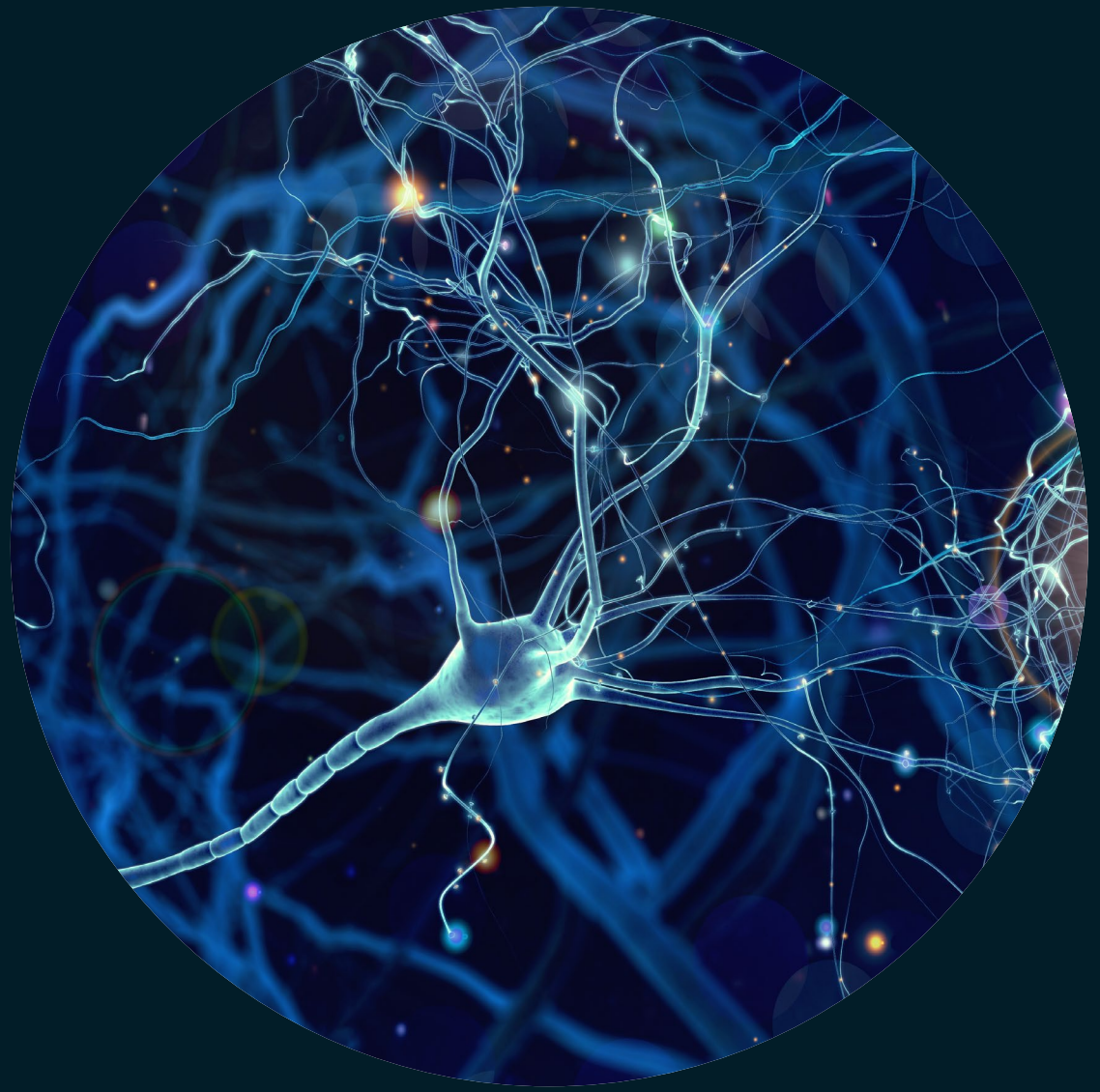

Multicenter Phase 2 Safety and Efficacy Study of MSC-NTF Cells (NurOwn®) in Progressive Multiple Sclerosis

J. Cohen, F. Lublin, C. Lock, D. Pelletier, T. Chitnis, M. Mehra, Y. Gothelf, R. Aricha, S. Lindborg, C. Lebovits, R. Kern

37th Congress of ECTRIMS
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Disclosures

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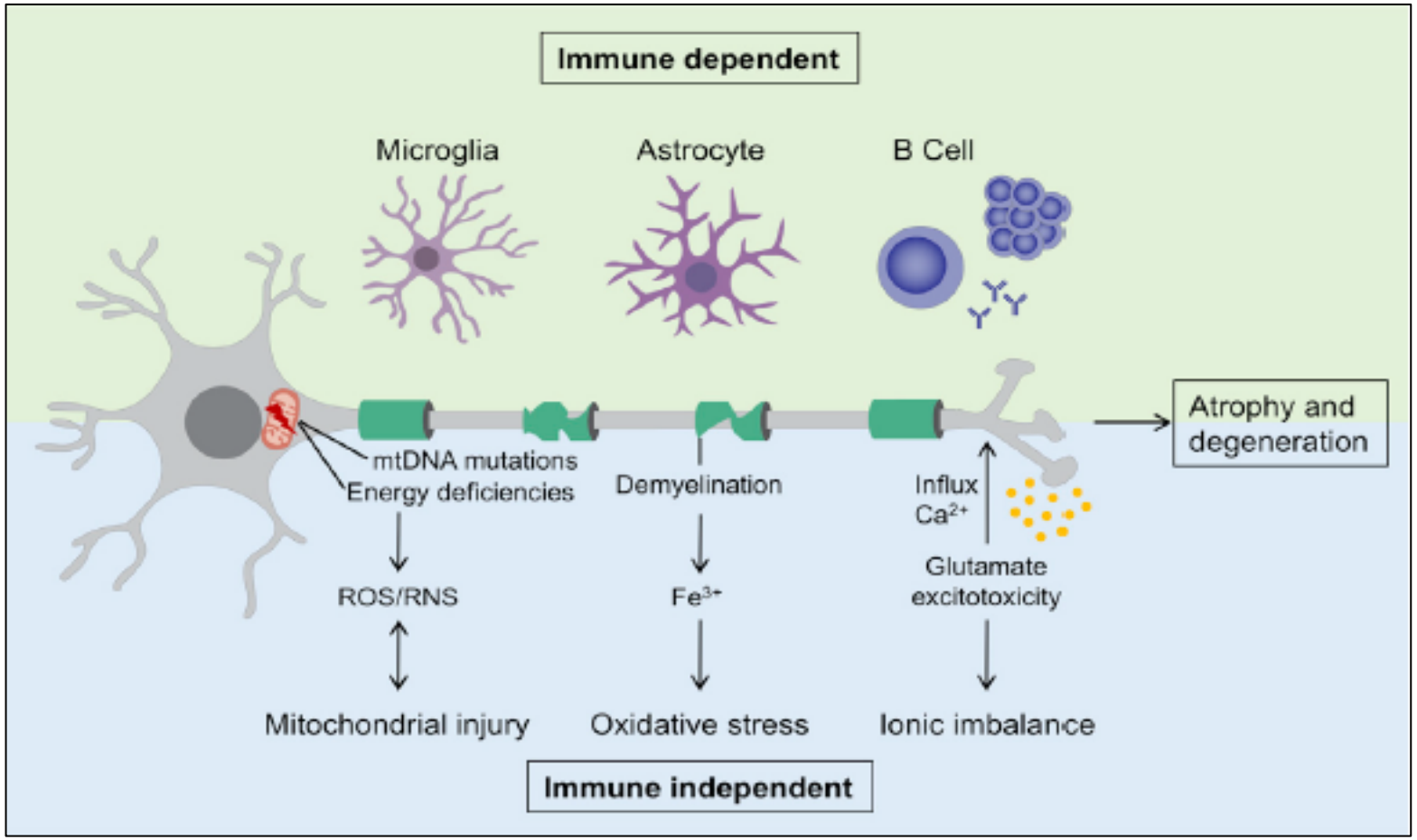
Jeffrey Cohen: Received personal compensation consulting for Adamas, Atara, Bristol-Myers Squibb, Convelo, MedDay, and Mylan; Editor of Multiple Sclerosis Journal
Fred Lublin: Consultant to and received research funding from Brainstorm Cell Therapeutics
Christopher Lock: Speakers' bureau, advisory boards, or consulting with Biogen, Bristol Meyers Squibb, EMD Serono, Sanofi Genzyme, InterX Inc., Diagnose early
Daniel Pelletier: Received research funding from Brainstorm Cell Therapeutics
Tanuja Chitnis: Received compensation for consulting from Biogen, Novartis Pharmaceuticals, Roche Genentech and Sonaofi Genzyme. Received research support from the National Institutes of Health, National MS Society, US Department of Defense, Sumaira Foundation, Brainstorm Cell Therapeutics, EMD Serono, I-mab Biopharma, Malinckrodt ARD, Novartis Pharmaceuticals, Octave Bioscience, Roche Genentch, and Tiziana Life Sciences.
Munish Mehra and Tigermed Biometrics team provided contract biostatistical services to Brainstorm Cell Therapeutics
Yael Gothelf, Revital Aricha, Stacy Lindborg, Chaim Lebovits, Ralph Kern are employed by Brainstorm Cell Therapeutics

MSC-NTF Cells (NurOwn®) Modulate Neuroinflammatory and Neuroprotective Pathways in Progressive MS



NurOwn MOA

Neuroinflammation↓

Osteopontin
MCP-1
CHIT-1
SDF-1
sCD-27

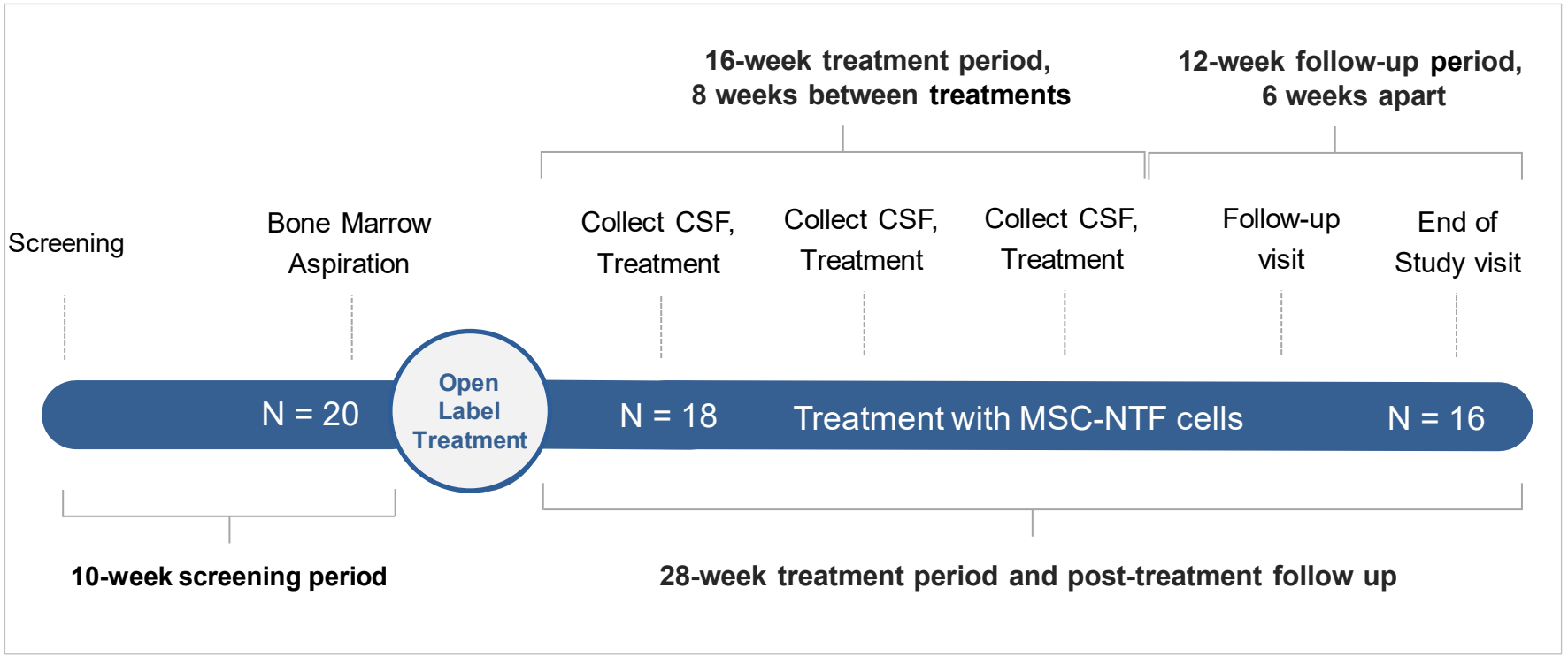
Neuroprotection↑

VEGF
HGF
Fetuin-A
NCAM-1
Follistatin

Baecher-Allan et al, Neuron 2018

NurOwn® Progressive MS Phase 2 Trial Design

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



Primary Outcome

Safety

Secondary Outcomes

Biomarkers (CSF & Serum)

Changes from baseline in

Timed 25-foot walking speed
9-hole peg test
SDMT
LCLA
MSFC-4
EDSS
MSWS-12

Exploratory Outcomes

Actigraphy

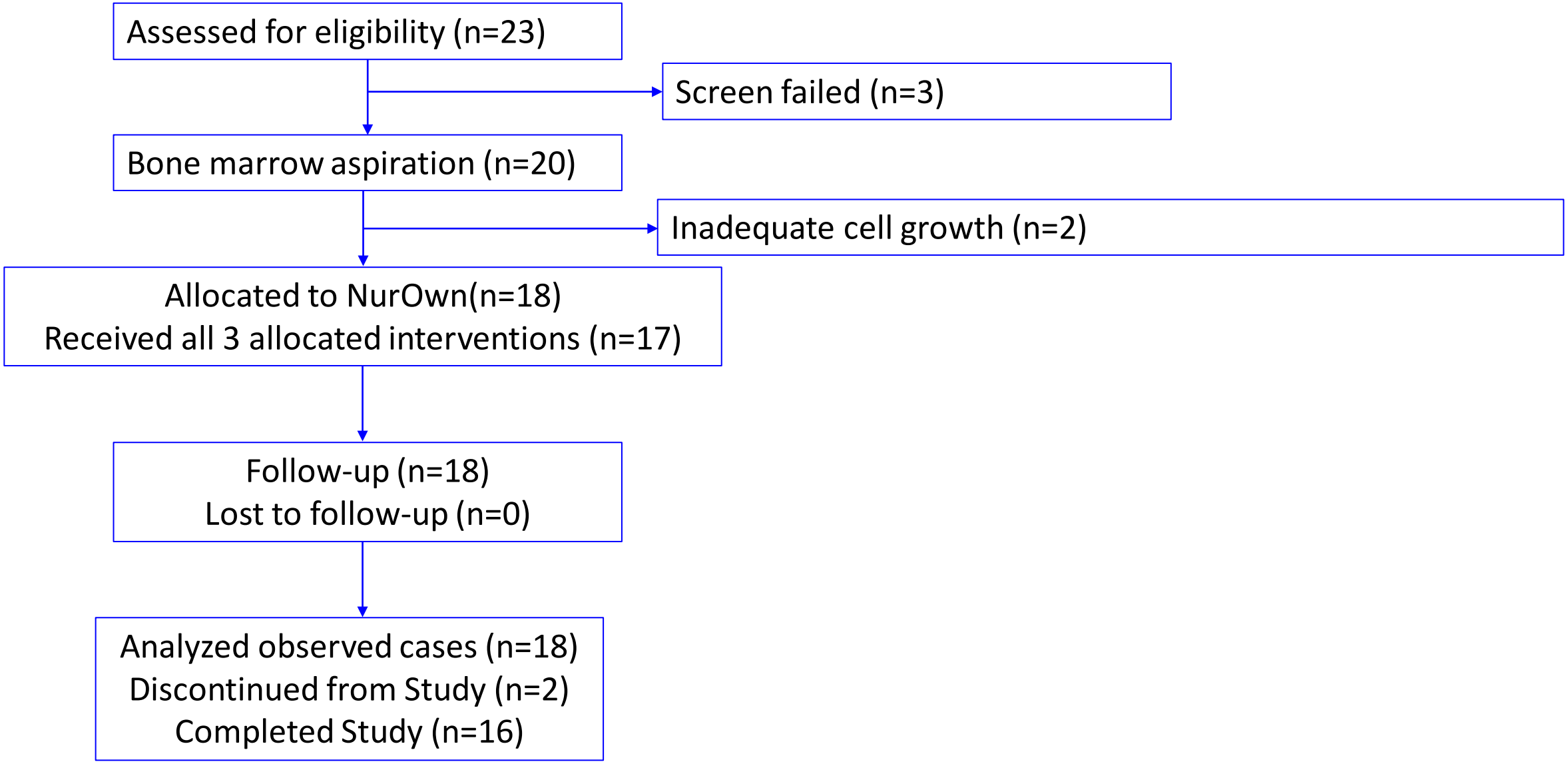
Quantitative Magnetic Resonance Imaging

ClinicalTrials.gov Identifier: NCT03799718

BCT-101 Demographics and Baseline Characteristics

Baseline Parameters	NurOwn (N=18)
Mean Age: Years(SD)	47 (9.6)
Females N(%)	10 (56%)
EDSS Score: Mean(SD)	5.4 (1.3)
T25FW Score (ft./sec.): Mean (SD)	2.4 (1.6)
9-HPT Score (sec.) – Combined Average: Mean(SD)	35.2 (15.7)
9-HPT Score (sec.) – Dominant Hand: Mean(SD)	30.3 (9.0)
9-HPT Score (sec.) – Non-Dominant Hand: Mean(SD)	40.1 (25.4)
MSWS-12 Score: Mean(SD)	75.6 (19.1)
LCLA Score – Binocular 2.5%: Mean(SD)	32.7 (8.9)
LCLA Score – Binocular 1.25%: Mean(SD)	23.3 (10.9)
SDMT Score: Mean(SD)	46.1 (11.5)
MSFC-4 Z score: Mean(SD)	0.03 (0.48)

CONSORT DIAGRAM



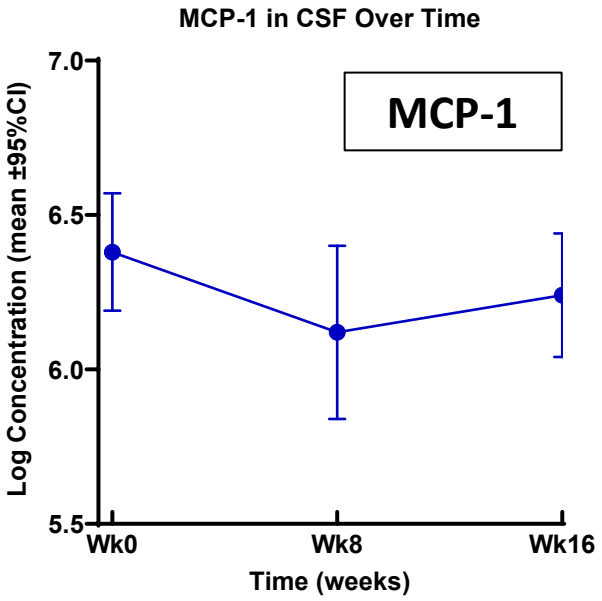
Safety: SAEs, Frequently Occurring TEAEs

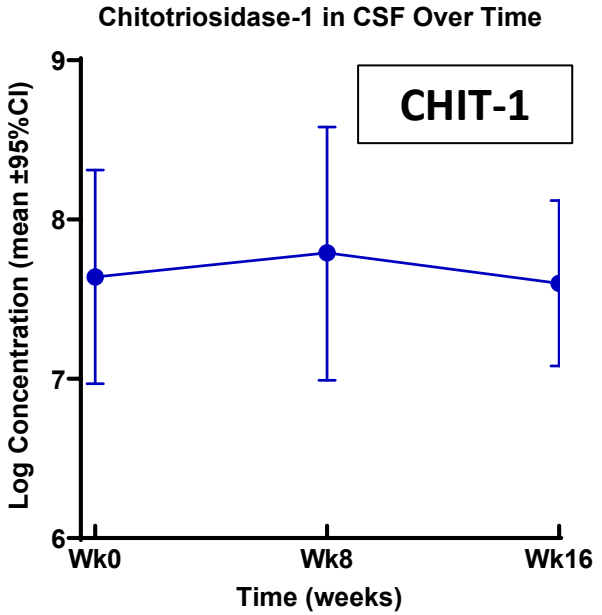
Two subjects had SAEs of Arachnoiditis and one of these discontinued the study.

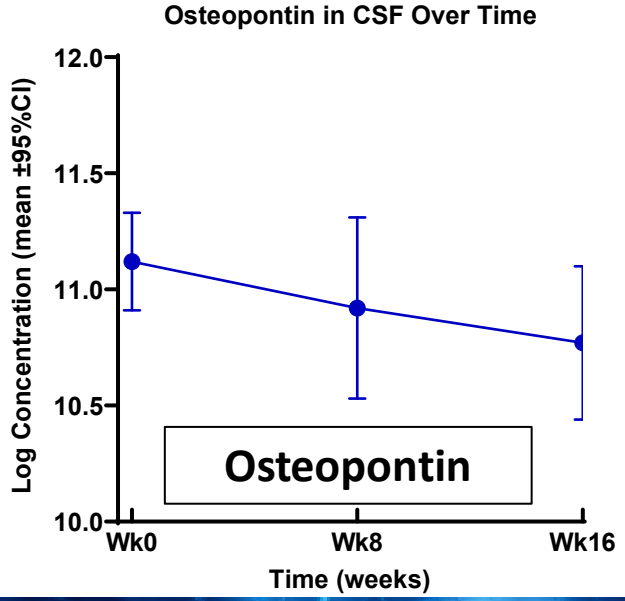
AE Preferred Term	# of Subjects (% out of 18)
Headache	16 (88.9)
Back pain	15 (83.3)
Urinary tract infection	6 (33.3)
Musculoskeletal pain	5 (27.8)
Injection site pain	4 (22.2)
Pyrexia	4 (22.2)
Arthralgia	3 (16.7)
Fall	3 (16.7)
Fatigue	3 (16.7)
Muscular weakness	3 (16.7)
Musculoskeletal stiffness	3 (16.7)
Pain in extremity	3 (16.7)

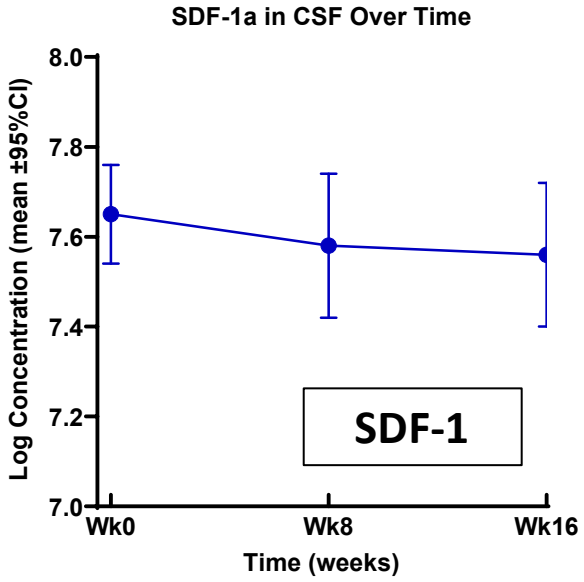
Other AEs in 2 subjects were: Hypoaesthesia, Micturition urgency, Musculoskeletal chest pain, Nausea, Neck pain, Radicular pain, Radiculopathy, Sensory disturbance. Some of the AE's in 1 subject only included Dizziness, Facial pain, Feeling cold, Neuralgia, Neuropathy peripheral, Pain, Paresthesia and Spinal Pain

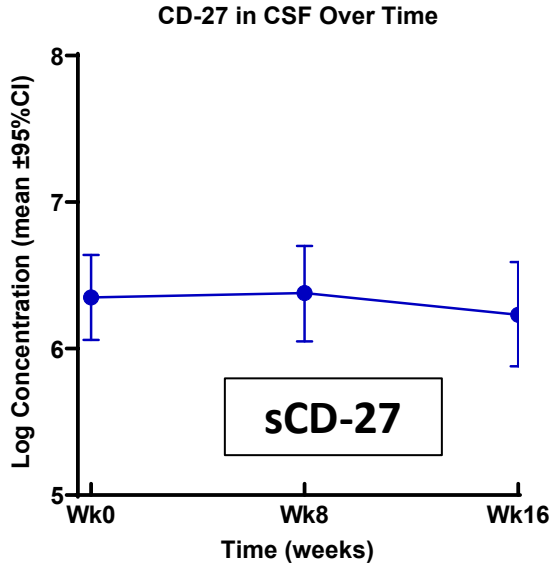
CSF Neuroinflammatory Biomarkers Decreased



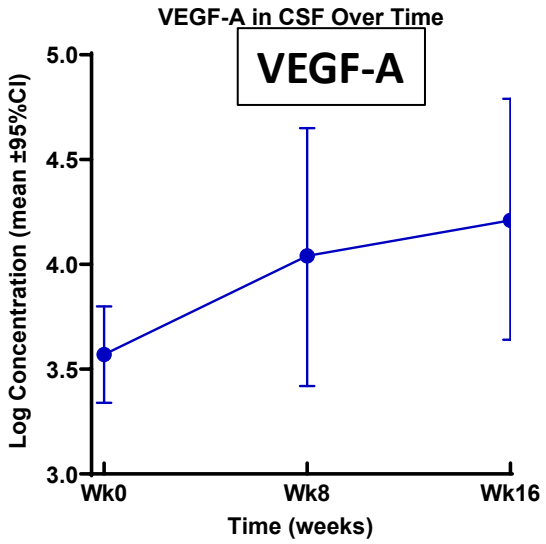


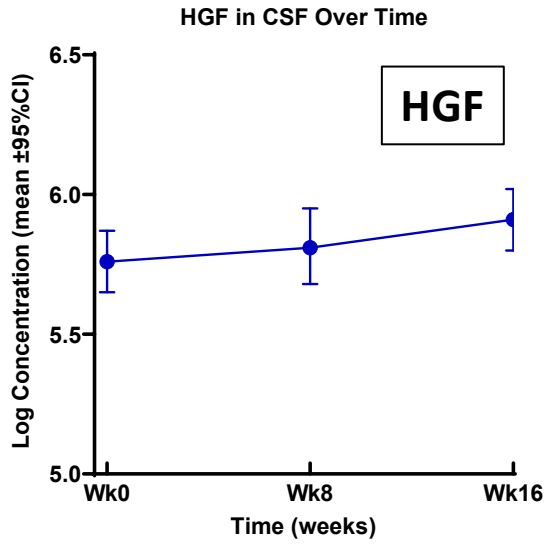


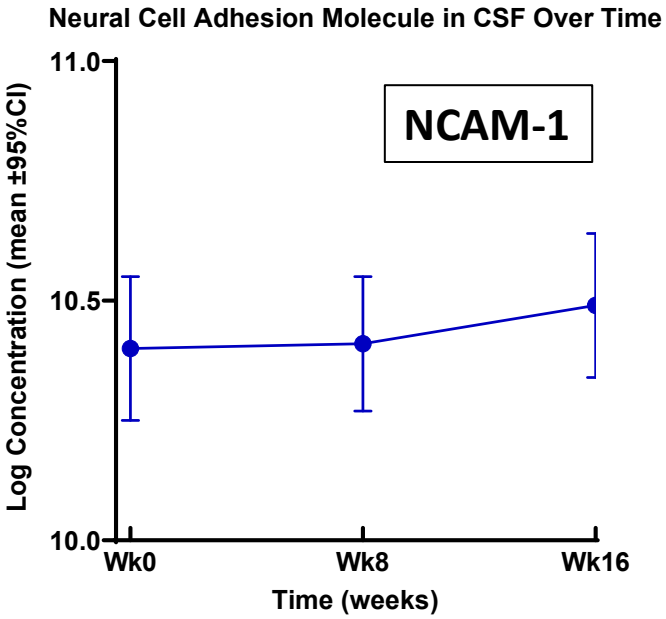


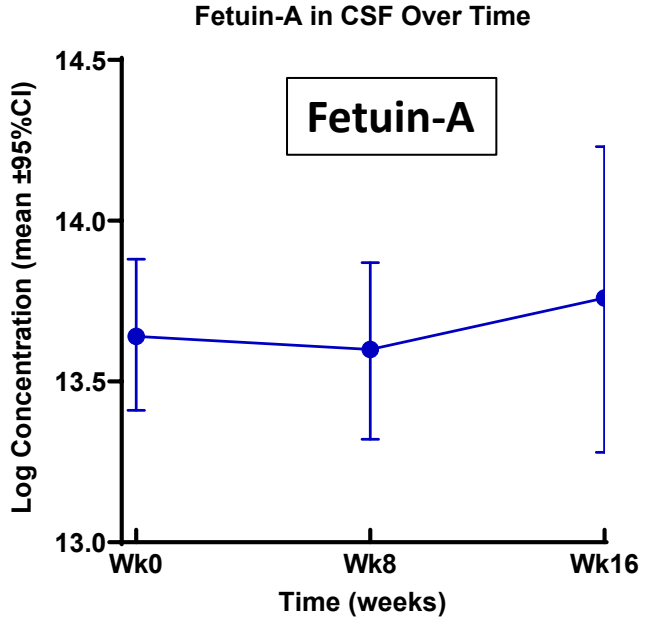


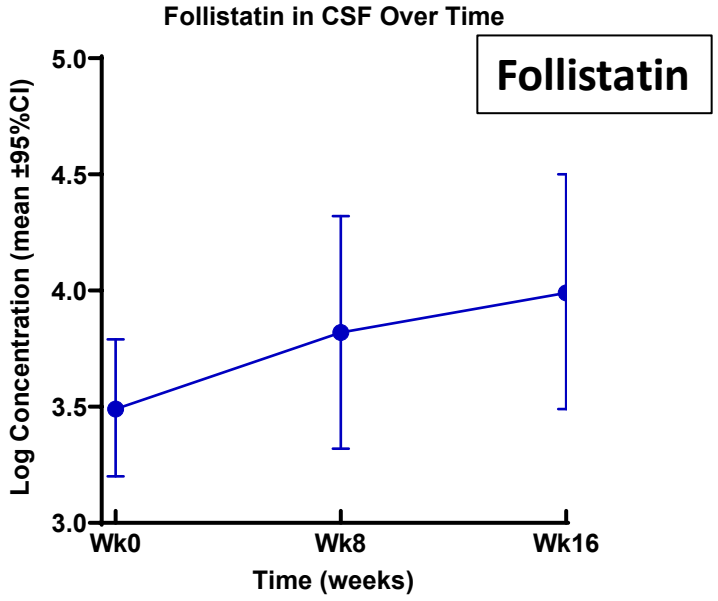
CSF Neuroprotection Biomarkers Increased











Demographics and Baseline Characteristics: NurOwn vs. CLIMB[1] vs. SPRINT-MS[2]

Baseline Parameters	BCT-101 NurOwn (N=18)	CLIMB Registry Observed Patients (N=48)	NN-102 (SPRINT-MS)	
			Ibudilast (N=121)	Placebo (N=123)
Mean Age: Years(SD)	47 (9.6)	55 (6.7)	55 (7.7)	57 (6.5)
Females N(%)	10 (56 %)	32 (67 %)	62 (51 %)	69 (56 %)
EDSS Score: Mean(SD)	5.4 (1.3)	5.2 (1.4)	5.5 (1.1)	5.4 (1.1)
T25FW Score (ft./sec.): Mean(SD)	2.4 (1.6)	3.2 (1.3)	2.7 (1.4)	2.7 (1.5)
9-HPT Score (sec.) – Combined Average: Mean(SD)	35.2 (15.7)	30.7 (11.5)	32.6 (12.6)	34.8 (14.0)
9-HPT Score (sec.) – Dominant Hand: Mean(SD)	30.3 (9.0)	29.0 (15.7)	30.9 (14.5)	32.7 (15.2)
9-HPT Score (sec.) – Non-Dominant Hand: Mean(SD)	40.1 (25.4)	32.1 (15.2)	34.5 (16.5)	36.4 (18.5)
MSWS-12 Score: Mean(SD)	75.6 (19.1)	NA	NA	NA
LCLA Score – Binocular 2.5%: Mean(SD)	32.7 (8.9)	27.5 (10.3)	29.7 (12.2)	27.2 (12.6)
LCLA Score – Binocular 1.25%: Mean(SD)	23.3 (10.9)	NA	NA	NA
SDMT Score: Mean(SD)	46.1 (11.5)	44.8 (10.7)	43.1 (14.7)	41.5 (14.1)
MSFC-4 Z score: Mean(SD)	0.03 (0.48)	0.04 (0.47)	0.08 (0.52)	-0.01 (0.51)

[1] CLIMB Registry from Tanuja Chitnis, MD, Brigham & Young. Based on 48 matched subjects out of 500, assessments between 1 and 2 years apart. Efficacy assessments were interpolated at Week 28 assuming linear change.

[2] SPRINT NN-102 Study Lead PI, Robert J. Fox, MD, MS, FAAN, Cleveland Clinic. Data obtained courtesy NIH/NINDS. Above efficacy data is at 24 Weeks

NA = data is not available for analysis

Responder Analysis, Over 28 Weeks: NurOwn vs. CLIMB[1] vs. SPRINT-MS[2]

Outcome	BCT-101 NurOwn (n=18)	CLIMB Registry Observed Patients (n=48)	NN-102 (SPRINT-MS)	
			Ibudilast (n=121)	Placebo (n=123)
T25W OR 9-HPT (≥25% improvement)	3/16 (19%)	2/47 (4%)	19/117 (16%)	13/121 (11%)
T25W (≥25% improvement)	2/14 (14%)	2/43 (5%)	18/114 (16%)	10/118 (9%)
9-HPT (≥25% improvement), Combined Average	2/15 (13%)	0/47 (0%)	2/117 (2%)	4/121 (3%)
9-HPT (≥25% improvement), Dominant Hand	1/15 (7%)	0/47 (0%)	0/116 (0%)	4/120 (3%)
9-HPT (≥25% improvement), Non-Dominant Hand	2/15 (13%)	0/46 (0%)	3/115 (3%)	7/120 (6%)
MSWS-12 (≥10-point improvement)	6/16 (38%)	NA	NA	NA
LCLA binocular 1.25% (≥8 letter improvement)	7/15 (47%)	NA	NA	NA
LCLA binocular 2.5% (≥8 letter improvement)	4/15 (27%)	3/47 (6%)	18/116 (16%)	15/120 (13%)
SDMT (≥3 point improvement)	10/15 (67%)	8/45 (18%)	48/117 (41%)	42/121 (35%)
SDMT (≥5 point improvement)	7/15 (47%)	1/45 (2%)	31/117 (27%)	31/121 (26%)
EDSS (Baseline EDSS ≤ 5.5 with Improvement ≥ 1.0)	0/6 (0%)	0/19 (0%)	4/42 (10%)	7/47 (15%)
EDSS (Baseline EDSS > 5.5 with Improvement ≥ 0.5)	3/10 (30%)	1/28 (4%)	6/74 (8%)	6/72 (8%)

NA = data is not available for analysis

Average Change from Baseline Over 28 Weeks, NurOwn vs. CLIMB vs. SPRINT-MS

	BCT-101	CLIMB Registry	NN-102 (SPRINT-MS)	
Outcome	NurOwn (N=18)	Observed Patients (N=48)	Ibudilast (N= 121)	Placebo (N=123)
T25FW Speed (feet/seconds)	0.10 (n=14)	-0.07 (n=43)	0.04 (n=114)	-0.06 (n=118)
9-HPT Time, Combined Average (seconds)	-0.23 (n=15)	0.49 (n=47)	2.14 (n=117)	0.28 (n=121)
9-HPT, Dominant Hand Time (seconds)	-1.95 (n=15)	0.03 (n=47)	1.97 (n=116)	1.87 (n=120)
9-HPT, Non-Dominant Hand Time (seconds)	1.48 (n=15)	0.93 (n=46)	2.53 (n=115)	-1.18 (n=120)
MSWS-12 (0 Best, 100 Worst)	-4.17 (n=16)	NA	NA	NA
LCLA binocular (1.25%)	5.0 (n=15)	NA	NA	NA
LCLA binocular (2.5%)	3.3 (n=15)	-1.07 (n=47)	-0.2 (n=116)	-0.6 (n=120)
SDMT (0 Worst, 120 Best)	3.8 (n=15)	0.10 (n=45)	1.1 (n=117)	-0.1 (n=121)
EDSS (0 Best, 10 Worst in 0.5 increments)	0.03 (n=16)	0.04 (n=47)	0.05 (n=116)	0.04 (n=119)
MSFC-4	0.18 (n=13)	-0.02 (n=40)	0.03 (n=110)	-0.05 (n=116)

NA = data is not available for analysis

Black font = improvement, Red font = worsening

Conclusions

- Repeated intrathecal administration of MSC-NTF cells (NurOwn®) was generally safe and well-tolerated
- CSF biomarkers at 3 consecutive time points (2 post-treatment) showed increases in neuroprotective biomarkers and decreases in neuroinflammatory biomarkers.
- **After 28-week follow-up, there were improvements in a variety of clinical outcomes, including T25FW, 9-HPT, LCLA and SDMT, that were not seen in matched progressive patients in the CLIMB registry or in the overall NN-102 SPRINT-MS Study cohort**
- These encouraging results should be confirmed in a prospective randomized placebo-controlled trial

Manufacturing

DANA-FARBER CANCER INSTITUTE

Dana-Farber Harvard Cancer Center

Cell Manipulation Core

Treatment Centers

Icahn School of Medicine at Mount Sinai

Cleveland Clinic

Stanford MEDICINE

Keck Medicine of USC

BRIGHAM HEALTH

BWH BRIGHAM AND WOMEN'S HOSPITAL

Funding

MS National Multiple Sclerosis Society

Data Access

CLIMB Registry Data: Tanuja Chitnis, MD

NN102 SPRINT-MS Study Data: NIH/NINDS. PI: Robert J. Fox, MD, MS, FAAN, Cleveland Clinic. Original Publication