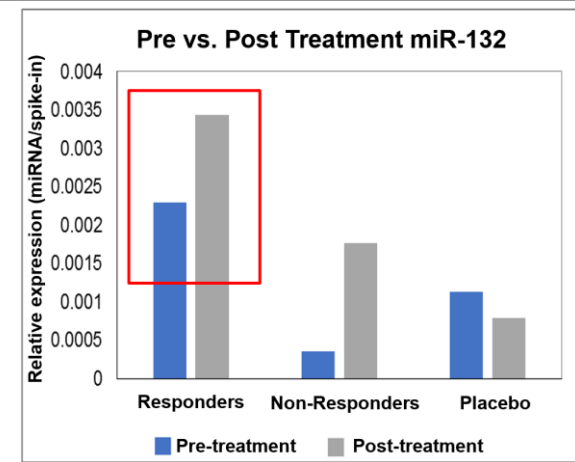
miR-132 is upregulated in MSC-NTF cells³



Decreased miR-132 correlates with AD Severity²



Phase 2 ALS: Single NurOwn treatment increased CSF miR-132 in responders



Phase 2 AD trial enrollment will be driven by biomarkers

Biomarker driven approach facilitates patient selection and improves chances of trial success

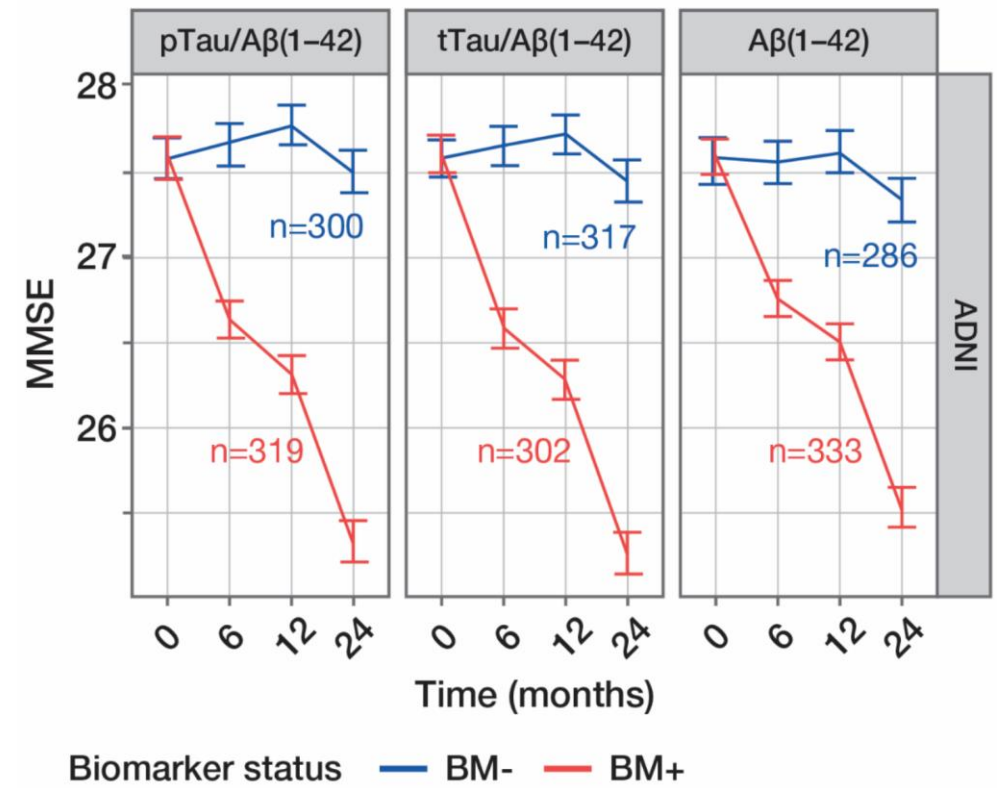
CSF amyloid and tau are linked to cognitive decline in AD

**SCIENTIFIC
REPORTS**
nature research

OPEN Predicting clinical decline and conversion to Alzheimer's disease or dementia using novel Elecsys $A\beta(1-42)$, pTau and tTau CSF immunoassays

Kaj Blennow^{1,2,10}, Leslie M. Shaw^{3,10}, Erik Stomrud^{4,5}, Niklas Mattsson^{4,6}, Jon B. Toledo^{3,7}, Katharina Buck⁸, Simone Wahl⁸, Udo Eichenlaub⁸, Valeria Lifke⁸, Maryline Simon⁹, John Q. Trojanowski³ & Oskar Hansson^{4,5*}

Trial biomarkers are predictive of clinical decline



Rationale for NurOwn[®] in Alzheimer's

- Targeting neuroinflammation offers an exciting and not yet fully evaluated therapeutic approach in Alzheimer's disease
- Robust effect on CSF biomarkers in Phase 2 ALS study
 - Robust effect on MCP-1/CCL2
 - MCP-1/CCL2 is associated with faster clinical progression
 - Increased neurotrophic factors in CSF
 - Increased miR-132 in CSF
 - Lower miR-132 correlates with reduced cognition
- Strong and consistent safety profile from 10 years in ALS



Phase 2 AD Trial: Led by Two World Renowned Investigators

Principal Investigator

Philip Scheltens, MD, PhD (Principal Investigator)

Professor of Cognitive Neurology: Amsterdam UMC

Director of the Alzheimer Centre: Amsterdam UMC

Extensive experience as PI of international AD trials



French National Coordinator

Bruno Dubois, MD, PhD

Professor of Neurology: Salpêtrière University Hospital

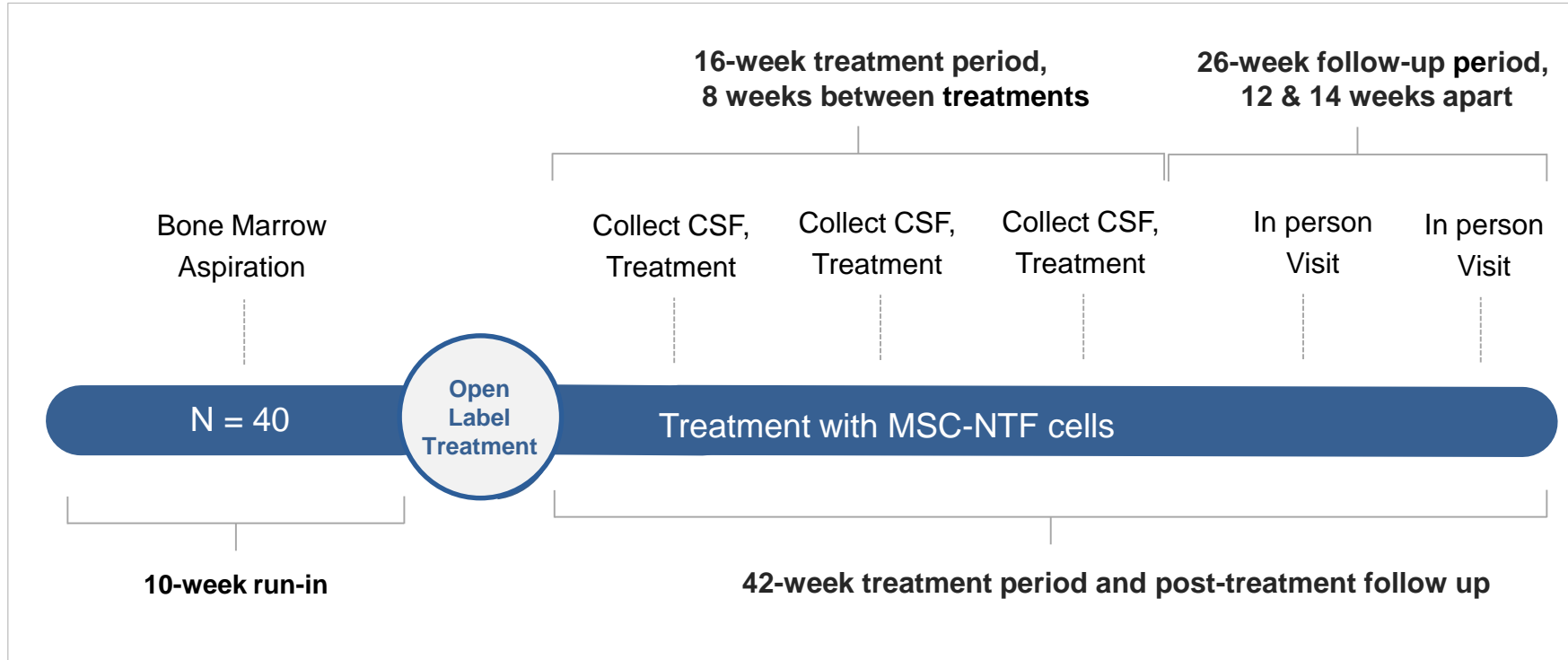
President: Scientific Committee of France-Alzheimer

President: International Fund Raising for Alzheimer's Disease



BCT-201-EU, AD Phase 2a Trial Design

52 week clinical trial



Primary Objective

To evaluate safety and tolerability of 3 intrathecal administrations of MSC-NTF cells

Secondary Objectives

To evaluate the modulation of CSF and blood biomarkers

To evaluate clinical outcomes measures to assess efficacy (cognition and function)

Clinical outcome measures: Cognition and activities of daily living

Clinical Dementia Rating Scale, Sum of Boxes

Neuropsychological Test Battery

Mini Mental State Examination

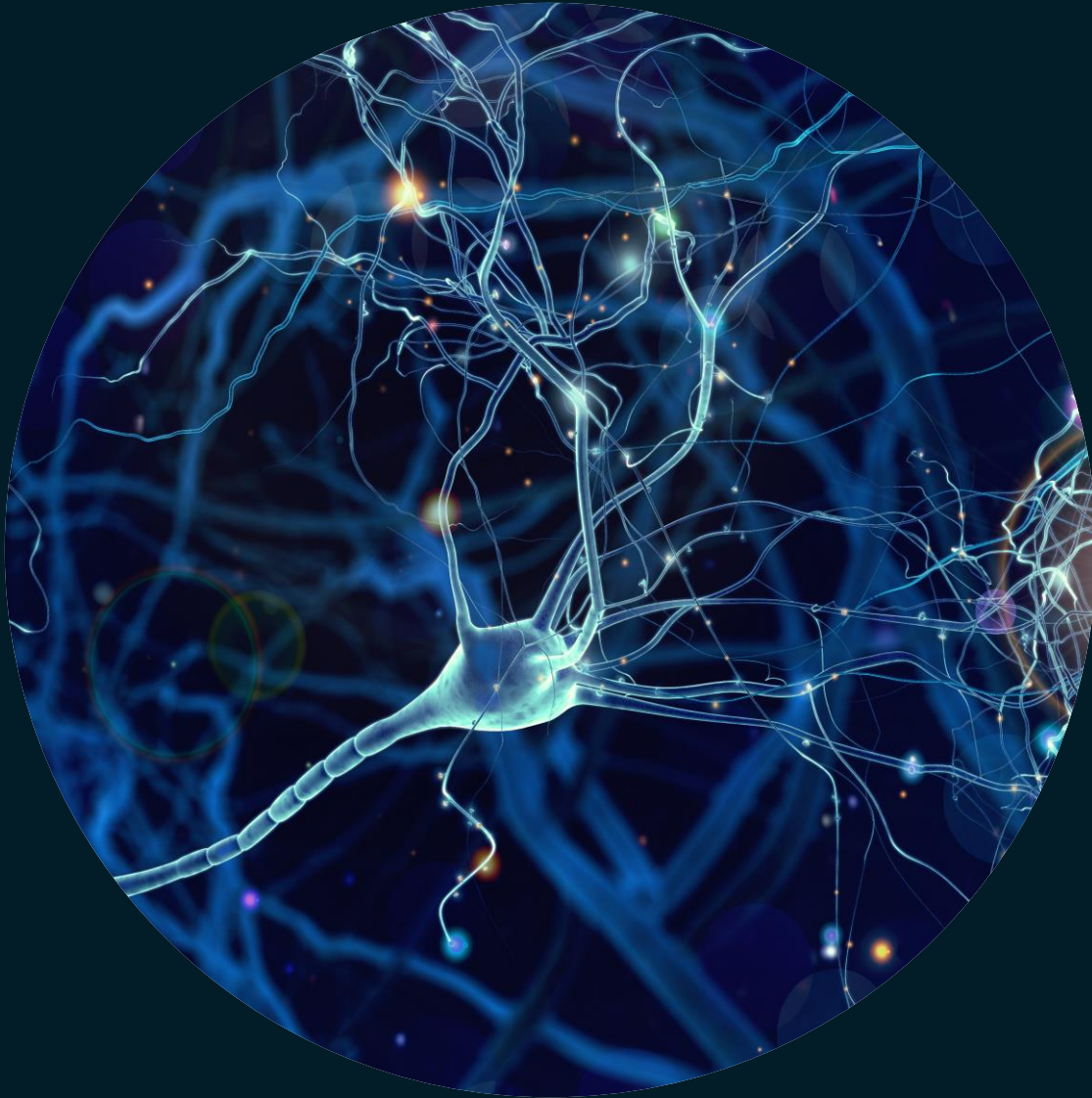
Amsterdam Instrumental Activities of Daily Living Questionnaire - Short Version

Biomarkers: paired serum and CSF samples

Neurotrophic, neurodegenerative and inflammatory factors

Markers associated with amyloid deposition

Markers of tau protein levels



Brainstorm Cell Therapeutics

NASDAQ: BCLI

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