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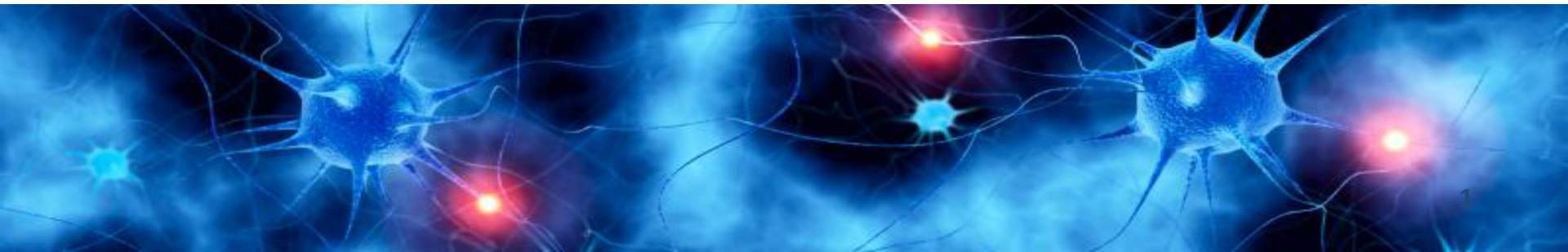
brainstorm
cell therapeutics

BCT-001-US Phase II Study Topline Results

NurOwn® in ALS

July 18, 2016



Safe Harbor Statement

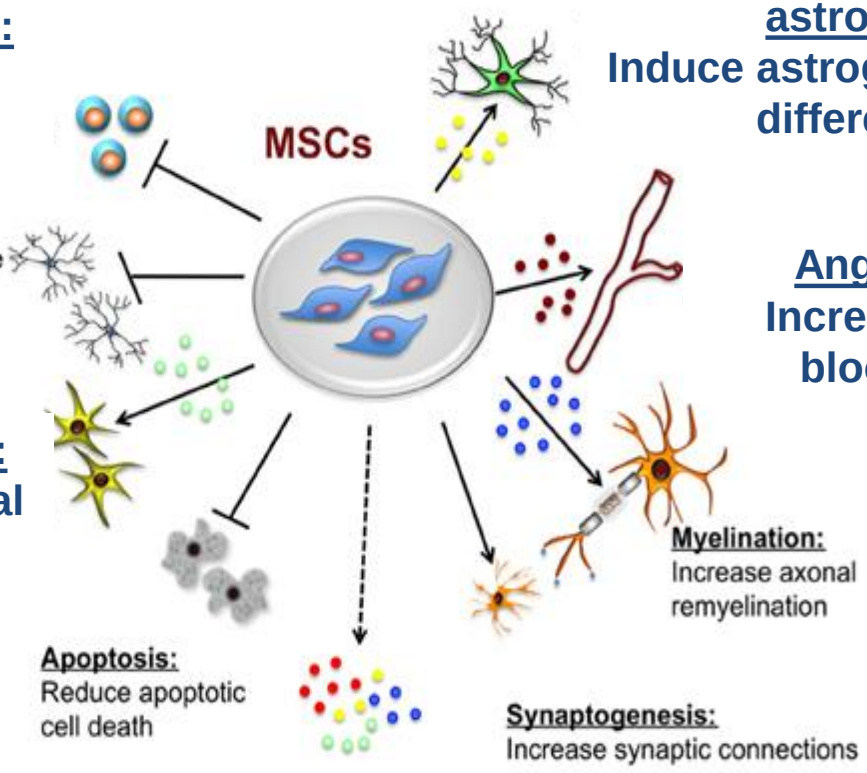
Statements in this announcement other than historical data and information constitute "forward-looking statements" and involve risks and uncertainties that could cause BrainStorm Cell Therapeutics Inc.'s actual results to differ materially from those stated or implied by such forward-looking statements. 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.

MSC therapeutic effects

The beneficial effects of MSCs are primarily mediated by paracrine mechanisms

Inflammation:
Reduce T lymphocyte activation

Increase reactive astrocytosis:
Induce astroglial growth and differentiation



Angiogenesis:
Increase cerebral blood vessels

Neurogenesis:
Induce neuronal growth and differentiation

Trophic factors:
Secretion of neurotrophic and angiogenic factors

From: Castillo-Melendez, M et al Frontiers in Neuroendocrine Science 24 Oct 2013

US clinical trial

A Phase 2, Randomized, Double Blind, Placebo Controlled Multicenter Study to Evaluate Safety and Efficacy of Transplantation of Autologous Mesenchymal Stem Cells Secreting Neurotrophic Factors (NurOwn®) in Patients With Amyotrophic Lateral Sclerosis[1]

- 3 Investigational sites
- 2 FDA approved manufacturing sites
- 48 ALS Patients, 16 patients/site
- 36 randomized to treatment, 12 randomized to placebo
- Combined IT + IM administration
- Treatment protocol 9 months (3 months pre- and 6 months post-transplant)

MASSACHUSETTS GENERAL HOSPITAL

University of Massachusetts Medical School

MAYO CLINIC

1. Clinicaltrials.gov identifier NCT02017912

Subject Disposition & Demographics

Disposition	MSC-NTF (N=36)	Placebo (N=12)	All Subjects (N=48)
Analysis Populations	n (%)	n (%)	n (%)
Safety (ITT)	36 (100.0)	12 (100.0)	48 (100.0)
Study Completion			
Completed	33 (91.7)	10 (83.3)	43 (89.6)
Discontinued	3 (8.3)	2 (16.7)	5 (10.4)

Demographics	MSC-NTF (N=36)	Placebo (N=12)	All Subjects (N=48)
Sex	n (%)	n (%)	n (%)
Male	25 (69.4)	10 (83.3)	35 (72.9)
Female	11 (30.6)	2 (16.7)	13 (27.1)
Age (years)	Descriptive Statistics		
n	36	12	48
Mean (SD)	50.3 (11.9)	53.5 (9.11)	51.1 (11.27)

Medical History

	MSC-NTF (N=36)	Placebo (N=12)	All Subjects (N=48)
El Escorial Criteria	n (%)	n (%)	n (%)
Possible	3 (8.3)	1 (8.3)	4 (8.3)
Laboratory-Supported Probable	5 (13.9)	1 (8.3)	6 (12.5)
Probable	16 (44.4)	7 (58.3)	23 (47.9)
Definite	12 (33.3)	3 (25.0)	15 (31.3)
ALS Medical History: Months Since Diagnosis			
n	36	12	48
Mean (SD)	9 (5.6)	9 (4.6)	9 (5.3)
ALS Medical History: Months Since First Symptom			
n	36	12	48
Mean (SD)	18 (3.8)	17 (3.1)	17 (3.6)

Overall Summary of Adverse Events

	MSC-NTF N=36	Placebo N=12
Number of Patients with at least one TEAE	36 (100%)	12 (100%)
Number of Patients with at least one Treatment-Related TEAE	35 (97.2%)	9 (75.0%)
Number of Treatment-Related Serious TEAEs	0	0
Number of Patients with at least one Treatment-Related Serious TEAE	0	0
Number of Patients with at least one SAE	9 (25%)	2 (16.6%)
Number of Patients with at least one Treatment-Emergent SAE	8 (22.2%)	1 (8.3%)
Number of Patients with Treatment-Related SAE	0	0
Number of Patients with TEAEs Resulting in Treatment Withdrawal	0	0
Number of Patients with TEAEs Resulting in Withdrawal from Study	0	0
Number of Patients with TEAEs Resulting in Death	0	0

- Systemic events such as pyrexia, chills, arthralgia and myalgia /musculoskeletal pain, and localized events such as injection site pain and procedural pain were more often reported in active-treatment patients.
- The largest differences in frequencies were for the localized reactions of injection site pain and back pain, and systemic reactions of pyrexia, headache, and arthralgia.
- Post-therapy serious adverse events (SAEs) tended to occur more frequently in active-treatment patients (8/36, 22.2%) than in placebo patients (1/12, 8.3%). Most SAEs were related to progression of underlying ALS, most commonly dysphagia. No SAEs were related to study treatment.
- Laboratory testing revealed a slight increase in absolute WBC and PMN counts in the active treatment group in the immediate post-transplantation period.
- Suicidal ideation scores from the C-SSRS progressed slightly in both treatment groups from pre- to post-transplantation study periods. No patients exhibited any suicidal behavior.

Responder analysis

Amyotrophic Lateral Sclerosis. 2010; 11: 178–180

informa
healthcare

ORIGINAL ARTICLE

Clinical significance in the change of decline in ALSFRS-R

CARMEN CASTRILLO-VIGUERA[1], DANIELA L. GRASSO[1], ELIZABETH SIMPSON[1], JEREMY SHEFNER[2] & MERIT E. CUDKOWICZ[1]

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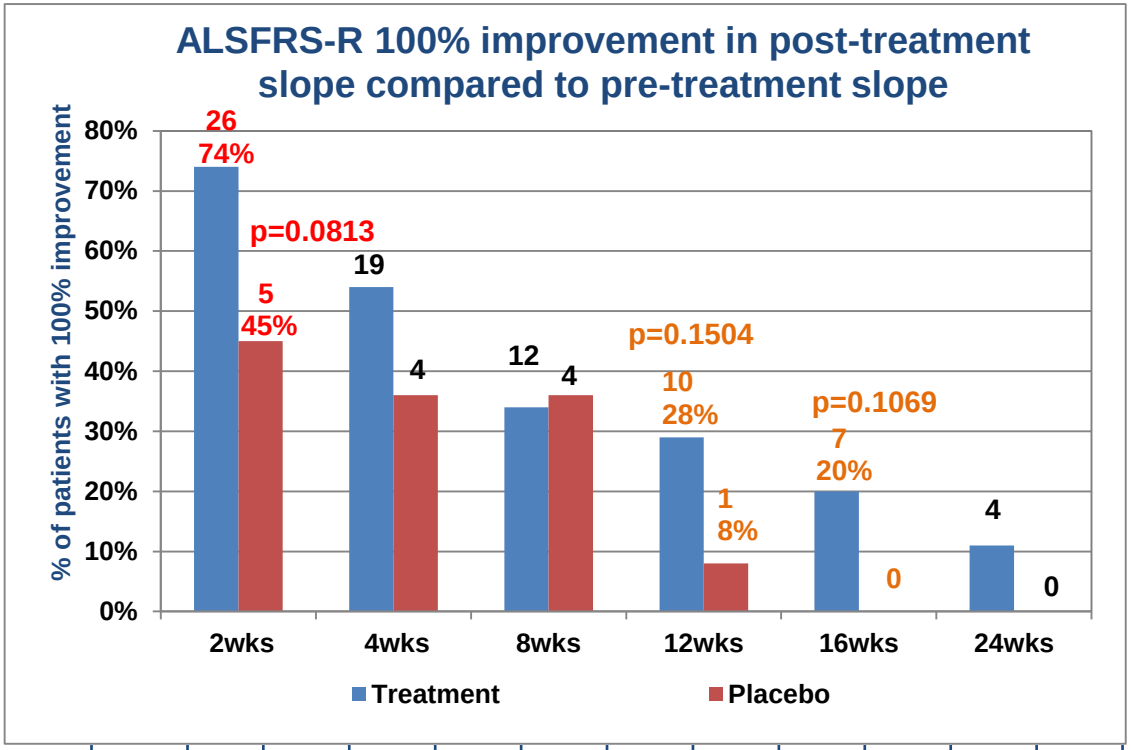
Abstract

Our objective was to survey ALS clinicians and researchers regarding what percentage reduction in the ALSFRS-R (Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised) slope they would consider clinically meaningful. A nine-question survey was provided to 65 members of the Northeast ALS Consortium (NEALS). They were asked to rate the clinical relevance of 10–50% changes in decline of the ALSFRS-R slope on a seven-point scale (1–7), where 1 = 'not at all clinically meaningful', 4 = 'somewhat clinically meaningful', and 7 = 'very clinically meaningful'. Ninety per cent of participants rated a 20% change in the decline of the ALSFRS-R score as the percentage in which a somewhat clinically significant change starts to be noted (i.e. score of 4 or higher). All participants endorsed a 25% or higher change in the ALSFRS-R score as at least somewhat clinically meaningful (score of 4 or higher). Ninety-three per cent of the participants viewed a 50% change in decline as very clinically meaningful (score of 7). This survey demonstrated that the majority of clinicians and clinical researchers surveyed believe that a therapy that resulted in a change of 20% or greater in the slope of the ALSFRS-R would be clinically meaningful.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3125671/

Efficacy
Responder Analysis



26 of 35	5 of 11	19 of 35	4 of 11	12 of 35	4 of 11	10 of 35	1 of 12	7 of 35	0 of 12	4 of 35	0 of 12
T	P	T	P	T	P	T	P	T	P	T	P
2wks		4wks		8wks		12wks		16wks		24wks	

T – Treatment; P – Placebo

Given the exploratory nature of this study, statistical significance was defined as a one-sided p value <0.1 (these p-values are highlighted in red above). In order to see trends in the data p-values that are ≥ 0.1 and < 0.2 are also highlighted in orange

Efficacy
Responder Analysis

ALSFRS-R % Improvement in post treatment slope compared to pre treatment slope over time

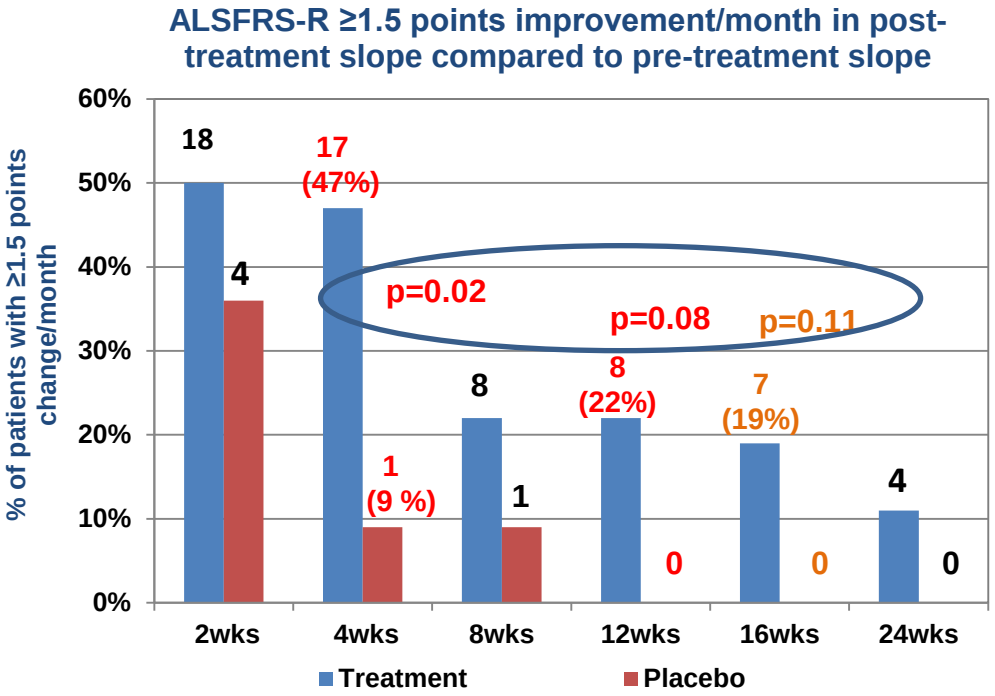
% improvement	2wks		4wks		8wks		12wks		16wks		24wks	
	T	P	T	P	T	P	T	P	T	P	T	P
	35	11	35	11	35	11	35	12	35	12	35	12
≥ 25% improvement	26 (74%)	5 (45%)	19 (54%)	5 (45%)	18 (51%)	5 (45%)	14 (40%)	3 (25%)	11 (31)%	3 (25%)	10 (29%)	3 (25%)
	p=0.0813											
≥ 50% improvement	26 (74%)	5 (45%)	19 (54%)	5 (45%)	18 (51%)	5 (45%)	14 (40%)	2 (17%)	10 (29%)	1 (8%)	8 (23%)	2 (17%)
	p=0.0813						p=0.1305		p=0.1504			
≥ 75% improvement	26 (74%)	5 (45%)	19 (54%)	5 (45%)	14 (40%)	4 (36%)	12 (34%)	1 (17%)	8 (23%)	1 (8%)	7 (20%)	1 (8%)
	p=0.0813											
≥ 100% improvement	26 (74%)	5 (45%)	19 (54%)	4 (36%)	12 (34%)	4 (36%)	10 (29%)	1 (8%)	7 (20%)	0 (0%)	4 (11%)	0 (0%)
	p=0.0813						p=0.1504		p=0.1069			

T – Treatment; P – Placebo
p-values are one-sided from Fisher's Exact test

Given the exploratory nature of this study, statistical significance was defined as a one-sided p value <0.1 (these p-values are highlighted in red above). In order to see trends in the data p-values that are ≥ 0.1 and < 0.2 are also highlighted in orange

Efficacy

Responder Analyses



18 of 36	4 of 11	17 of 36	1 of 11	8 of 36	1 of 11	8 of 36	0 of 12	7 of 36	0 of 12	4 of 36	0 of 12
T	P	T	P	T	P	T	P	T	P	T	P
2wks		4wks		8wks		12wks		16wks		24wks	

p-values using one-sided Fishers Exact Test

Given the exploratory nature of this study, statistical significance was defined as a one-sided p value <0.1 (these p-values are highlighted in red above). In order to see trends in the data p-values that are ≥ 0.1 and < 0.2 are also highlighted in orange

Efficacy
Responder Analysis

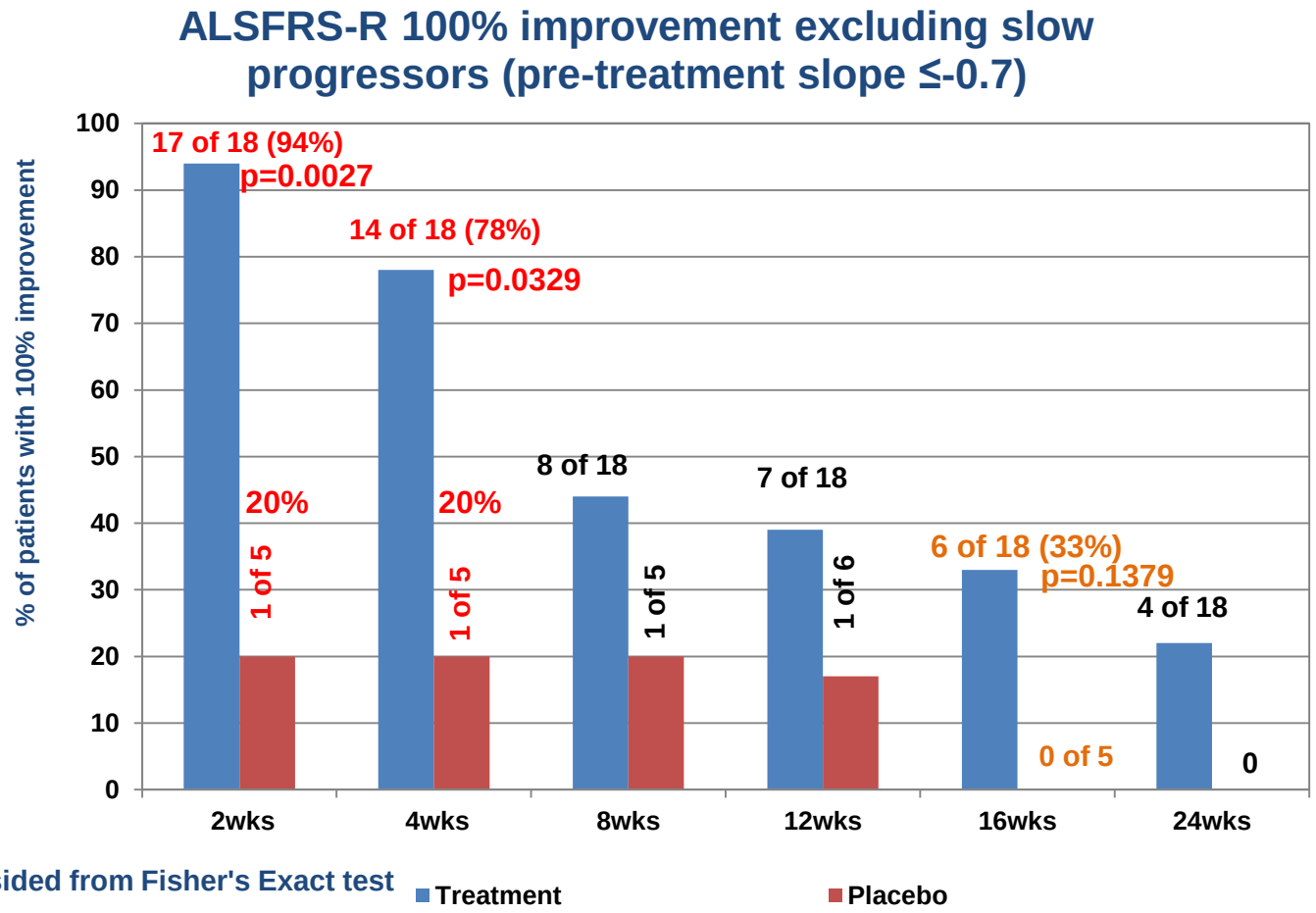
ALSFRS-R points improvement/month in post treatment slope compared to pre-treatment slope over time

Change points/months	2wks		4wks		8wks		12wks		16wks		24wks	
	T 35	P 11	T 35	P 11	T 35	P 11	T 35	P 12	T 35	P 12	T 35	P 12
≥0.5 points	64%	36%	47%	36%	42%	36%	36%	17%	25%	8%	22%	17%
	p=0.1029											
≥1 points	53%	36%	47%	27%	28%	9%	22%	17%	22%	8%	22%	8%
≥1.5 points	50%	36%	47%	9%	22%	9%	22%	0%	19%	0%	11%	0%
			p=0.0227				p=0.0802		p=0.1134			
≥2 points	42%	18%	33%	9%	11%	0%	14%	0%	11%	0%	6%	0%
	p=0.1442		p=0.1143									
≥2.5 points	42%	18%	28%	0%	11%	0%	6%	0%	3%	0%	3%	0%
	p=0.1442		p=0.0491									

T – Treatment; P – Placebo
p-values are one-sided from Fisher's Exact test

Given the exploratory nature of this study, statistical significance was defined as a one-sided p value <0.1 (these p-values are highlighted in red above). In order to see trends in the data p-values that are ≥ 0.1 and < 0.2 are also highlighted in orange

Responder Analysis (excluding all patients with pre-treatment slope ≤-0.7 (Slow Progressors)



p-values are one-sided from Fisher's Exact test

Given the exploratory nature of this study, statistical significance was defined as a one-sided p value <0.1 (these p-values are highlighted in red above). In order to see trends in the data p-values that are ≥ 0.1 and < 0.2 are also highlighted in orange

ALSFRS-R Slope Change Responder Analyses excluding all patients with pre-treatment slope ≤-0.7
(Subgroup Analysis: Slow Progressors)

% of total (% improvement)	2 wks		4 wks		8 wks		12 wks		16 wks		24 wks	
	T	P	T	P	T	P	T	P	T	P	T	P
	18	5	18	5	18	5	18	5	18	5	18	5
25% improvement	17 (94%)	1 (20%)	14 (78%)	2 (40%)	14 (78%)	2 (40%)	11 (61%)	2 (33%)	10 (56%)	1 (17%)	9 (50%)	2 (33%)
	p=0.0027		p=0.1421		p=0.1421				p=0.1179			
50% improvement	17 (94%)	1 (20%)	14 (78%)	2 (40%)	14 (78%)	2 (40%)	11 (61%)	2 (33%)	9 (50%)	1 (17%)	7 (39%)	1 (17%)
	p=0.0027		p=0.1421		p=0.1421				p=0.1711			
75% improvement	17 (94%)	1 (20%)	14 (78%)	2 (40%)	10 (56%)	1 (20%)	9 (50%)	2 (33%)	7 (39%)	1 (17%)	7 (39%)	1 (17%)
	p=0.0027		p=0.1421		p=0.1854							
100% improvement	17 (94%)	1 (20%)	14 (78%)	1 (20%)	8 (44%)	1 (20%)	7 (39%)	1 (17%)	6 (33%)	0 (0%)	4 (22%)	0 (0%)
	p=0.0027		p=0.0329						p=0.1379			

T – Treatment; P - Placebo
p-values are one-sided from Fisher's Exact test

Given the exploratory nature of this study, statistical significance was defined as a one-sided p value <0.1 (these p-values are highlighted in red above). In order to see trends in the data p-values that are ≥ 0.1 and < 0.2 are also highlighted in orange

Biomarkers

- Cerebral-spinal fluid (CSF) samples were collected from patients, as specified per a protocol amendment, after the first 8 patients had already been treated

- A total of 35 patients out of 48 had corresponding samples from visits pre- and post-transplantation available for analysis. Levels of neurotrophic factors and inflammatory factors in each sample were measured

- A statistically significant increase in levels of Vascular Endothelial growth Factor (VEGF), Hepatocyte Growth Factor (HGF) from pre- to post-transplantation was observed in the samples of those patients who responded to NurOwn

- There was also a statistically significant reduction in inflammatory markers such as Monocyte Chemoattractant Protein-1 (MCP-1) and Stromal Cell-Derived Factor 1 (SDF-1) over this period, in patients treated with NurOwn that was not observed in the placebo group

Conclusions

- BCT-001 achieved its primary objective, demonstrating that NurOwn was safe and well tolerated.
- Single administration of NurOwn produced a clinically meaningful beneficial response in terms of both the ALSFRS-R rating scale and CSF biomarkers.
- In the ITT population, across all definitions of "responder", a higher percentage of NurOwn-treated subjects were responders compared to placebo, at all except one timepoint studied out to 24 weeks.
- In a pre-specified subgroup analysis that excluded slowly progressing subjects, NurOwn-treated subjects showed marked outperformance compared to placebo-treated subjects.
- Increased levels of growth factors in CSF and decreased inflammatory markers observed after two weeks are further evidence for a biological effect.
- Results suggest that larger confirmatory trial with repeat dosing at 8 to 12 weeks is warranted.

Next Steps

- **Request for FDA Meeting**
- **A Multi-Dose Double Blind Randomized Placebo Controlled Adequately Powered Trial in US and Israel**