HEALEY ALS Platform Trial

March 19, 2026

Massachusetts General Hospital
Founding Member, Mass General Brigham

HARVARD MEDICAL SCHOOL

Healey & AMG Center

Sean M. Healey & AMG Center for ALS
at Massachusetts General Hospital

TACKLE ALS "DON'T BE SORRY LETS BEAT THIS"

ALS ASSOCIATION

MDA Muscular Dystrophy Association

SALSA For a Cure

alsFINDINGaCURE

NEALS Network of Excellence for ALS

I AM ALS

TAMBOURINE

NEUROLOGICAL CLINICAL RESEARCH INSTITUTE

BARROW Neurological Institute

ALS ONE

RUN2REVIVE MIND · BODY · POTENTIAL

Berry Consultants Statistical Innovation

1850 MELIORA

ucb

biohaven pharmaceuticals

CLENE NANOMEDICINE

prilenia

THE ARTHUR M. BLANK FAMILY FOUNDATION

BASEBALL WINTER MEETINGS SAN DIEGO 2015

SEELOS THERAPEUTICS

Calico

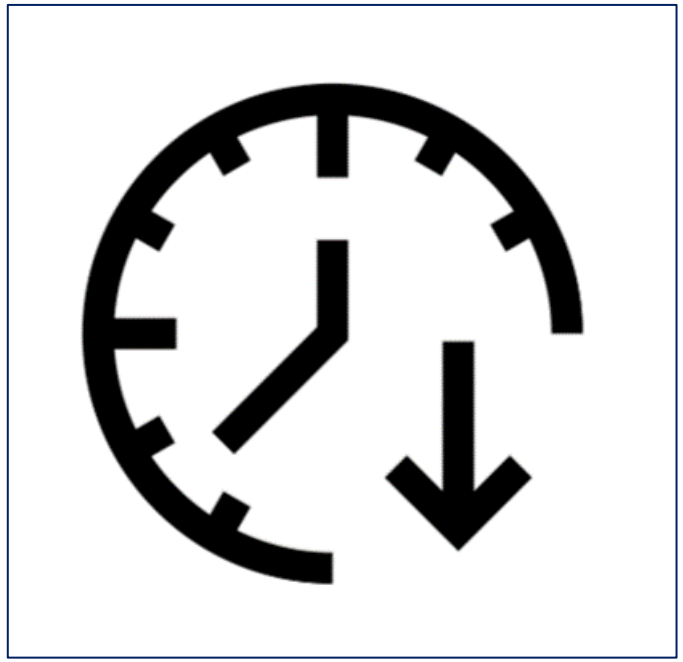
DENALI

Neurizon

AMG The AMG Foundation

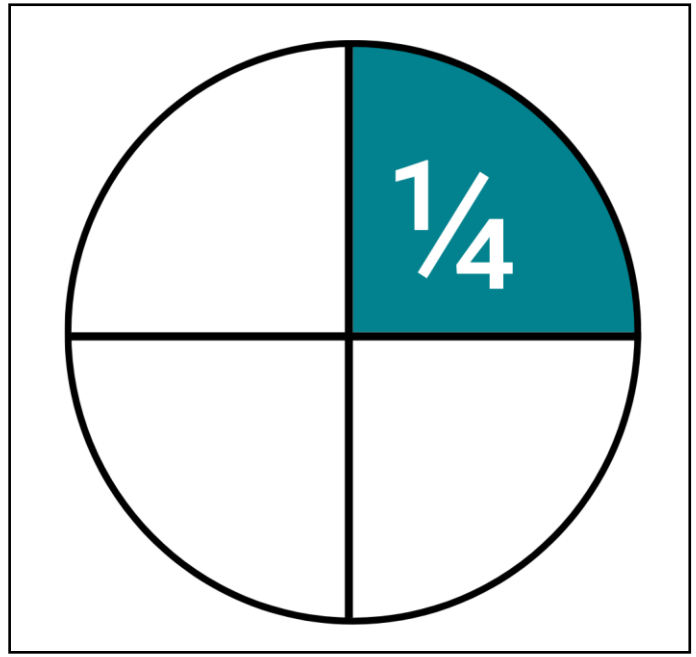
The HEALEY ALS Platform Trial has transformed the ALS trial landscape

Platform trials have several advantages over traditional trials



Cuts time in 1/2

Cuts costs by 1/3

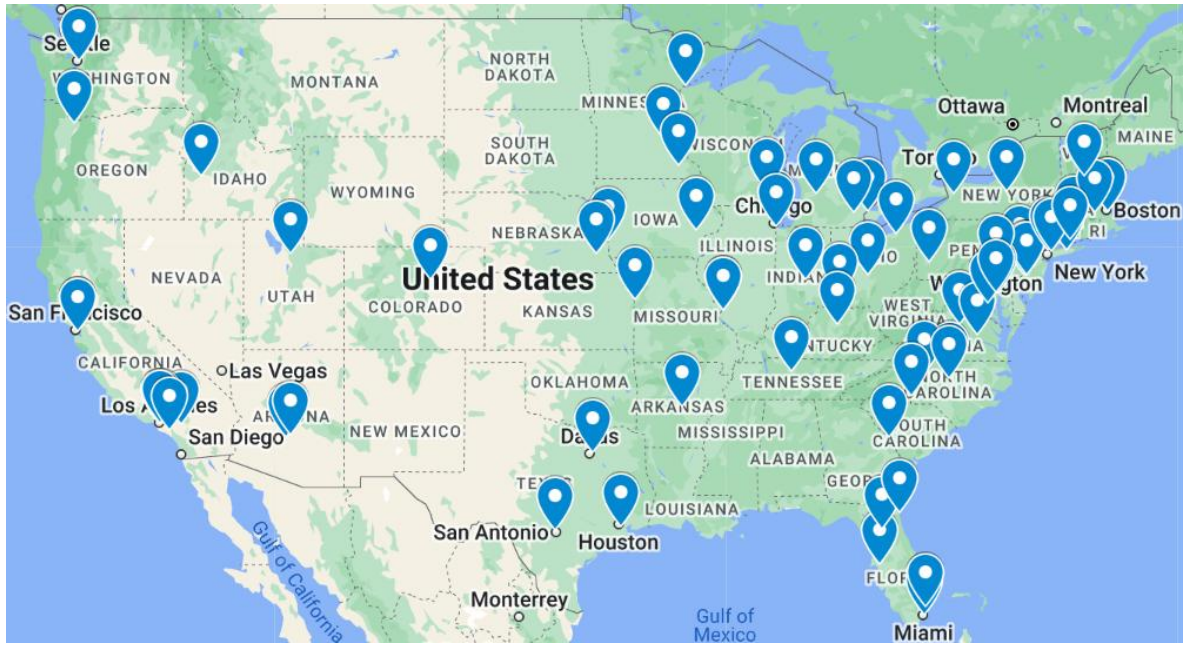


Reduces placebo

Five years of innovation and impact

5 YEARS

Thank You



Study drugs tested: **7**

Study drugs that offered Expanded Access: **3**

Study participants: **1,373**

IRB approved Platform Trial sites to date: **88**

Study visits: **25,632**

Current study staff nationwide: **946**

Biosamples: **271,643**
Includes plasma, serum, urine, whole blood, isolated DNA, and CSF

10
Publications
Published in the JAMA and Lancet Families of journals, Nature Aging, Muscle and Nerve and Annals of Neurology

Multiple
Publications in the pipeline
Including Regimen F and G results, papers on biostatistics, biomarkers and digital outcomes

48
Poster presentations

78
Oral presentations

Sharing experience with
29
Disease-specific networks

114
Companies we have engaged
52
Companies that applied

~180
Total webinars hosted
~60,000
Total views on YouTube

The trial learns from its experience and adapts

Revised the Master Protocol to:

- Increase statistical power
- Streamline operations
- Add even more patient-centered features

Study Duration

9 months RCT followed by ATE

Inclusion Criteria

2 years since symptoms onset

Visit Schedule

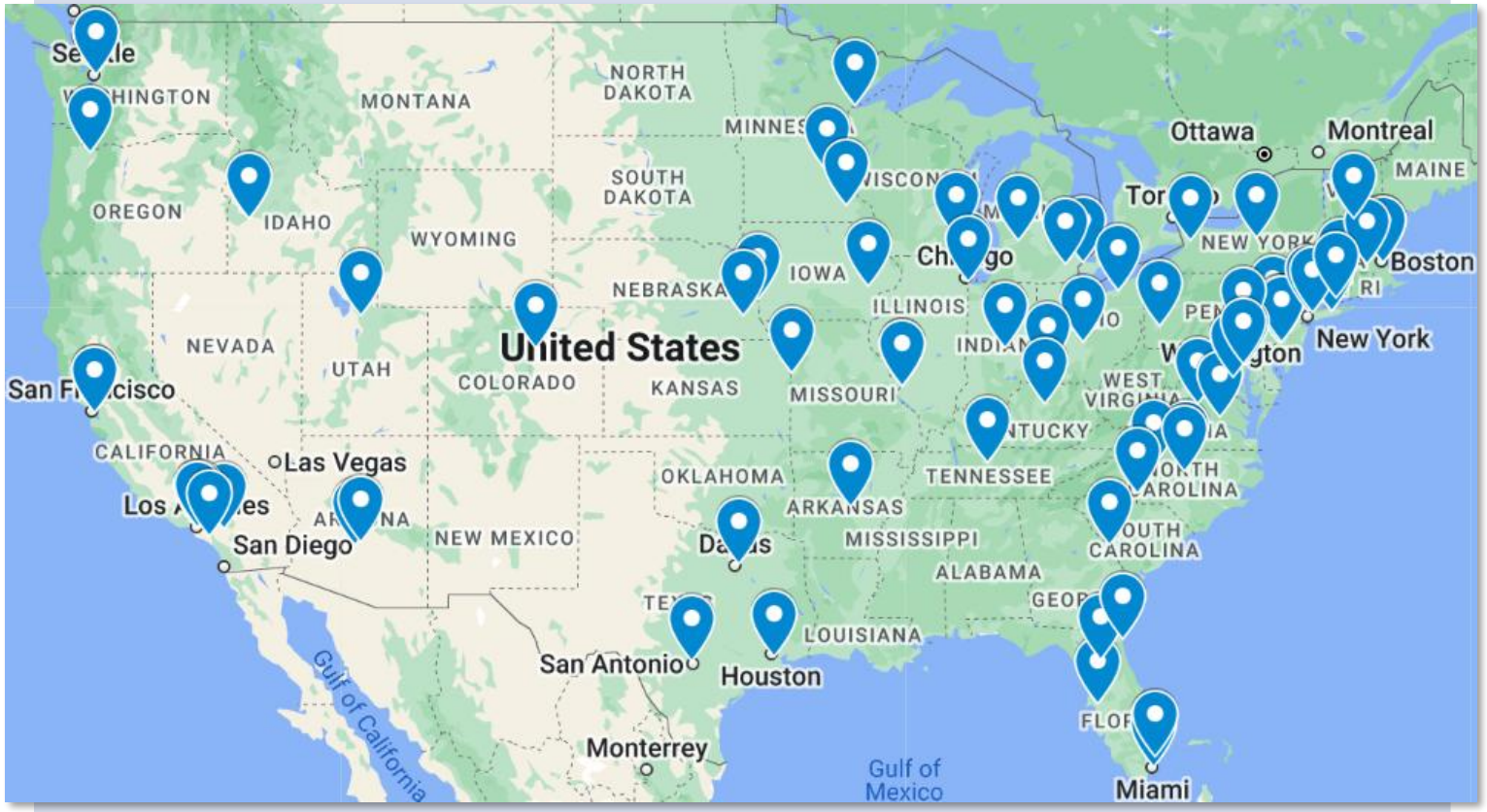
Increased remote visits (patient-centered)

Biomarkers

New biomarkers

New regimens will enroll under the revised Master Protocol

The trial operates across a network of ALS centers of excellence in the US



Site Map & Contacts:

https://bit.ly/3g2NZr5

NEALS Network of Excellence for ALS

HEALEY ALS Platform Trial Communications

Catherine Small
Patient Navigator

Patient Navigation – Central resource for people living with ALS

Phone: 833-425-8257 (HALT ALS)

E-mail: healeyalsplatform@mgh.harvard.edu

We provide information on our website, community webinars, ALS Link emails, and Mass General Neurology's social media (LinkedIn, Facebook, X)

https://bit.ly/4jtw4In
HEALEY ALS Platform Trial News & Webinars

https://bit.ly/4ubNb8f
Community Webinar Sign Up

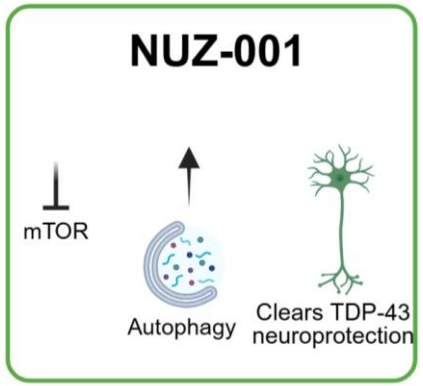
https://bit.ly/3V2MBt6
ALS Link Email List Sign Up

Regimen I (NUZ-001)

Industry Partner

Neurizon

Mechanism of action



Regimen co-leads

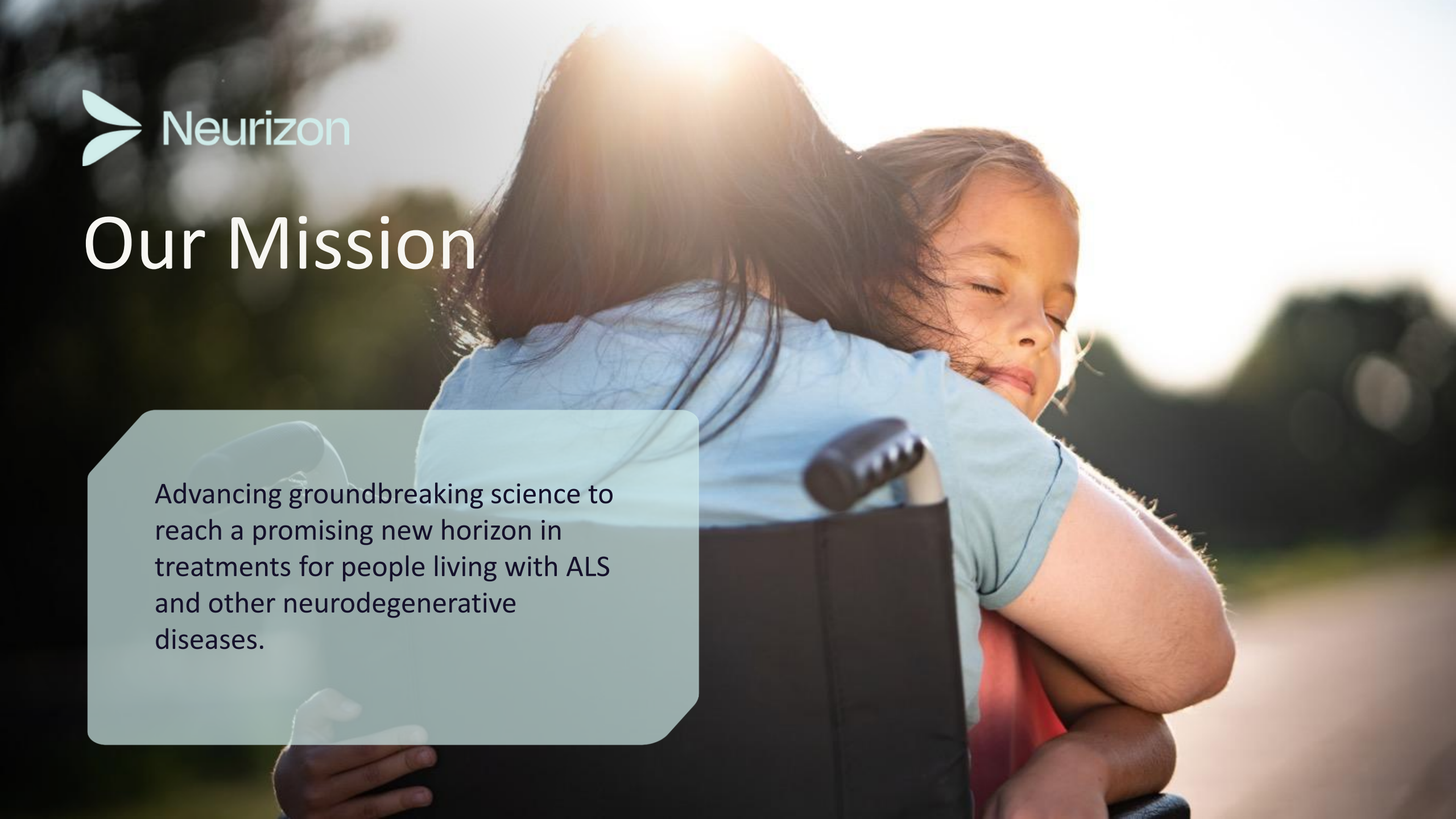
James Berry, MD, MPH
Mass General Brigham

Michael Weiss, MD
University of Washington

NUZ-001 (Regimen I)
HEALEY ALS Platform Trial

Speakers:
Dr. Chris Freitag- Chief Medical Advisor
Sharon Tamir- ALS Program Lead
Neurizon Therapeutics

Neurizon



Neurizon

Our Mission

Advancing groundbreaking science to reach a promising new horizon in treatments for people living with ALS and other neurodegenerative diseases.

NUZ-001 is an investigational therapy being developed for people living with ALS

In most people with ALS, a protein called TDP-43 becomes mislocalized and forms harmful aggregates inside motor neurons, contributing to cellular stress and degeneration.

NUZ-001 is designed to:

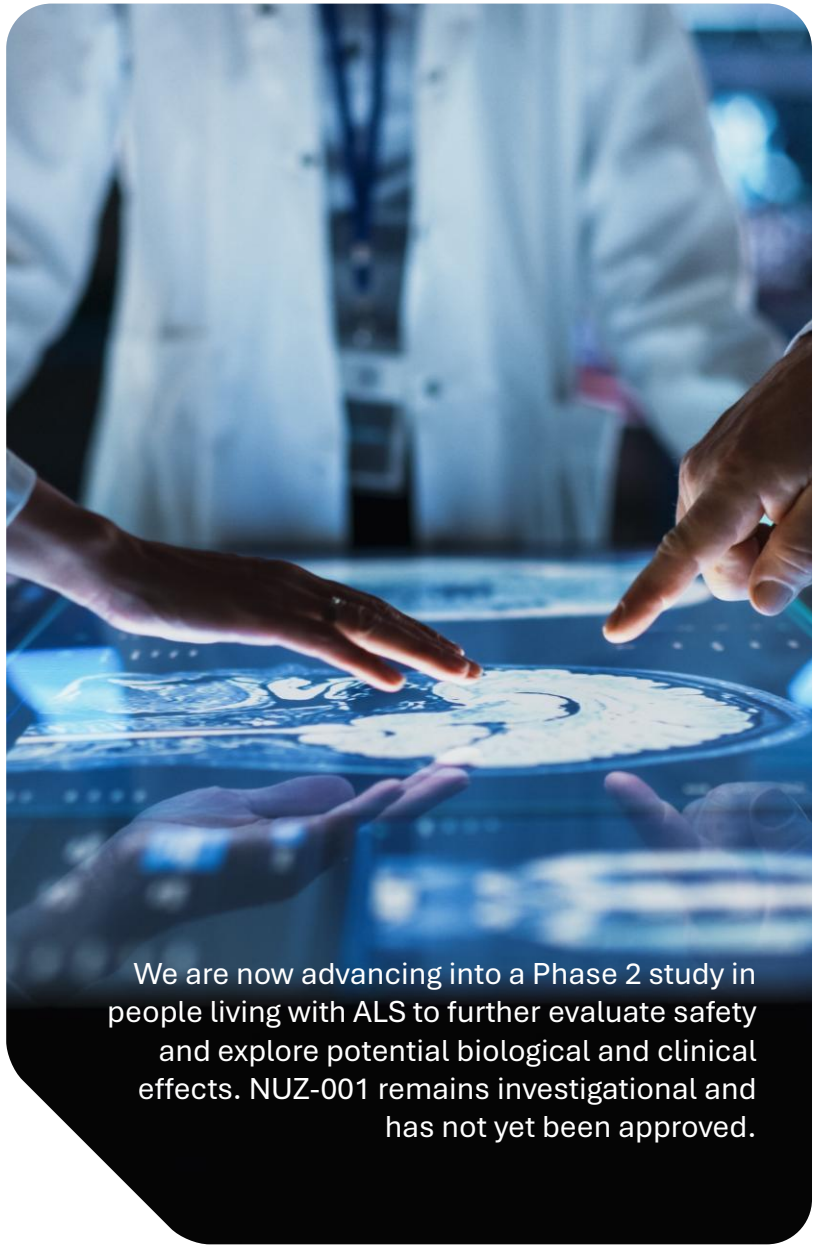
- Strengthen the cell's own internal natural clearance systems
- Switch on protective pathways that help clear away toxic protein buildup and support cell survival
- Address underlying disease biology and not just symptoms

Safety Data:

- Phase 1 study completed, demonstrating safety and tolerability in a small group of participants
- Supported by extensive nonclinical animal safety data generated over more than 20 years in another indication

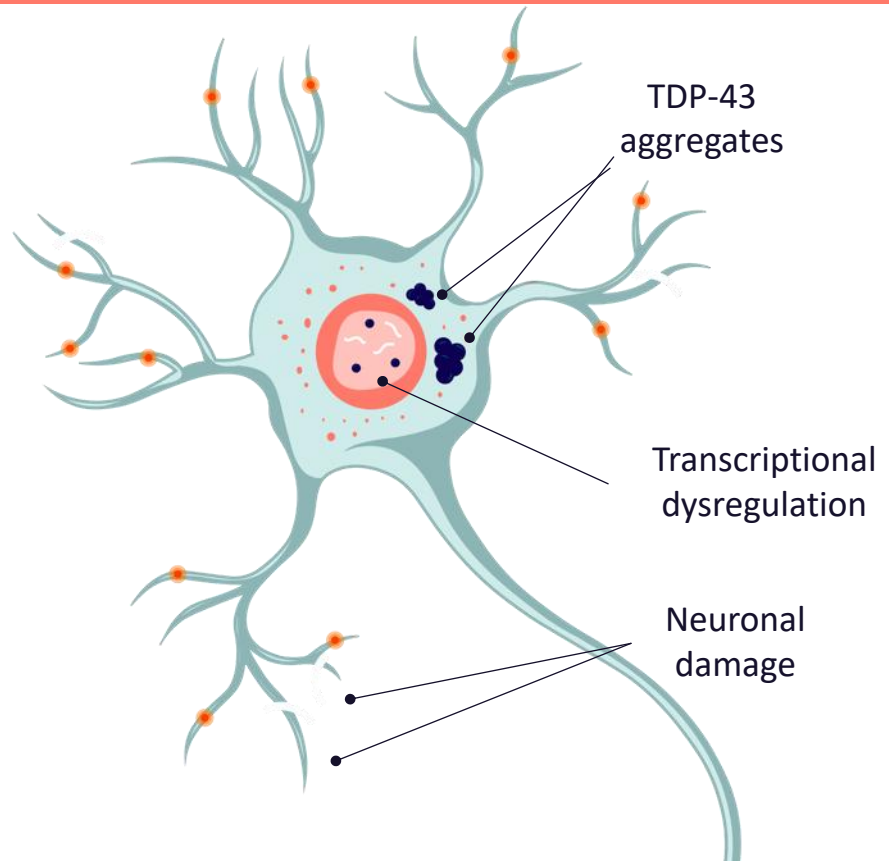
Today we will share:

- Why TDP-43 biology is central to sporadic ALS
- What we have learned from preclinical research and Phase 1 studies
- How these findings inform our upcoming Phase 2 clinical trial

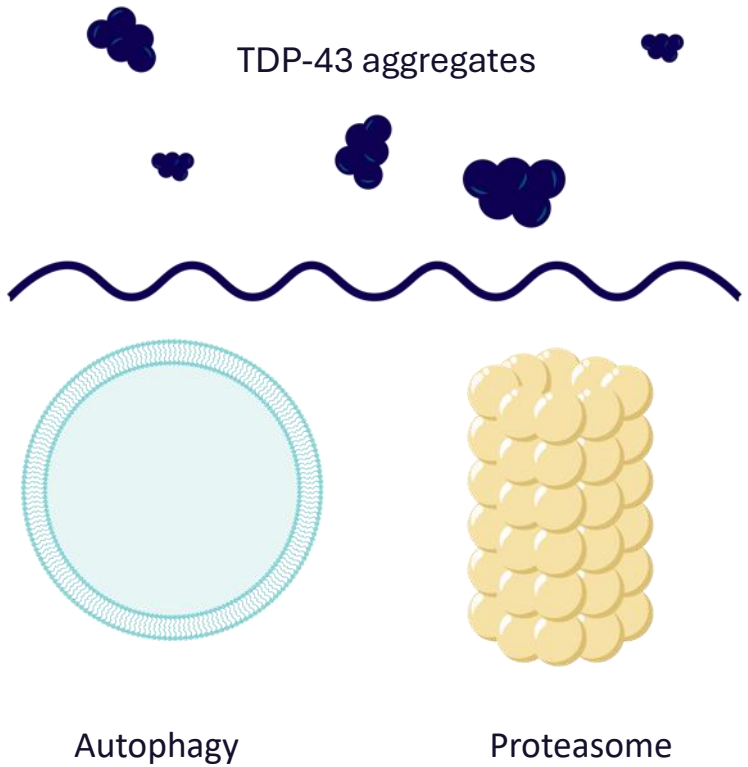


Protein Aggregation and Reduced Protein Clearance are Drivers of Neuronal Pathology in ALS

TDP-43 protein aggregation is a major driver of neuronal damage in ALS

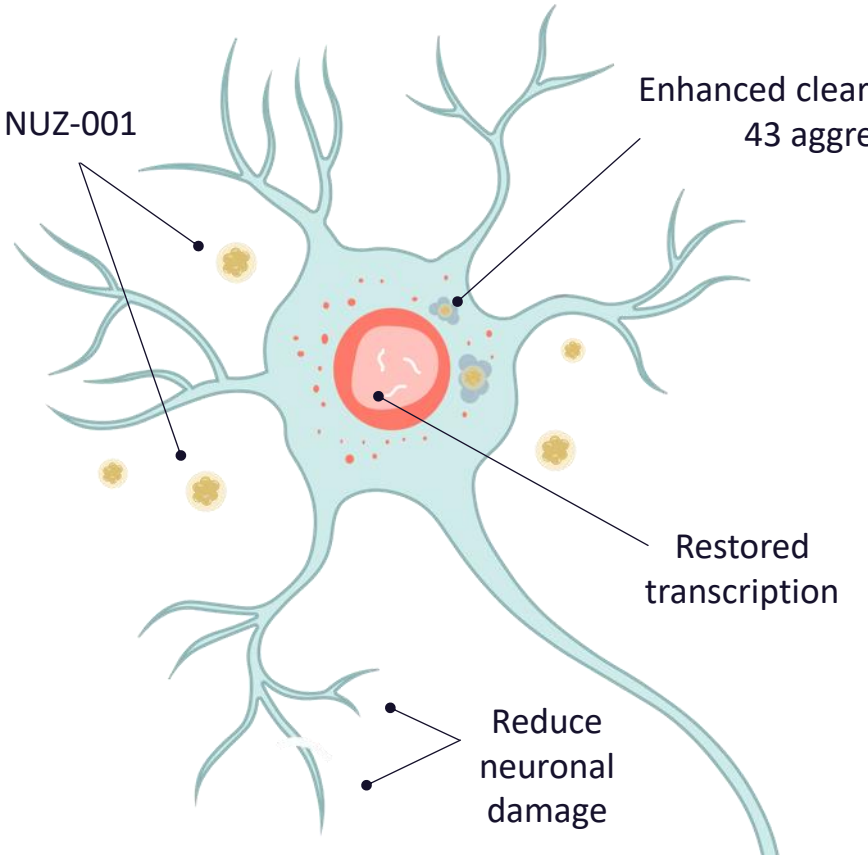


Protein aggregates block endogenous protein clearance pathways

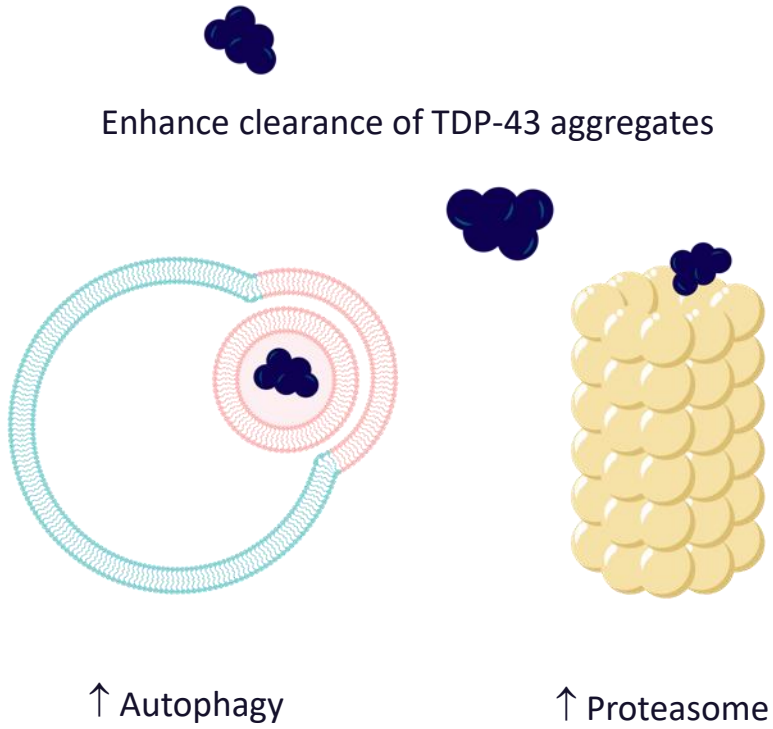


NUZ-001 Enhances Endogenous Protein Clearance Pathways to Remove Toxic Protein Aggregates

NUZ-001 enters neuron and binds molecular target

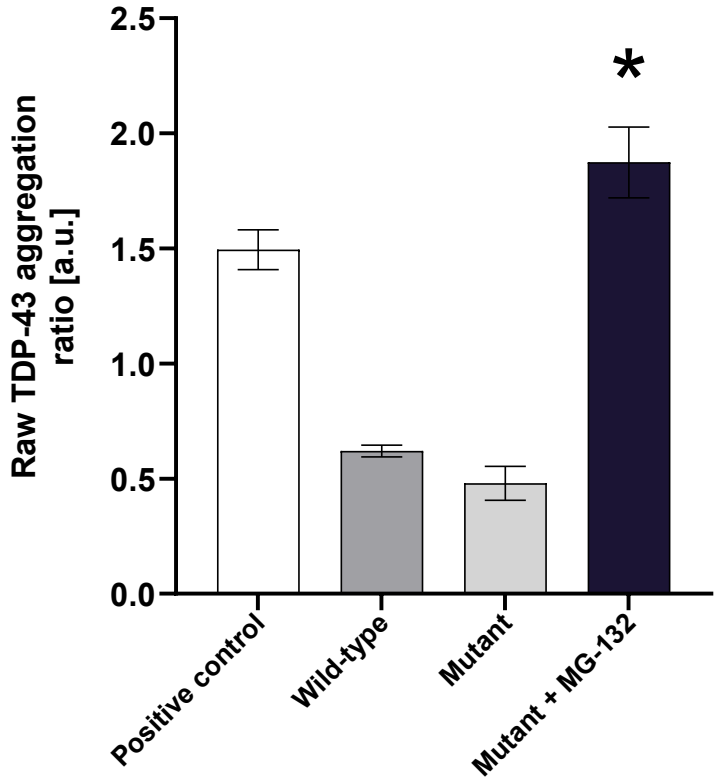


NUZ-001 enhances endogenous protein clearance pathways

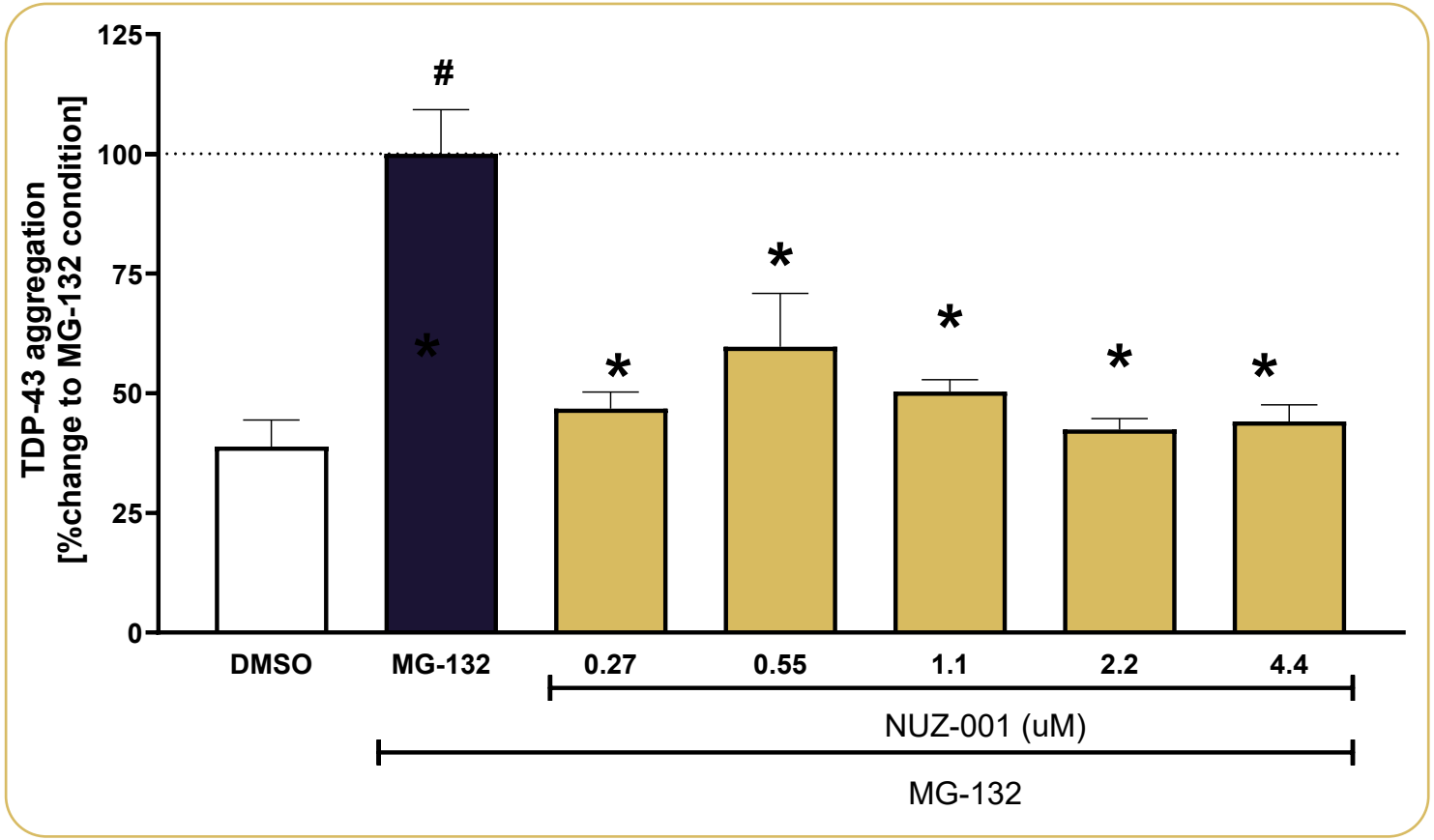


NUZ-001 Prevents TDP-43 Aggregation in ALS Neuronal Model Under Stress

Proteasome inhibitor, MG-132, induces TDP-43 aggregation in an ALS mutant neuronal model



NUZ-001 prevented TDP-43 aggregation in ALS mutant neuronal model



Human iPSC-derived motor neurons were treated with NUZ-001 at multiple concentrations for 6 days. TDP-43 aggregation was evaluated 24 hr following the last treatment. * p<0.05 vs MG-132 treatment. # p<0.05 DMSO

Key insights from Phase 1 ALS MEND and Open Label Extension (OLE) Study

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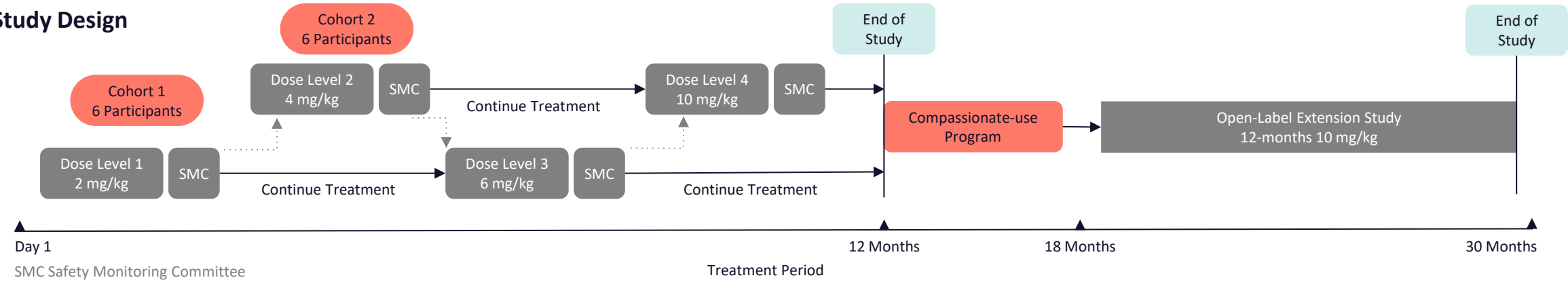
Phase 1 ALS MEND and Open Label Extension (OLE) Study Design

The Phase 1 MEND Study was an open-label, multicentre study involving 12 participants with ALS that commenced in October 2022, followed by a compassionate-use program and later a 12-month open-label extension study.

Study Design



Study Completed

- Phase 1 MEND Study top-line results released in Q1 CY2024
- 12 participants continued treatment with NUZ-001 under a compassionate-use program
- 10 participants rolled-over into a 12-month Open-Label Extension (OLE) Study.
- Top-line results demonstrated long-term safety and preliminary efficacy signals of ALS treatment with NUZ-001
- NUZ-001 has been safely used for more than 3 years, with three participants still receiving treatment under the TGA's Special Access Scheme
- Recommended Phase 2 dose selected as 10 mg/kg

Phase 1 Open Label Extension
Safety and Tolerability Summary

Study drug was well tolerated during long-term administration in the OLE, with no dose-limiting toxicities and no treatment-related deaths.

	Total (n)	Related to Treatment (n)
Adverse Events	25	3
Serious Adverse Events	5	0

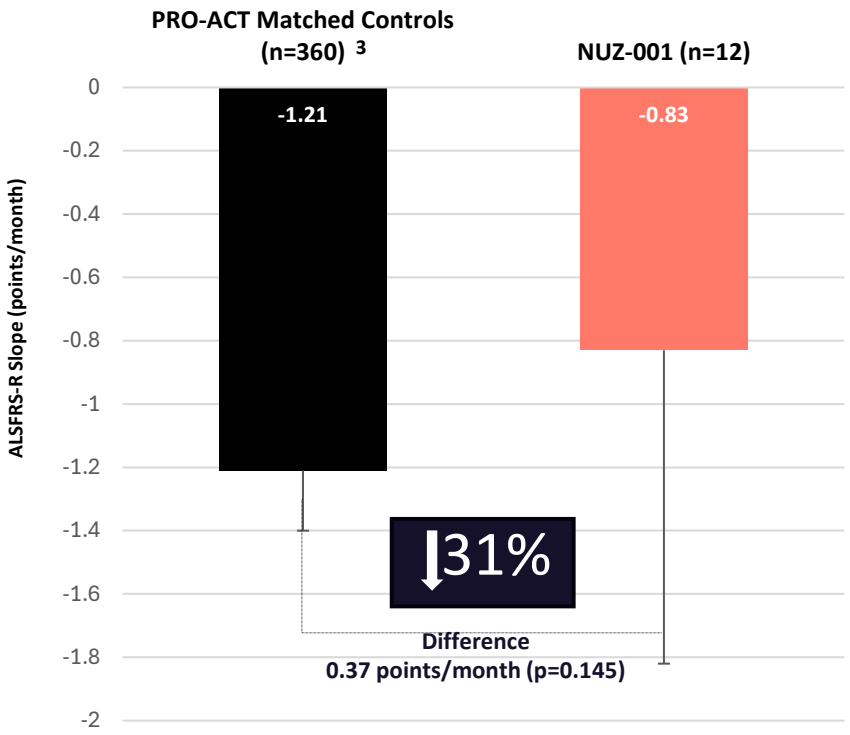
- No participants withdrew from study
- No serious adverse events related to study drug
- Three (30%) participants reported AEs possibly related to study treatment, mild to moderate
  - Raised liver enzyme, Increased hair growth, Dry mouth at night
- Four (40%) participants experienced serious adverse events, all unrelated to study drug
  - Polymyalgia Rheumatica, Pneumonia, Respiratory Failure, Soft Tissue Injury, Suicide Attempt – Overdose

- No unexpected safety findings observed in the OLE compared with Phase 1 MEND.
- 3 participants still receiving treatment under the TGA's Special Access Scheme.

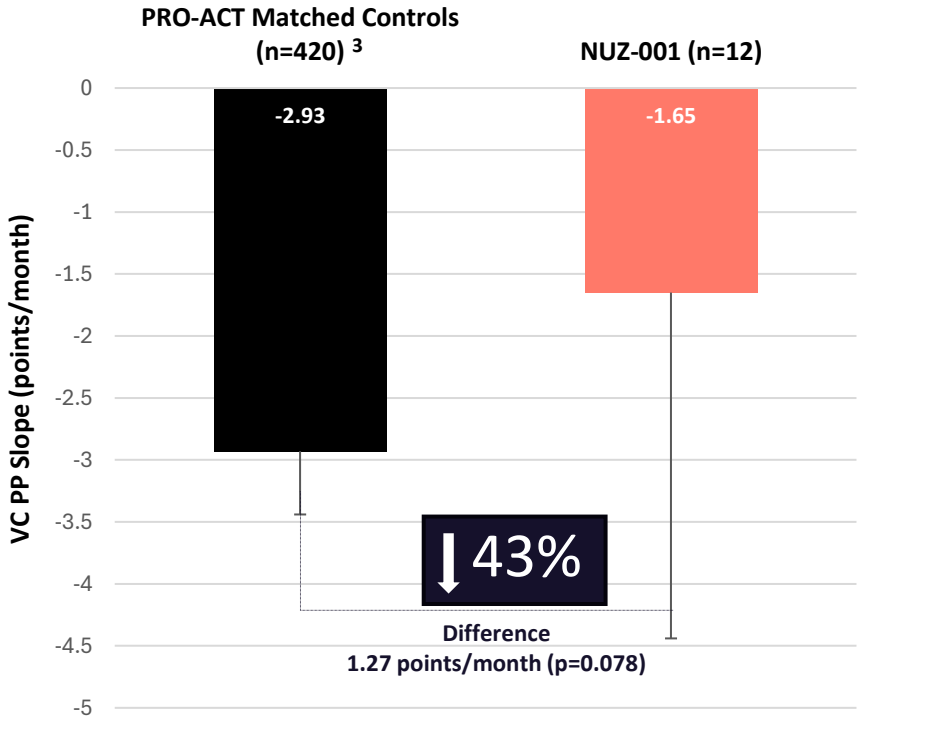
Phase 1 Open Label Extension
Preliminary Efficacy ALSFRS-R and SVC

Treatment with NUZ-001 across combined Phase 1 and OLE studies showed slower progression of ALS in all participants by 31% for ALSFRS-R and 43% for SVC percent predicted (PP) when compared to matched controls from the PRO-ACT historical database[1].

Motor Function – ALSFRS-R



Respiration – SVC PP[2]



1. Atassi N, Berry J, Shui A, Zach N, Sherman A, Sinani E, Walker J, Katsovskiy I, Schoenfeld D, Cudkowicz M, Leitner M. The PRO-ACT database: design, initial analyses, and predictive features. Neurology. 2014 Nov 4;83(19):1719-25. doi: 10.1212/WNL.0000000000000951.Epub 2014 Oct 8. PMID: 25298304; PMCID: PMC4239834
2. Forced vital capacity (FVC) was used when SVC was not collected
3. Matched on time since onset, baseline ALSFRS-R, pre-baseline ALSFRS-R slope, and disease onset location

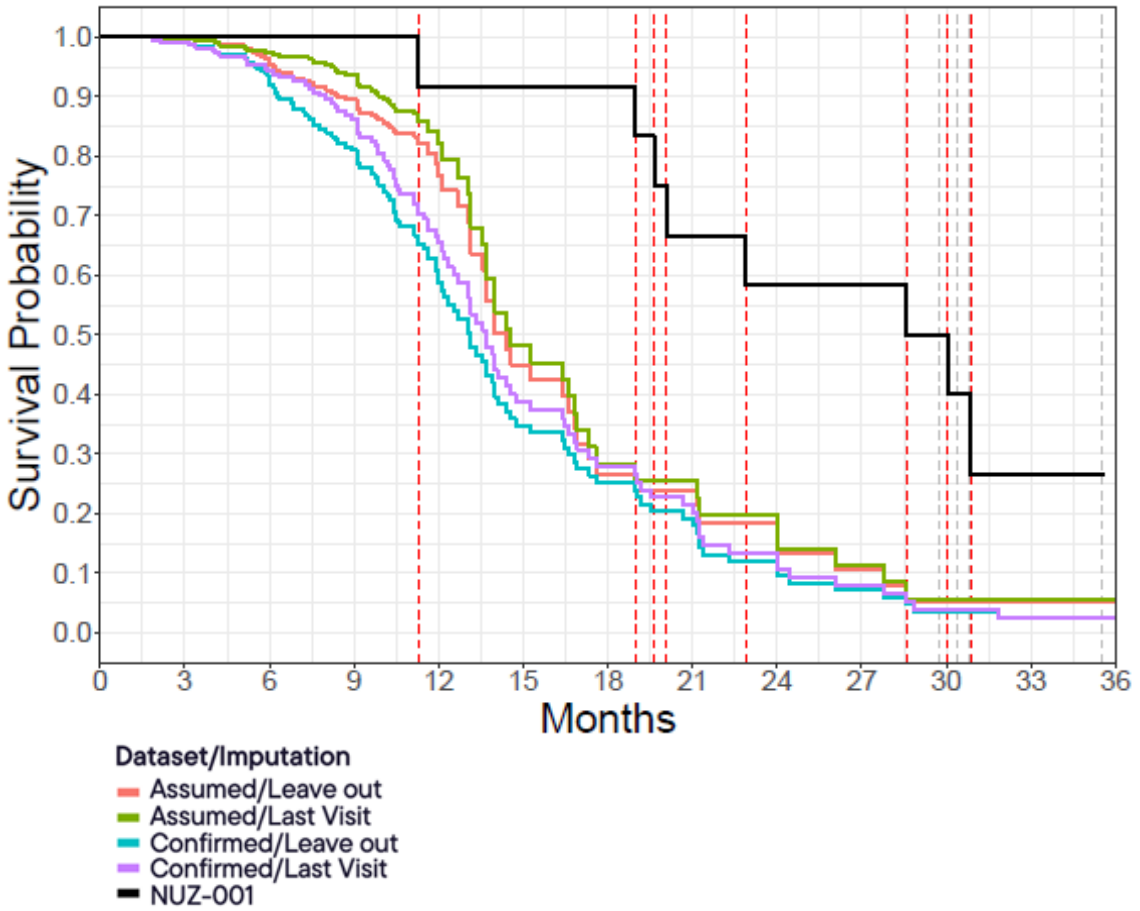
Phase 1 Open Label Extension

Survival Probability Analysis

Treatment with NUZ-001 resulted in significantly longer survival of participants with ALS, (X^2=10.95, p=0.00094), when compared to matched controls[1] from the PRO-ACT database[2]

Analysis suggests that treatment with NUZ-001 reduces the risk of death by 70.2%:

Hazard ratio of 0.298 (95% CI: (0.135, 0.659), p = 0.0028)



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Phase 1 Open Label Extension
Conclusion

These results support the potential of NUZ-001 as a disease-modifying therapy for ALS and provide strong justification for advancing the program into further clinical development with the HEALEY ALS Platform Trial

Highlights (Based on a small study population of 12 participants)

Primary Objectives
- Long-term treatment with NUZ-001 at the recommended Phase 2 dose was well-tolerated

Slowed Functional Decline
- Sustained slowing in disease progression by 31% compared to PRO-ACT matched control ALS participants

Respiratory Stabilisation
- 43% reduction in VC PP compared to PRO-ACT matched controls

Survival*
- Longer survival compared to PRO-ACT matched controls
- Estimated life extension of ~16 months

Biomarker Trends
- Encouraging biomarkers trends in NfL and urinary $p75^{ECD}$

Patient Satisfaction
- No study discontinuations; 3 of the 4 remaining participants continue to access NUZ-001 under the TGA's Special Access Scheme**

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* Data cut 15 Aug 2025

** As of 03 Feb 2026

HEALEY ALS Platform Trial Regimen ‘I’ for NUZ-001

36-week Double blind Placebo Controlled Period

36-week Active Treatment Extension Period

Inclusion/Exclusion Criteria

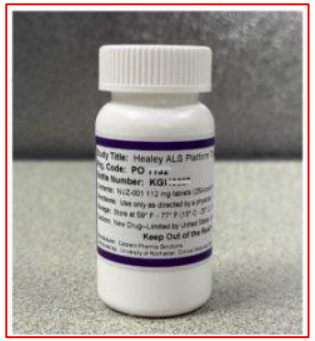
NUZ-001 10 mg/kg

3:1 Randomization
n=160 participant

Placebo

NUZ-001 10 mg/kg

NUZ-001 Dosing:
Once daily with oral tablets



Primary Endpoint

- Change from baseline through Week 36 in disease severity, measured by the ALSFRS-R total score and survival

Secondary Endpoints

- Change from baseline through Week 36 in secondary efficacy measures (e.g., respiratory function via slow vital capacity (SVC))
- Survival through Week 36 (death or equivalent endpoint)

Key Inclusion Criteria

- Sporadic or familial ALS diagnosed as clinically possible, probable, lab-supported probable, or definite ALS defined by revised El Escorial criteria.
- Age 18 years or older.
- Time since onset of weakness due to ALS ≤ 24 months.
- Participants must either not take riluzole or be on a stable dose of riluzole for ≥ 30 days prior to the Master Protocol Screening Visit.
- Participants must either not take edaravone or have completed at least one cycle (typically 14 days) of edaravone prior to the Master Protocol Screening Visit.
- Participants must have the ability to swallow pills and liquids.

Key Exclusion Criteria

- Clinically significant unstable medical condition (other than ALS) that would pose a risk to the participant. Use of investigational treatments for ALS Exposure at any time to any gene therapies under investigation for the treatment of ALS (off-label use or investigational).
- Anything that would place the participant at increased risk or preclude the participant's full compliance with or completion of the study, in the SI's opinion.

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For more information: **ClinicalTrials.gov ID** NCT07410806

Biomarkers: Understanding Disease Activity and Treatment Response

Neurofilament Light Chain (NfL):

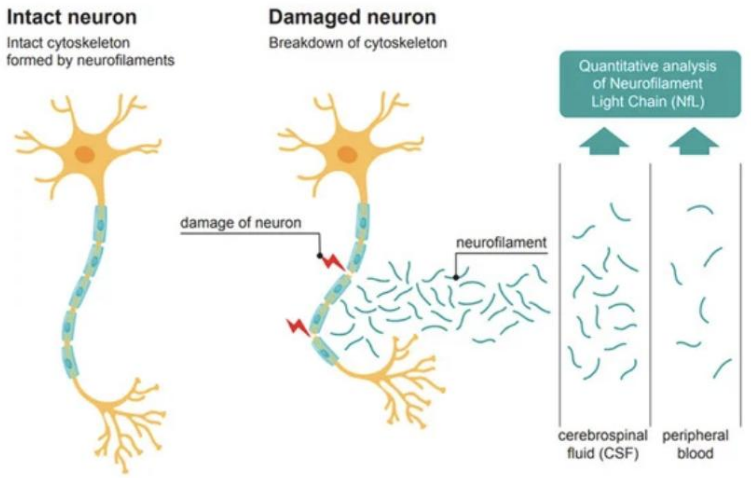
A protein found in CSF & blood that increases when motor neurons
are under stress or damaged cerebrospinal fluid (CSF) required at baseline and Week 24 visits)

Protein Assays (TDP-43) & Proteomics:

Cutting-edge technologies used to explore the body's biological response to disease and treatment

RNA & DNA expression:

Measures gene expression changes to understand disease activity and treatment effects



p75 neurotrophin receptor:

Helps track nerve cell stress and disease progression with urine sample

Mitochondrial health markers:

Indicators of cellular stress, energy function, and nerve cell well-being

Innovative Digital Biomarker

Speech intelligibility in ALS is both a functional outcome (how well a person communicates) and a biological signal of disease progression, making it highly relevant for patient care, prognosis, and clinical research.

Earlier Detection of Changes

Speech analysis can sometimes detect small changes related to ALS up to six months earlier than traditional rating scales.

Reflects Multiple Important Functions

Speaking involves many body systems, including muscles, breathing, and thinking.

Focus on What Matters to Patients

Communication is a key part of quality of life. Speech-based assessments directly measure how well someone can communicate.

What we measure

- Speech intelligibility and naturalness outcomes
- Speech timing and sequencing
- Voice quality, breath support and contributes to speech intelligibility and naturalness

Our Strategic Progress for People Living with ALS

- Our focus remains on advancing our ALS clinical program by commencing enrolment in the HEALEY ALS Platform Trial for NUZ-001
- Accelerated approval may be possible on Phase 2 data
- NUZ-001 has been granted Orphan Drug Designation by the U.S. FDA
- Studies are on-going for a liquid formulation of NUZ-001, for ease of use

Expanded Access Protocol (EAP) Compassionate Use - we are exploring options to offer EAP in the future

For more information, please check out:

Learn More About the Clinical Trial

HEALEY ALS Platform Trial- Master Protocol (including inclusion/exclusion criteria)
https://clinicaltrials.gov/study/NCT04297683

Regimen I NUZ-001 Details:
https://clinicaltrials.gov/study/NCT07410806

Learn More About Neurizon Therapeutics

https://www.neurizon.com

Thank You!

To the individuals and families living with ALS, the caregivers who stand beside them, and the clinicians dedicated to their care, thank you for your strength, your trust, and your commitment to advancing research for the entire ALS community.