

NurOwn for ALS

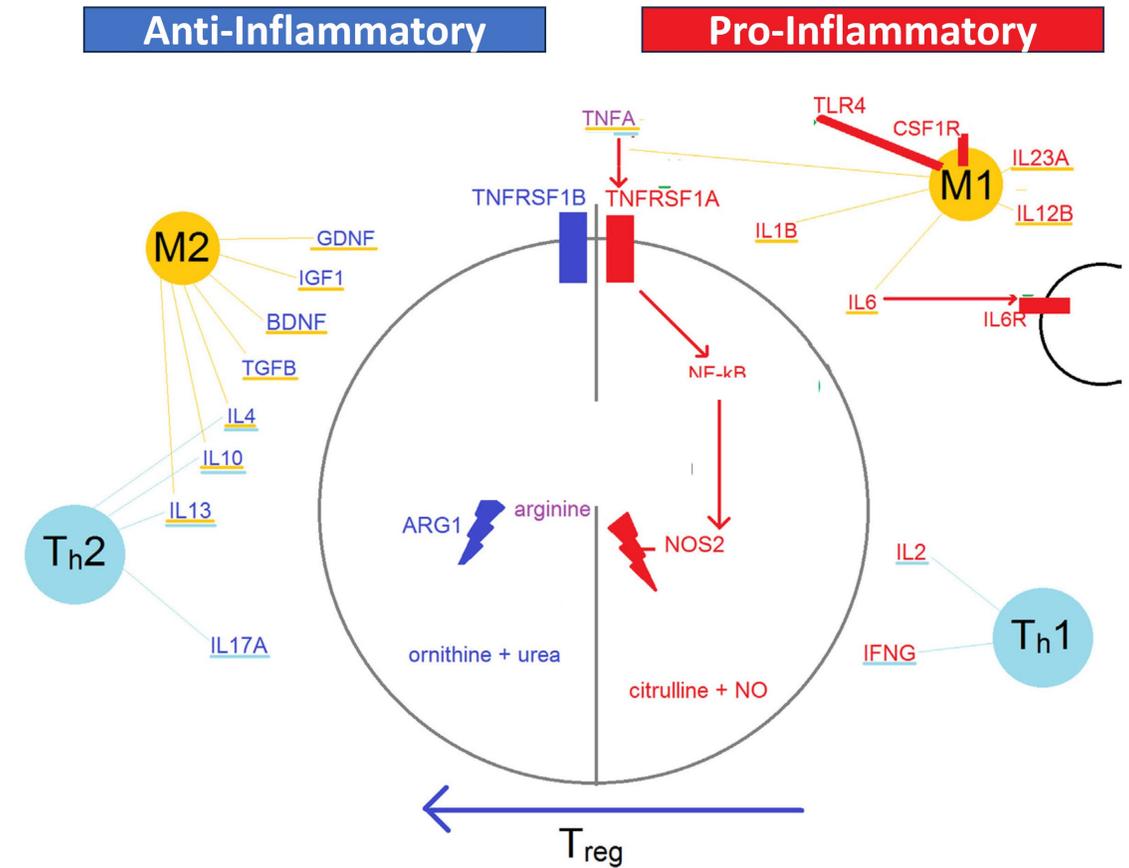
Biomarker exploration of NurOwn multimodal mechanism of action on neuroinflammation, neuroprotection and neurodegeneration

Bob Dagher, MD
Executive Vice President
Chief Development Officer

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Complex & Multi-faceted Mechanisms Underlying ALS

- Neurodegeneration may be linked to deficient neuroprotection and neuroinflammation¹
- Stem cell treatment potential to synergistically tackle interrelated pathological mechanisms
- MSCs play key role in immunomodulation



Stem Cells Exhibit Multiple Physiological Actions

Function of NSC's fundamental physiological role¹

Neuroprotection & trophic support via diffusible factors, gap junctions & exosomes

- Scavenging ROS & excitotoxins
- Promoting angiogenesis
- Mobilizing endogenous NSCs
- Replacing interneurons
- Glial support
 - e.g., astrocytes & oligodendrocytes
- Inducing neural self-repair
- Reducing inflammation & scarring
- Repairing the blood-brain barrier
- Promoting endogenous neurite outgrowth
- Providing extracellular matrix
- Restoring normal metabolism to injured host cells

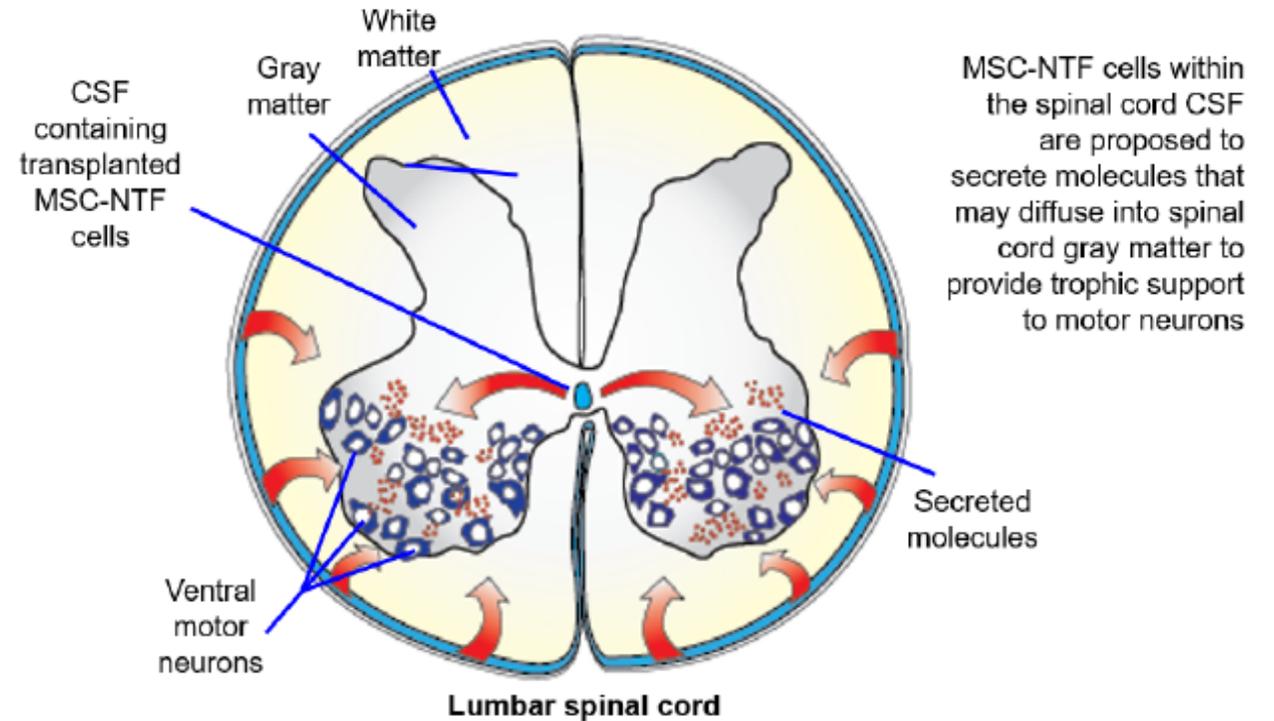
Stem Cell Therapy Success Lessons

- Treat as early in the disease process as possible¹
 - Protecting established neural circuits/networks much more tractable than reconstructing or replacing them
- Transplanted stem cell to participate in homeostatic processes of target organ (brain & spinal cord)
- Need for consistency with biological imperatives of the target organ and the cell
 - Match cells that belong in milieu and follows their biological function
 - Promote reciprocal cross-talk among different cell types for balanced homeostasis
- Cells must reach target of action for requisite amount of time, in requisite dose



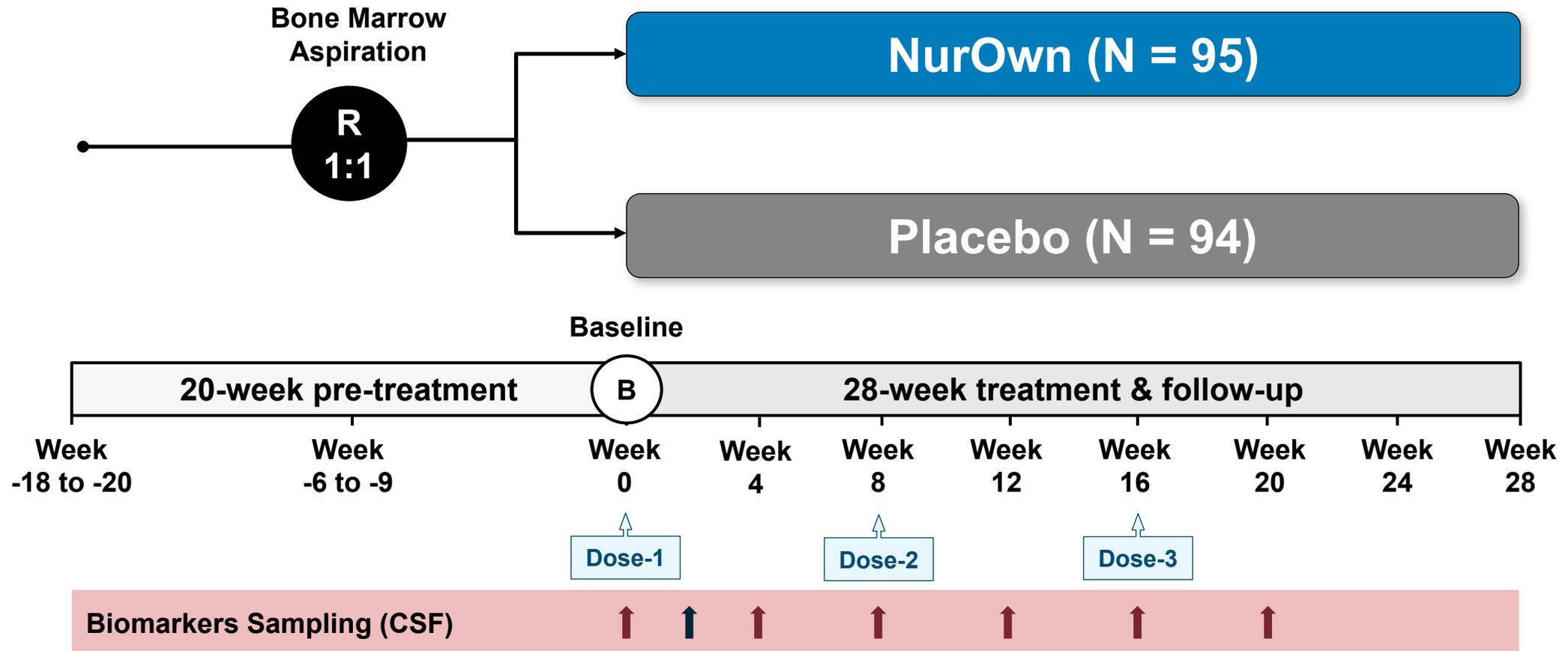
NurOwn (MSC-NTF): A Novel Stem Cell Therapy

- Modulates neuroinflammatory and neurodegenerative disease processes
 - Promotes neuronal survival
 - Improves neurological function
- Autologous cells recognized as individual's own cells
 - Safer choice in avoiding unwanted immune responses



Ref: FDA CMC Reviewer – FDA Advisory Committee (CTGTAC) on NurOwn September 27, 2023

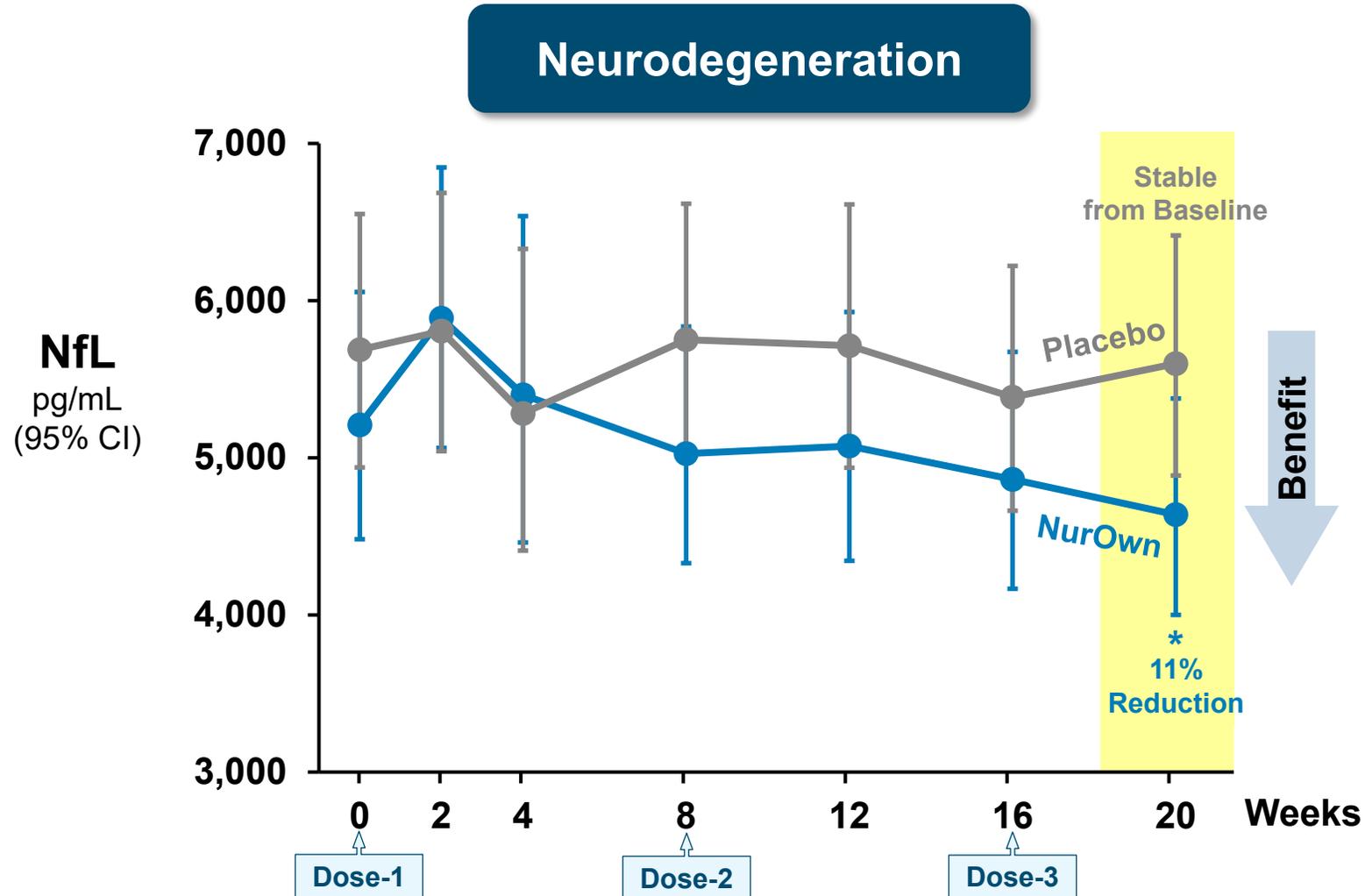
BCT-002-US: NurOwn Phase 3 Trial in ALS



BCT-002-US: Biomarkers from Different Pathways

Biological Pathway	Biomarkers
Neurodegeneration	NfL, pNfH, DR6, Caspase-3, TWEAK, UCH-L1, miR-142-5p, Tau
Neuroinflammation	
Anti-inflammatory	LAP (TGF- β 1), Fetuin-A, IL-37, MSR1, miR-146a-5p, miR-146b-5p
Pro-inflammatory	MCP-1, CHI3L1/YKL-40, Chitotriosidase-1, IP-10, S100B, SDF-1a, TREM-2, ICAM-1, GFAP, OPG
Neuroprotection	Galectin-1, BDNF, VEGF, Clusterin/ApoJ, NMNAT1, GDF-15, HGF, G-CSF, LIF
Others	miR-124-3p, miR-132-3p, miR-20a-5p, miR-9-3p, miR-34a-5p, miR-206, Follistatin, miR-19b-3p, Osteopontin, miR-199-5p, miR-126-3p, miR-30b-5p,

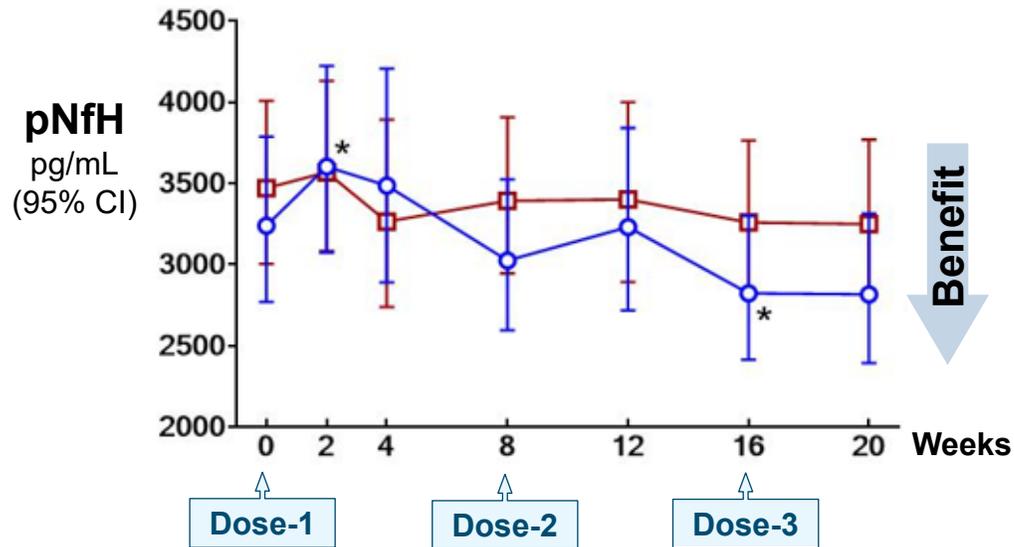
NurOwn Significantly Lowers NfL vs Placebo



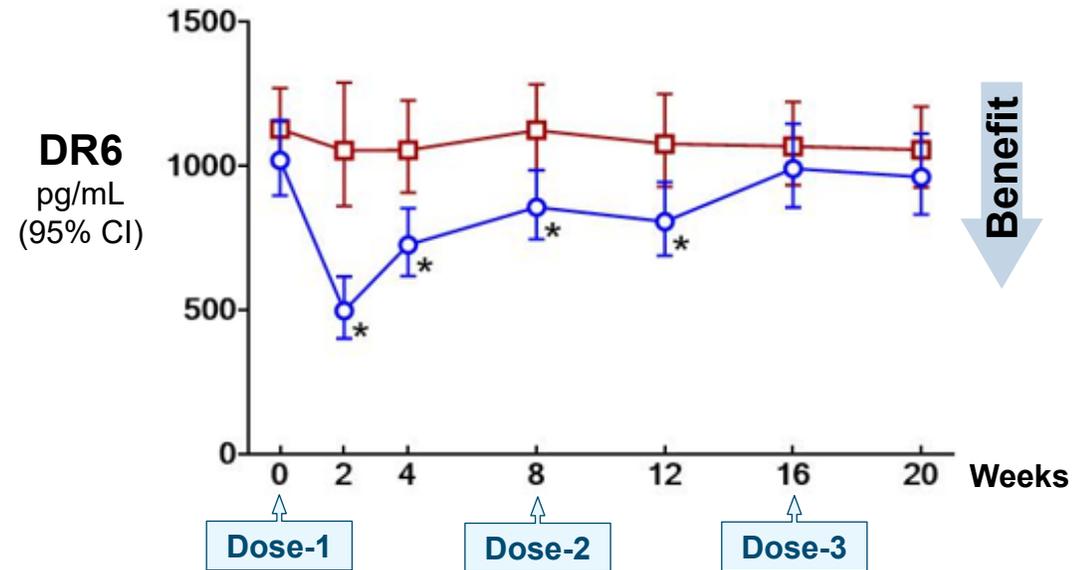
* $p < 0.05$

NurOwn Positive Impact on Neurodegeneration Biomarkers

pNfH: Neurodegeneration



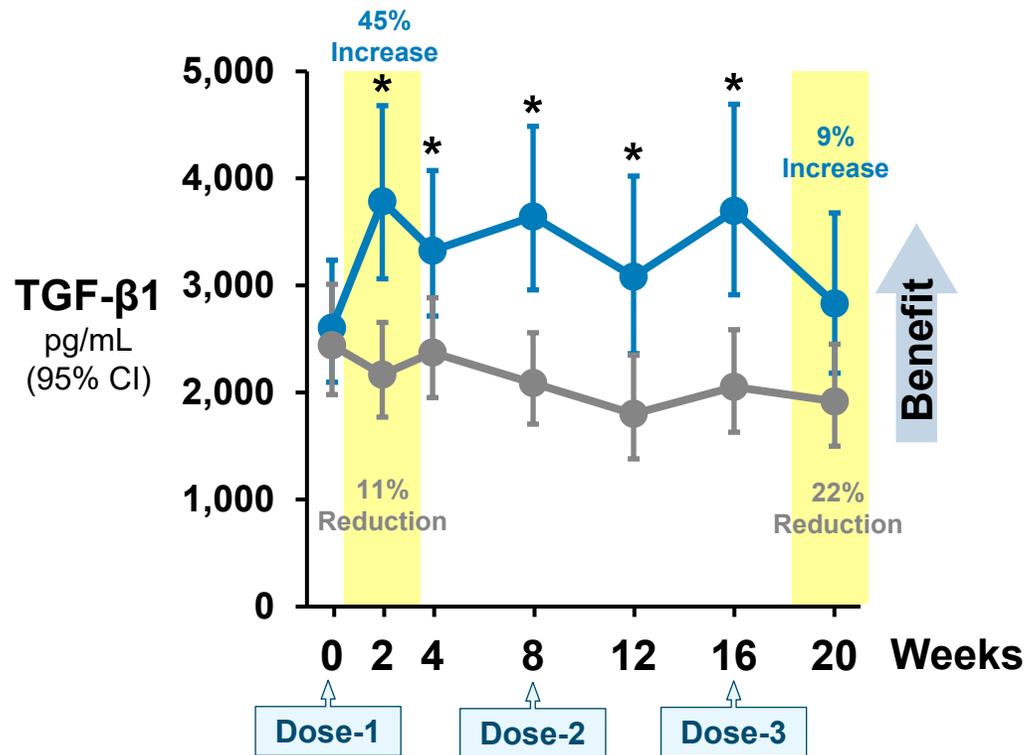
DR6: Neurodegeneration



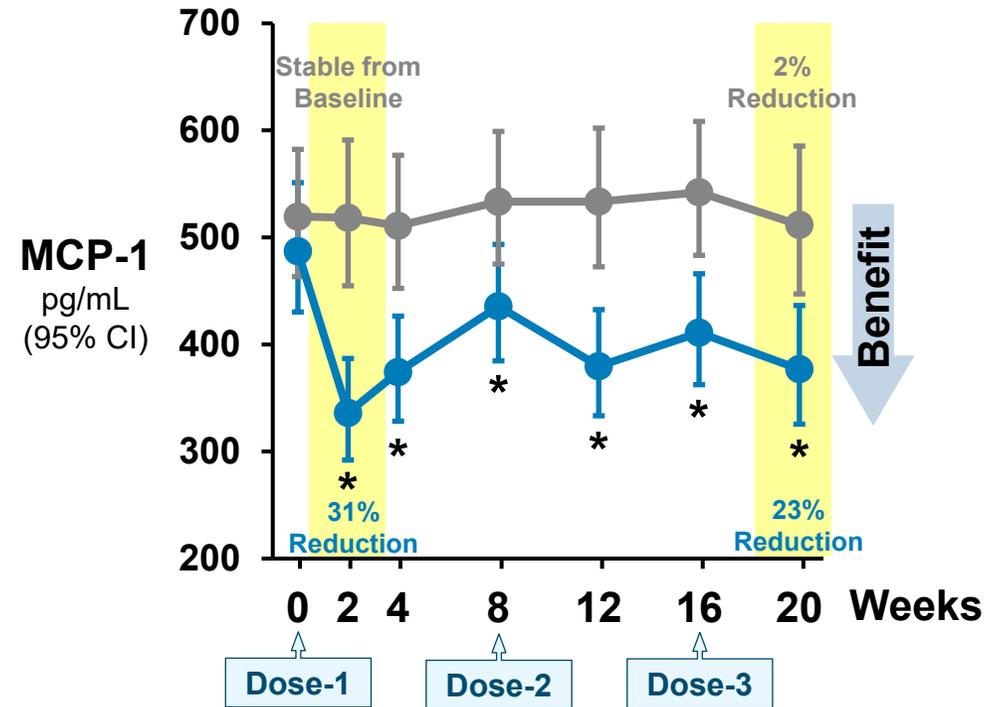
* p < 0.05

NurOwn Significantly Impacts Inflammatory Biomarkers

Anti-inflammatory



Pro-inflammatory



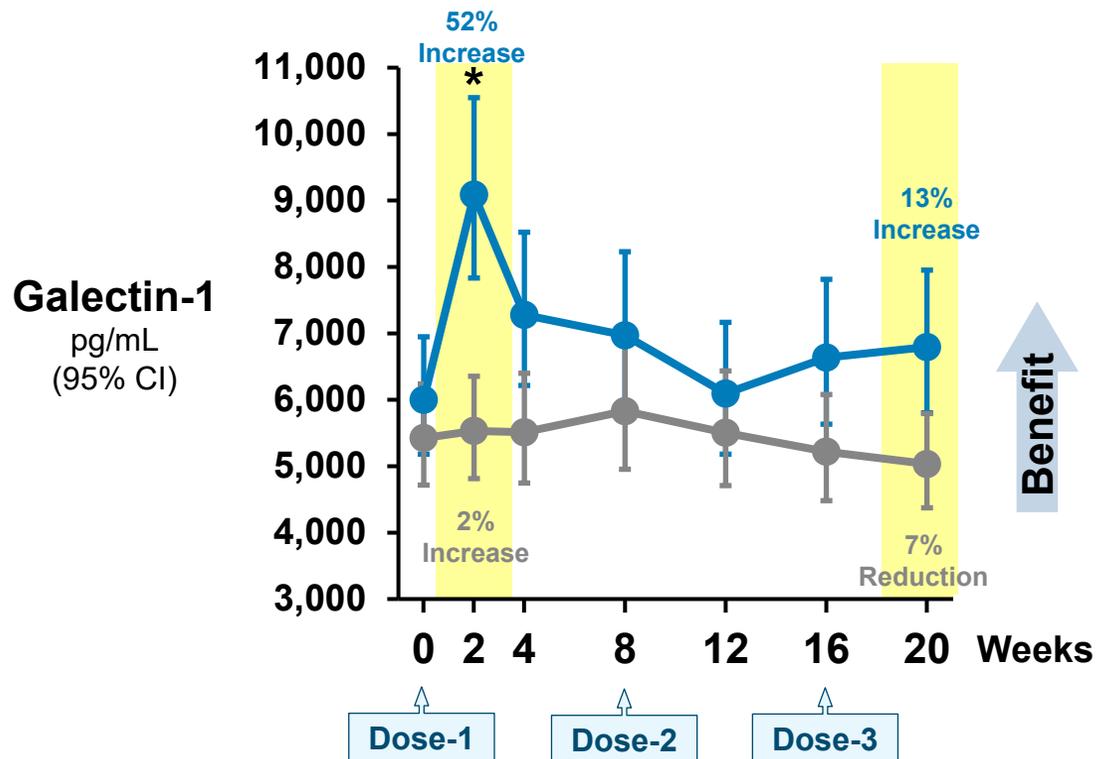
● NurOwn
(N = 95)

● Placebo
(N = 94)

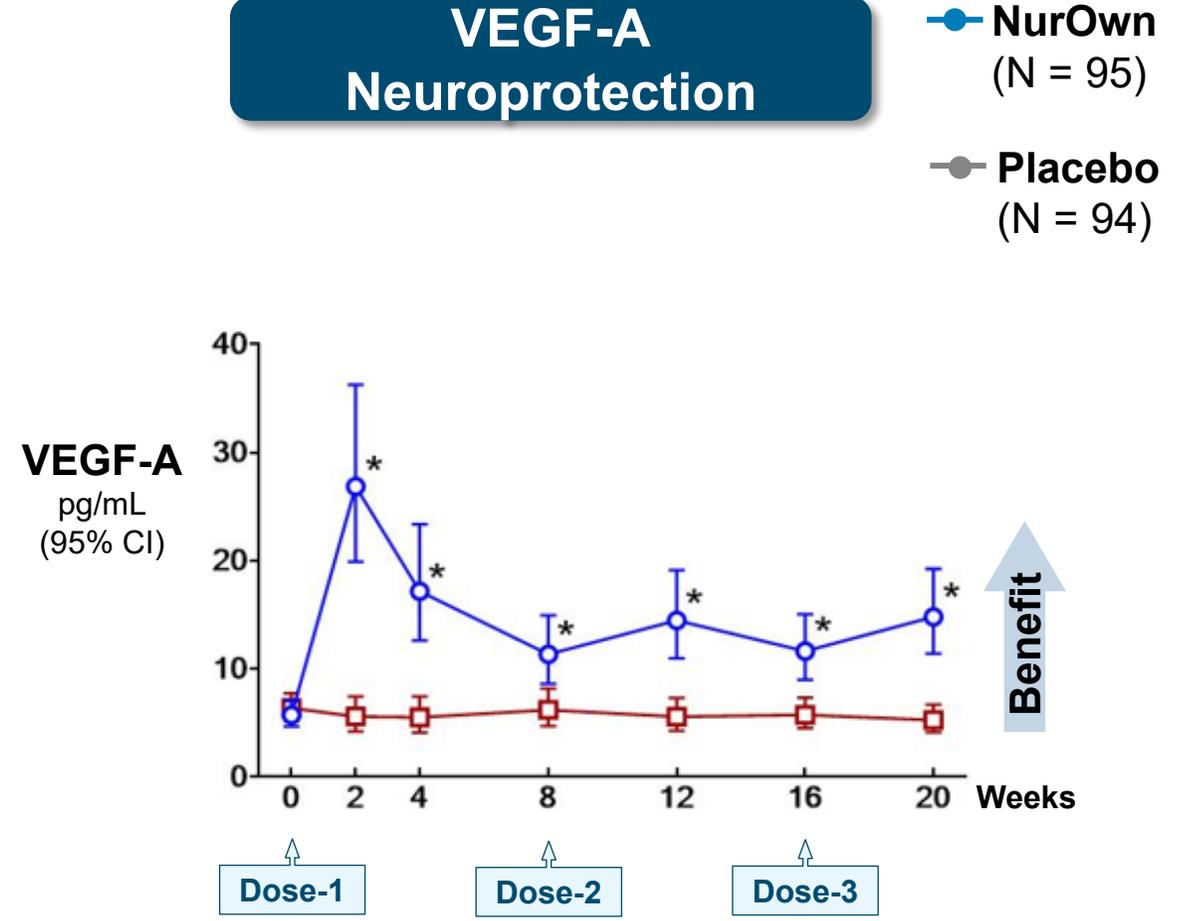
* p < 0.05

NurOwn Significantly Impacts Neuroprotection Biomarkers

Galectin-1 Neuroprotection



VEGF-A Neuroprotection

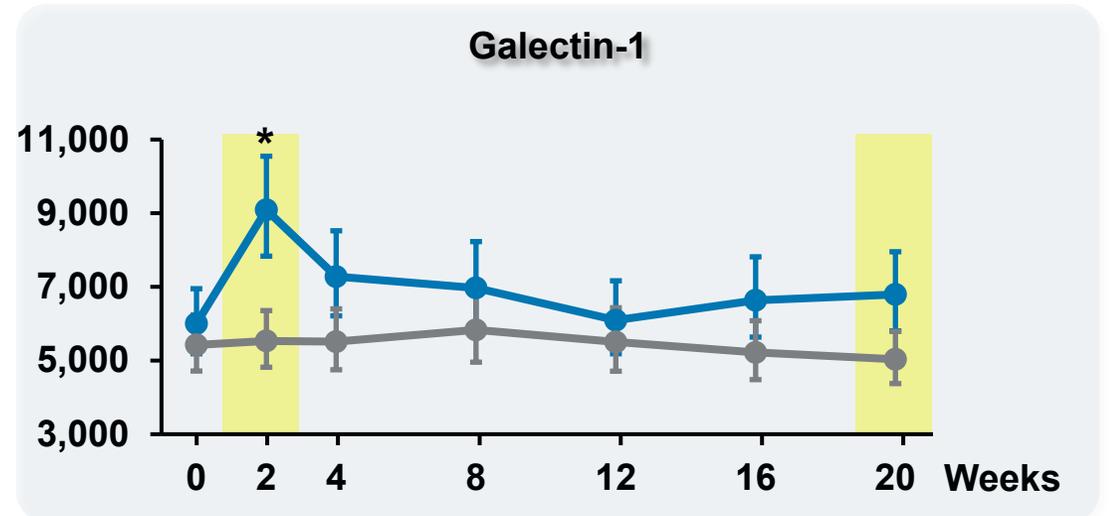
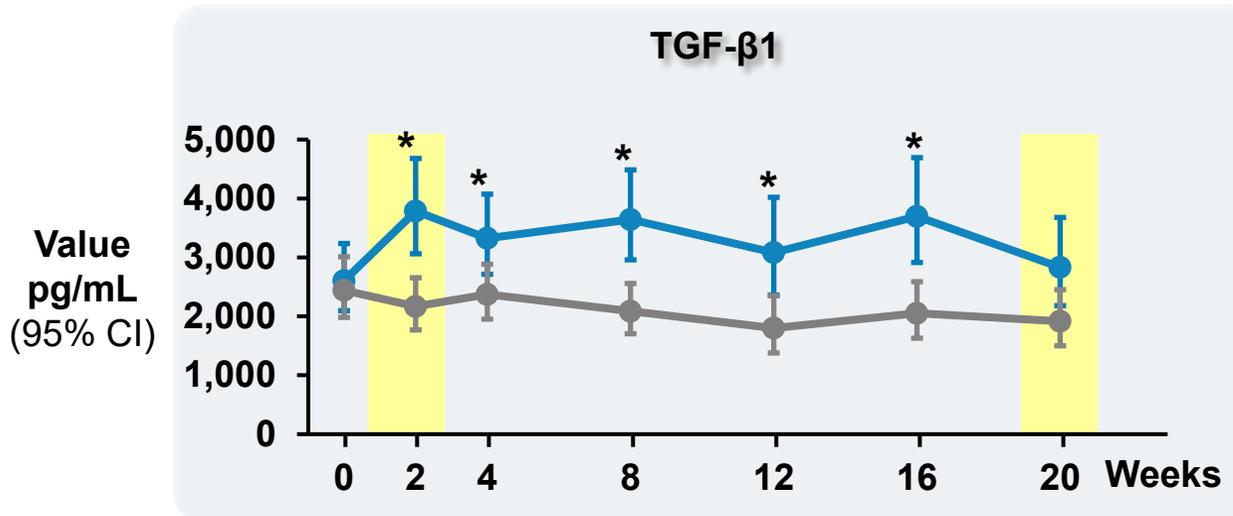
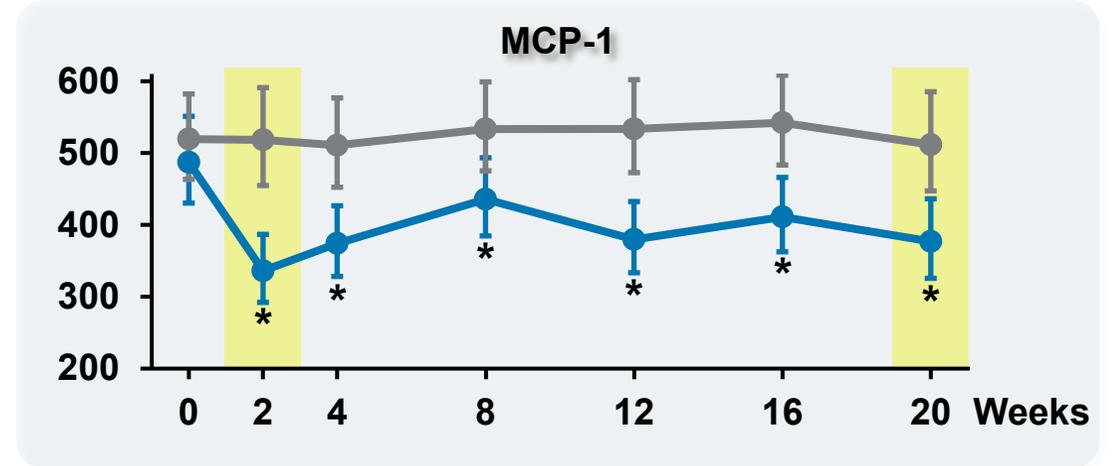
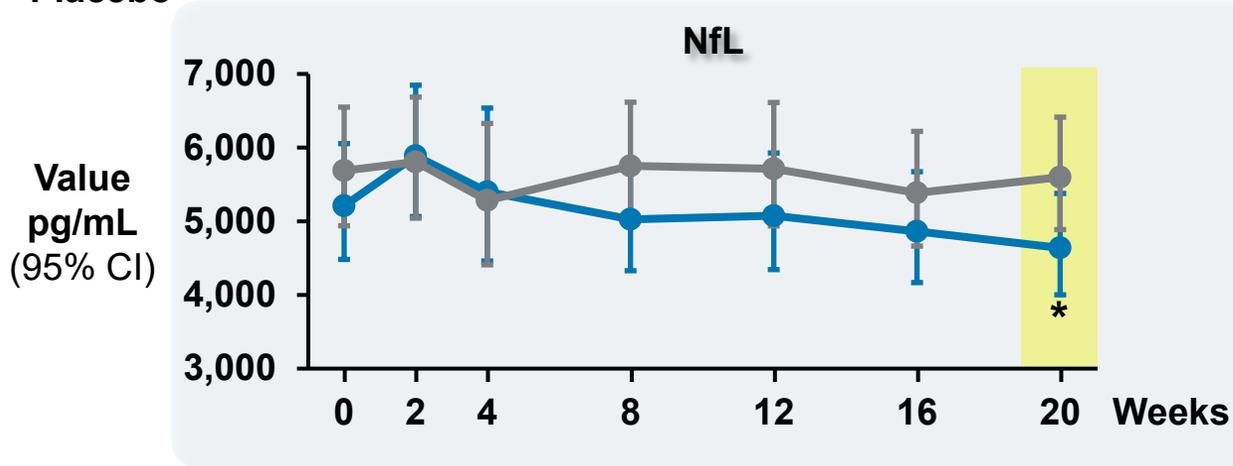


* p < 0.05

Totality of Evidence Supports NurOwn MOA

Average Z-score = 2.24
p < 0.0001

● NurOwn
● Placebo



* p < 0.05

NurOwn Phase 3 Trial in ALS: Data Summary

- ✓ Clinical results in overall population did not reach significance
 - ✓ Results in subgroups with less advanced disease show consistent treatment effect of NurOwn across endpoints and over time
 - ✓ Supportive results from biomarkers data
 - ✓ Data collected support safety of repeat intrathecal administration
- Positive benefit/risk profile in participants with **mild to moderate disease**

Thank you