Neurizon Therapeutics Limited
ABN 35 094 006 023
www.neurizon.com

New NUZ-001 Mechanistic Data presented at BIO International Convention 2026

- **New preclinical data to be presented at the BIO International Convention 2026 expanding the mechanistic evidence base for NUZ-001 across multiple validated neural dysfunction models**
- **New findings include data linking NUZ-001 activity to restoration of STMN2, a key neuronal maintenance protein disrupted downstream of TDP-43 pathology in ALS**
- **Additional new data show that NUZ-001 restores stress-disrupted proteostasis-associated protein expression in human neurosphere and zebrafish models, supporting consistent activity across 2D, 3D and in vivo systems**
- **Presentation further strengthens the emerging mechanistic profile of NUZ-001 as a multi-pathway modulator of endogenous protein proteostasis and neuronal stress-response biology**

23 June 2026 – Melbourne Australia: Neurizon® Therapeutics Limited (ASX: NUZ & NUZOA; OTCQB: NUZTF) ("Neurizon" or "the Company"), a clinical-stage biotech company dedicated to advancing innovative treatments for neurodegenerative diseases, is pleased to provide an update on new preclinical mechanism-of-action data for its lead amyotrophic lateral sclerosis (“ALS”) candidate, NUZ-001, which will be presented at the BIO International Convention 2026 ("BIO 2026").

The data further strengthen the growing body of evidence supporting NUZ-001’s ability to restore key cellular pathways implicated in ALS, including protein homeostasis, neuronal stress adaptation and TDP-43-associated dysfunction, while reinforcing the scientific rationale underpinning the ongoing Phase 2/3 HEALEY ALS Platform Trial.

BIO 2026 is one of the world’s leading biotechnology and lifescience partnering forums, bringing together global biopharma companies, investors, researchers and business development professionals. Participation provides Neurizon with an important platform to share the scientific and clinical progress of NUZ-001, including findings that continue to strengthen the mechanistic and translational profile in ALS and other neurodegenerative diseases.

The presentation highlights new data across multiple validated preclinical neuronal dysfunction models showing that NUZ-001 engages biological pathways directly relevant to neuronal health, protein clearance and disease-associated stress responses. Together, the findings are intended to further expand the scientific foundation supporting NUZ-001 and to demonstrate the consistency of its activity across complementary experimental systems.

Summary of key findings:

The presentation includes three key new findings:

1. **STMN2-related findings in motor neurons**
   New results indicate that NUZ-001 prevents the decline of STMN2, an axonal maintenance and regeneration factor that is disrupted when TDP-43 function is impaired. Because TDP-43 pathology is a central feature of the majority of ALS cases, the preservation of STMN2 biology is increasingly recognised as one of the most important downstream indicators of TDP-43 function and a potentially meaningful marker of neuronal resilience in ALS.

2. **Human neurosphere proteostasis data**
   In stress-exposed human neurosphere models, NUZ-001 restored the expression of multiple regulators associated with protein homeostasis, including markers linked to mitochondria and lysosomal function, autophagy, mitophagy and broader cellular clearance systems. These findings extend earlier cellular observations by demonstrating a coordinated restorative effect in a more complex 3D human neural model.

3. **Zebrafish proteostasis-regulatory expression data**
   In zebrafish larval stress models, NUZ-001 treatment restored expression patterns across a panel of proteostasis-regulatory candidates. These in vivo data are important because they demonstrate that the biological activity of NUZ-001 is not restricted to in vitro systems and (may) reflect a reproducible stress-adaptive mechanism across model types.

Relevance of the new mechanism-of-action data:

Recent Neurizon announcements have highlighted that NUZ-001 increases activity across both autophagy and proteasomal clearance pathways, reduces p62 and LC3 markers in human iPSC-derived neurons, and shows in vivo biological activity in zebrafish models alongside disease-dependent restoration of BDNF and protection from pathological stress phenotypes. The new BIO 2026 data build on that foundation by moving beyond isolated pathway markers and showing a broader pattern of restoration across proteins and pathways involved in maintaining neuronal protein quality control under stress.

Taken together, the new motor neuron, neurosphere and zebrafish findings support a model in which NUZ-001 may act on key proteostasis regulators, with consequences for TDP-43-associated neuronal dysfunction, helping restore endogenous systems that govern protein clearance, stress adaptation and neuronal health. This is particularly relevant for ALS, where disruption of TDP-43 biology and failure of cellular protein quality control mechanisms are considered central drivers of motor neuron degeneration. The consistency of NUZ-001's activity across multiple complementary models strengthens confidence that the programme is targeting biologically relevant pathways implicated in disease progression.

Management commentary:

Interim Executive Chairman, Sergio Duchini, said: *"These findings provide important additional validation of the biological activity of NUZ-001 and further strengthen the mechanistic framework supporting its ongoing clinical development. What is particularly encouraging is the consistency of the signal across multiple independent model systems, spanning cellular 2D and 3D human neural models and in vivo settings. Together, these data continue to build confidence that NUZ-001 is engaging pathways directly relevant to ALS biology, including TDP-43 dysfunction, proteostasis and neuronal resilience. As our Phase 2/3 HEALEY ALS Platform Trial progresses, we believe these findings further support NUZ-001's potential as a differentiated therapeutic approach for ALS."*

Presentation details:

Neurizon's Dr Martin Engel will present these new findings at BIO International Convention 2026 on Tuesday, 23 June at 11:30AM PDT. The presentation, titled "NUZ-001 in ALS: From mechanism to registrational trial" follows this release.

-ENDS-

This announcement has been authorised for release by Sergio Duchini, Interim Executive Chair, on behalf of the Board of Neurizon Therapeutics Limited.

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About Neurizon Therapeutics Limited

Neurizon Therapeutics Limited (ASX: NUZ) is a clinical-stage biotechnology company dedicated to advancing treatments for neurodegenerative diseases. Neurizon is developing its lead drug candidate, NUZ-001, for the treatment of ALS, which is the most common form of motor neurone disease. Neurizon's strategy is to accelerate access to effective ALS treatments for patients while exploring the potential of NUZ-001 for broader neurodegenerative applications. Through international collaborations and rigorous clinical programs, Neurizon is dedicated to creating new horizons for patients and families impacted by complex neural disorders. NUZ-001 is an investigational product and is not approved for commercial use in any jurisdiction.

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Neurizon

NUZ-001 in ALS: From mechanism to registrational trial

Dr Martin Engel,
Head of Scientific and Commercial Partnerships

Bio International Convention 2026

ABN 35 094 006 023

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NUZ-001: a late-clinical stage ALS program designed to target the core ALS pathology

Restoring cellular protein homeostasis to halt ALS neurodegeneration, now in a registrational Phase 2/3 trial.

Neurizon Therapeutics

- Late clinical-stage biotechnology company – Phase 2/3 Registrational Trial
- Disease-modifying platform therapy in neurodegeneration

Lead Compound: NUZ-001

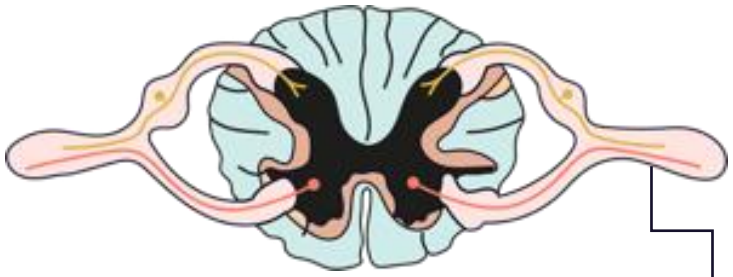
- Small oral molecule oral – once daily with >3 years favourable patient safety profile
- Enhances autophagy and proteosomal clearance
- Targets 97% of MND/ALS patients: prevents TDP-43 aggregation & restores loss of function

Path to Market

- Orphan Drug Designation (FDA & EMA) with IP protection until 2041
- Established GMP manufacturing & supply
- Topline Readout ~ 12 month
- Regulatory & Commercial infrastructure ready

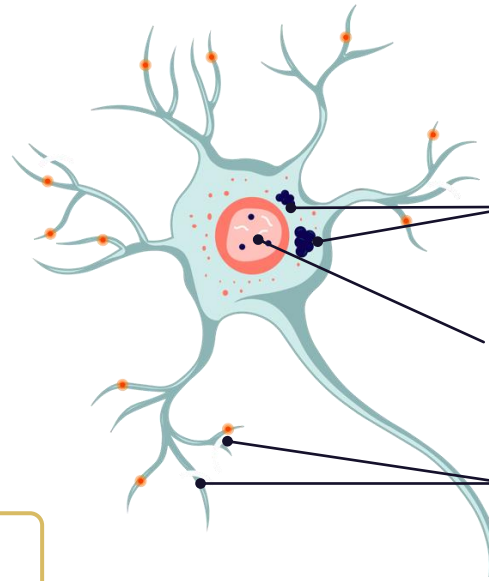
97% of ALS is driven by TDP-43 aggregation

Spinal Cord

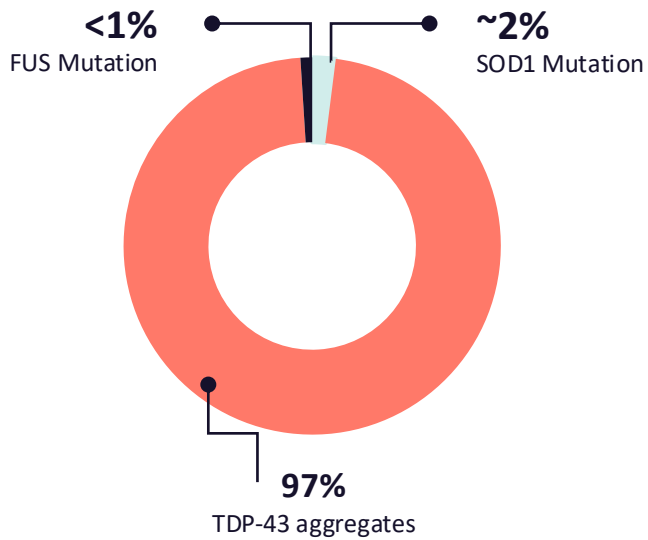


Motor Neuron -> Muscle connection

Motor Neuron



ALS Patient Population[1]



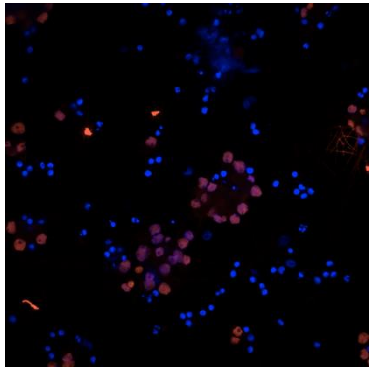
Current ALS therapies target downstream neuronal stress
→ extend life expectancy by 2-6 month[2]

FUS = Fused in Sarcoma; SOD1 = Superoxide Dismustase 1; TDP-43 = Transactive response DNA-binding protein 43 **1**. Ling SC, Polymenidou M, Cleveland DW. Converging mechanisms in ALS and FTD: disrupted RNA and protein homeostasis. Neuron. 2013 Aug 7;79(3):416-38. doi: 10.1016/j.neuron.2013.07.033. **2**. Quigley, Savannah E., Kellen H. Quigg, and Stephen A. Goutman. 2025. "Genetic and Mechanistic Insights Inform Amyotrophic Lateral Sclerosis Treatment and Symptomatic Management: Current and Emerging Therapeutics and Clinical Trial Design Considerations." CNS Drugs 39 (10): 949–93. https://doi.org/10.1007/s40263-025-01217-0..

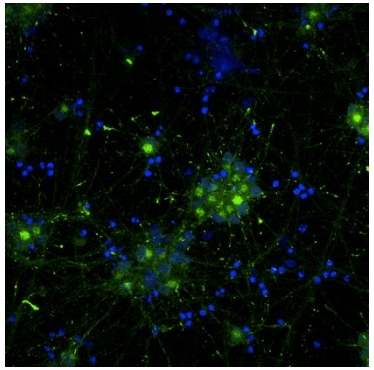
NUZ-001 prevents TDP-43 aggregation and restores neuronal function in human iPSC models

iPSC Motor Neurons

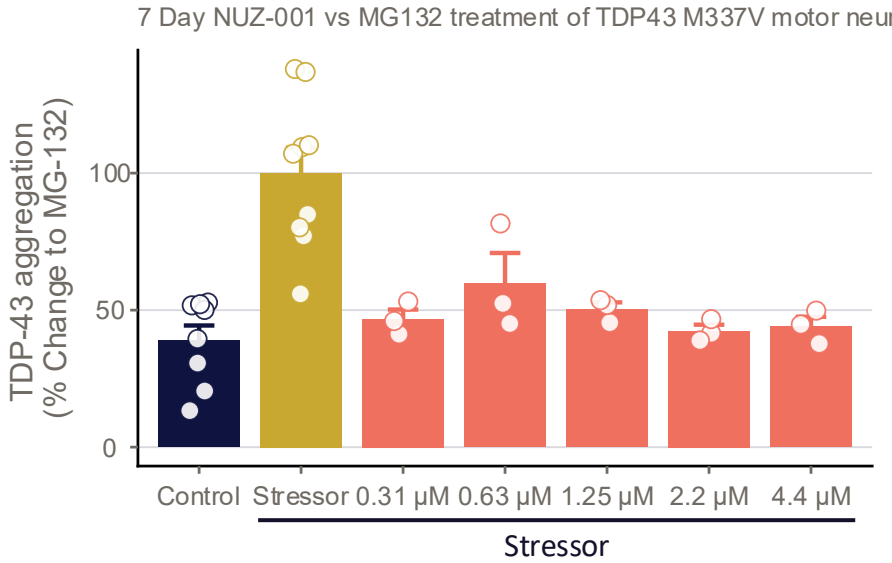
TDP43/DAPI

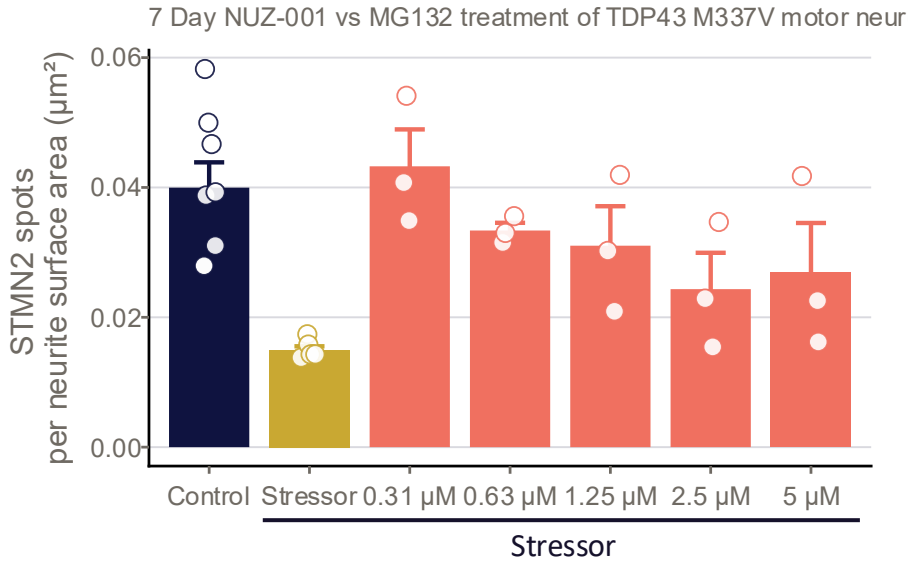


STMN2/DAPI



NUZ-001 prevents the formation of TDP-43 aggregates and loss of Stathmin-2[1] expression



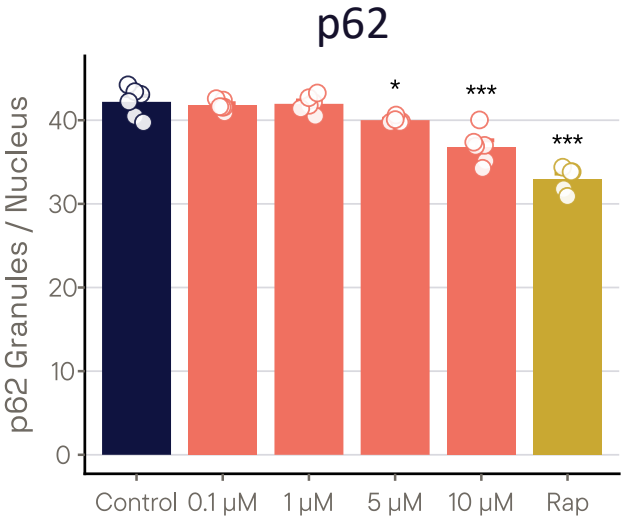


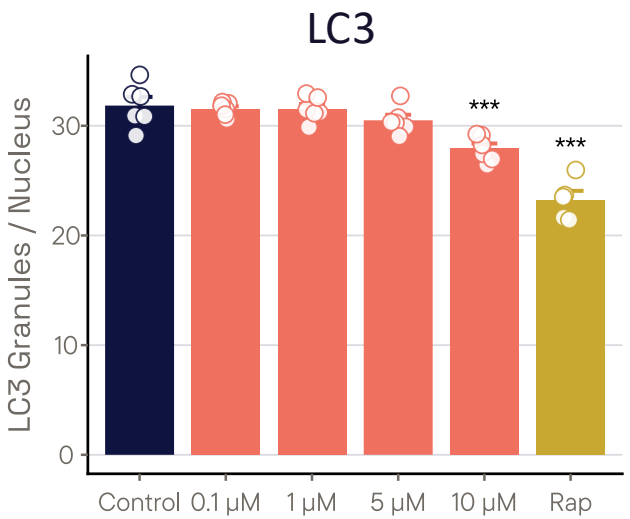
STMN2 = Stathmin-2; TDP-43 = Transactive response DNA-binding protein 43

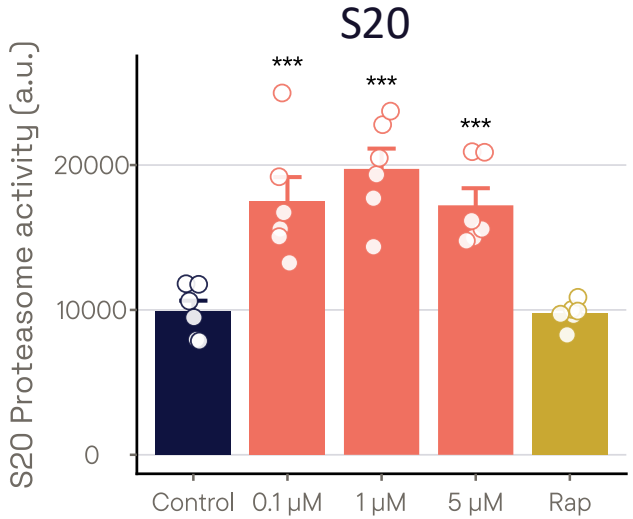
1. Klim, Joseph R., Luis A. Williams, Francesco Limone, et al. 2019. "ALS-Implicated Protein TDP-43 Sustains Levels of STMN2, a Mediator of Motor Neuron Growth and Repair." Nature Neuroscience 22 (2): 167–79. https://doi.org/10.1038/s41593-018-0300-4..

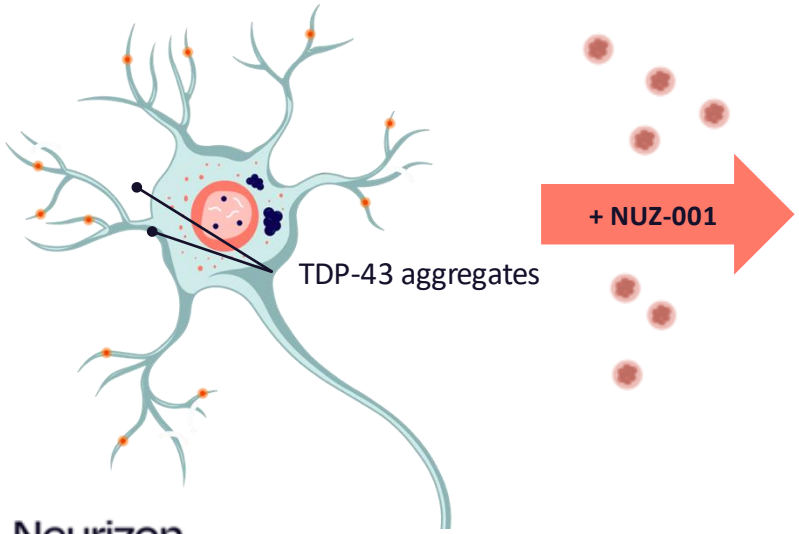
NUZ-001 enhances cellular protein clearance mechanisms

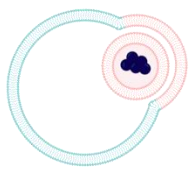
iPSC
Glutamatergic
Neurons











↑ Autophagy
(p62, LC3)

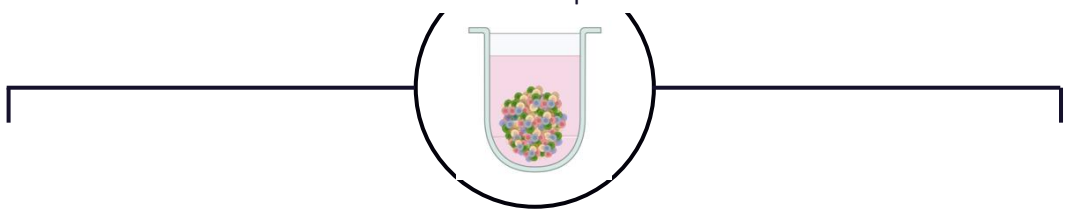
↑ Proteasome
(S20)

Enhances clearance of protein aggregates

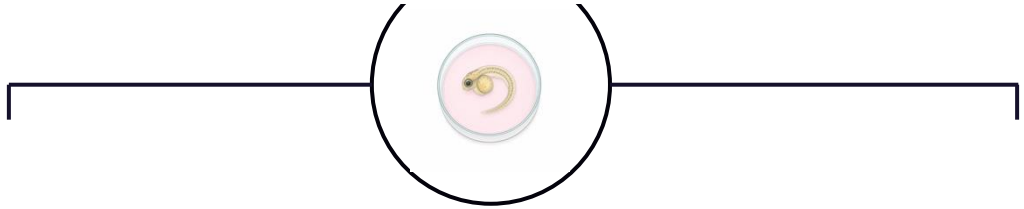
Neurizon

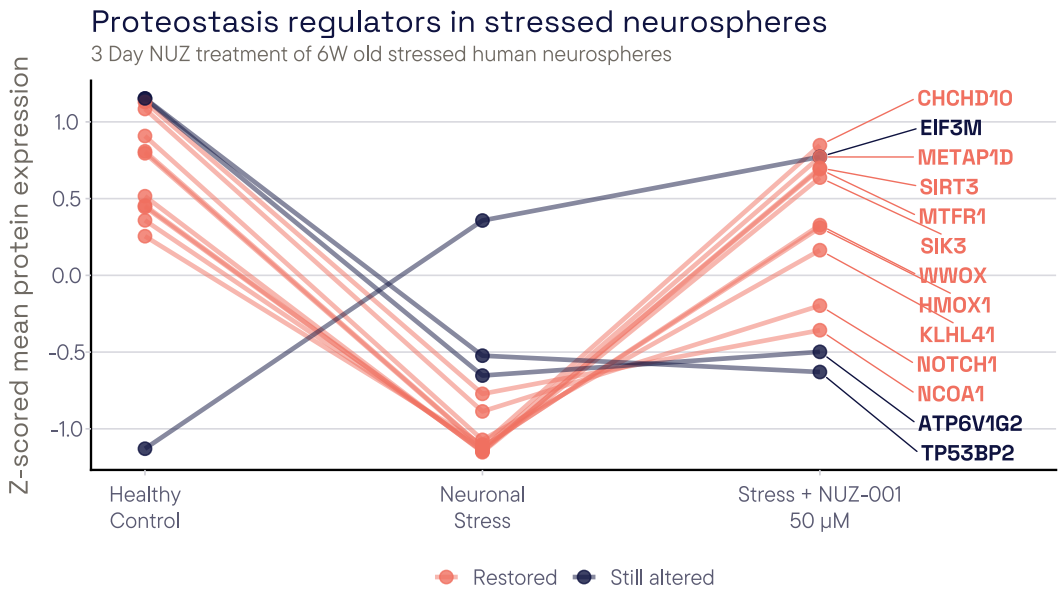
NUZ-001 rebalances proteosomal activity across multiple preclinical neuronal stress models

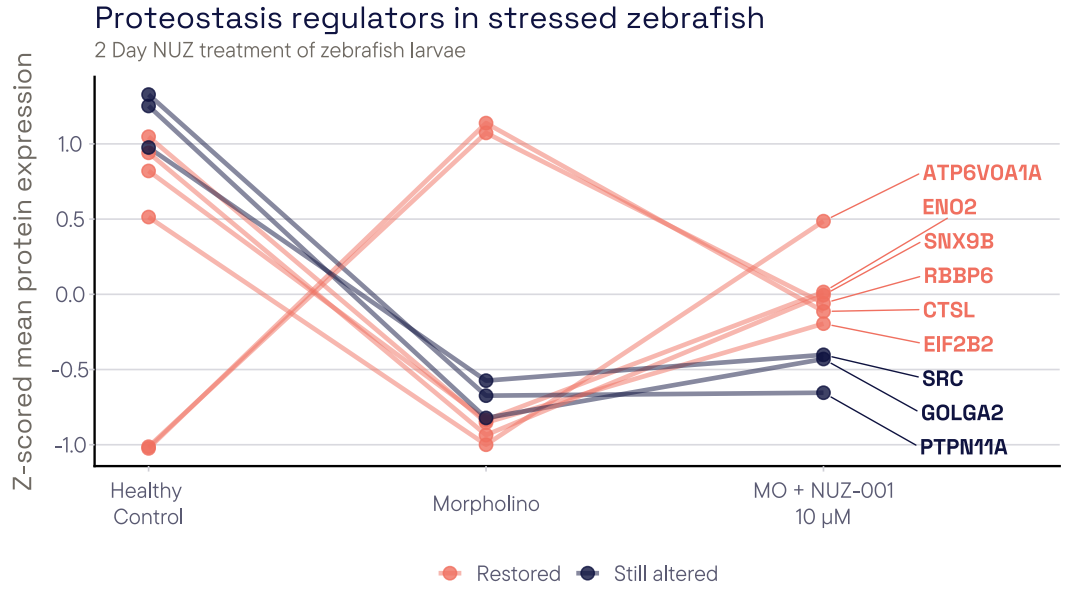
Human Neurospheres



Zebrafish Larvae







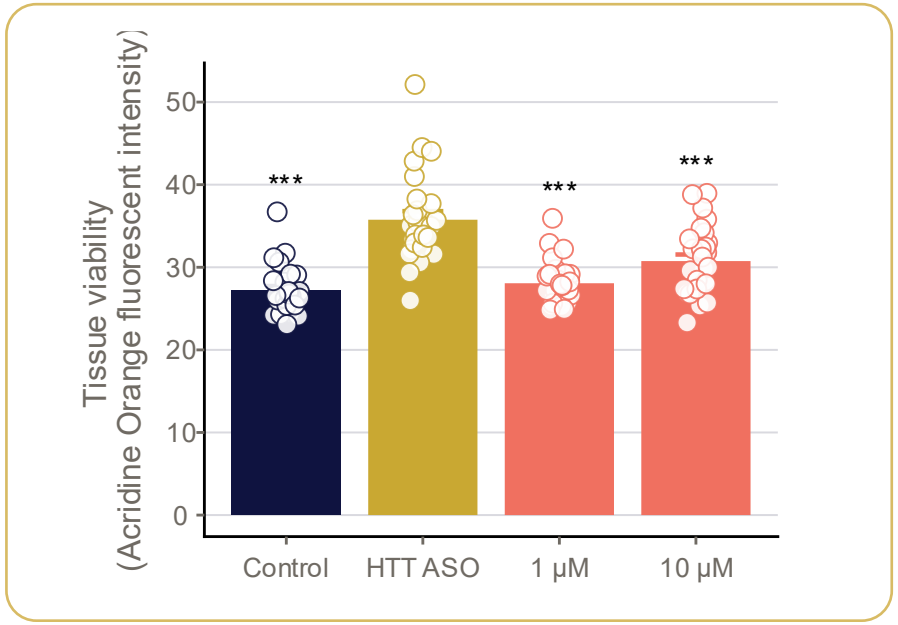
Consistent rebalancing of proteostasis across 2D, 3D and in vivo models confirms reproducible mechanism → a critical translational validation step.

NUZ-001: Disease-agnostic, mechanism driven, platform potential

NUZ-001 is rebalancing proteostasis with potential across multiple proteinopathies

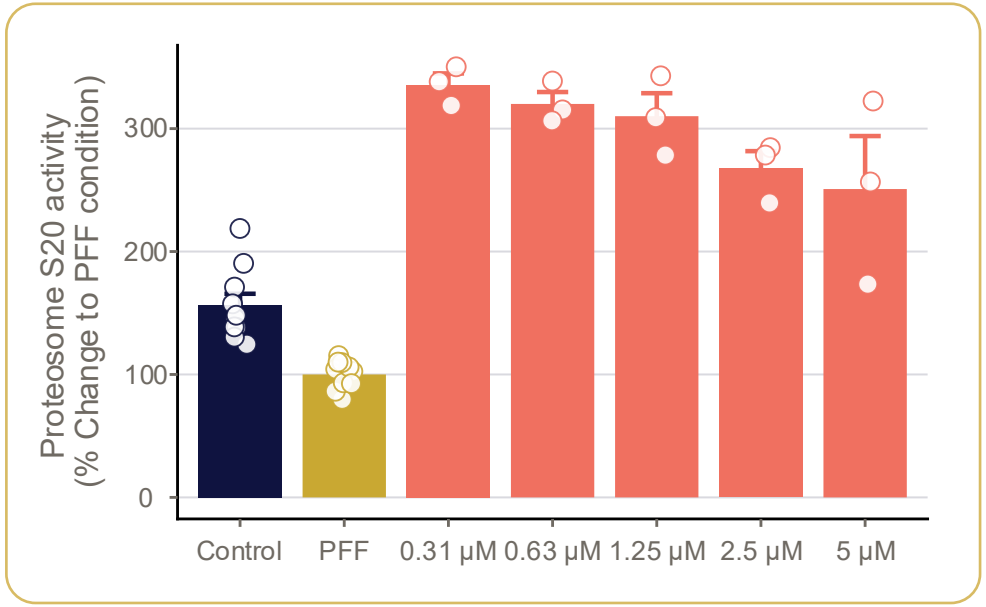
TDP-43	mHTT	α-Synuclein	Tau	Amyloid beta
ALS/AD/PD/**FTD**/CTE	**HD**	AD/**PD**	AD/PD/FTD/CTE/PSP	AD/PD

NUZ-001 attenuates apoptosis induced by Huntington (htt) reduction



*Zebrafish HD model: hTT KO ASO. ***p<0.001 vs. Htt ASO treated.*

NUZ-001 enhances proteasomal activity following treatment with α-synuclein



*human iPSC-derived neurons during α-synuclein Preformed Fibrils treatment (PFF). *p<0.05 vs untreated (Control)*

AD = Alzheimer's Disease; ALS = Amyotrophic Lateral Sclerosis; CTE = Chronic Traumatic Encephalopathy; FTD = Frontotemporal Dementia; HD = Huntington Disease; PD = Parkinson's Disease; PSP = Progressive Supranuclear Palsy

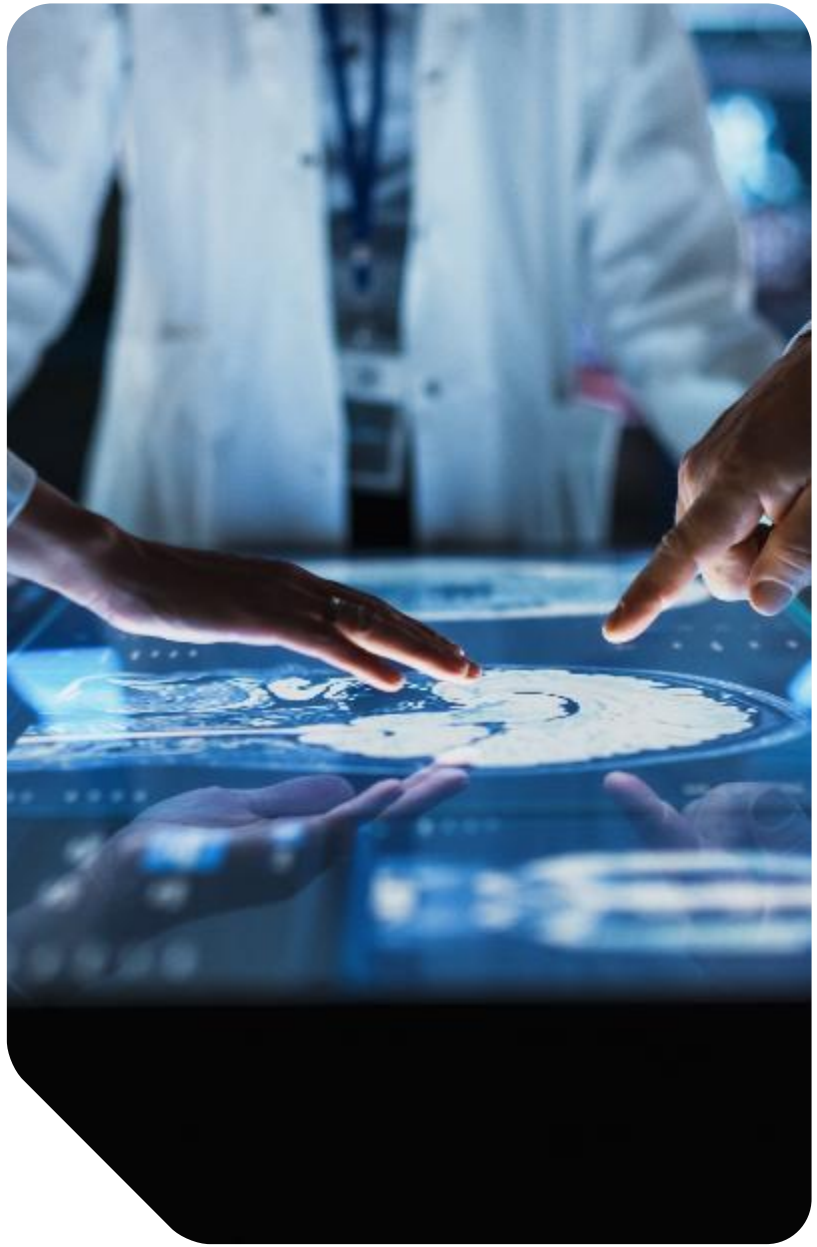
Australian Phase 1 and Open Label Extension Study

Early Clinical Development of NUZ-001 in MND/ALS

Early Clinical Development of NUZ-001 in MND/ALS started in Australia in collaboration with FightMND, which funded the Phase 1 trial.

- Neurizon conducted a Phase 1 and Open Label Extension study in Australia involving a small group of people living with ALS/MND (n=12)
- The study evaluated safety, tolerability and exploratory clinical measures
- NUZ-001 appeared generally safe and well tolerated
- No study discontinuations; several participants continue to access NUZ-001 under the TGA's Special Access Scheme
- The program generated important early insights supporting further clinical development

The scientific and clinical data generated from these studies contributed to the selection of NUZ-001 for inclusion in the HEALEY ALS Platform Trial in the United States.

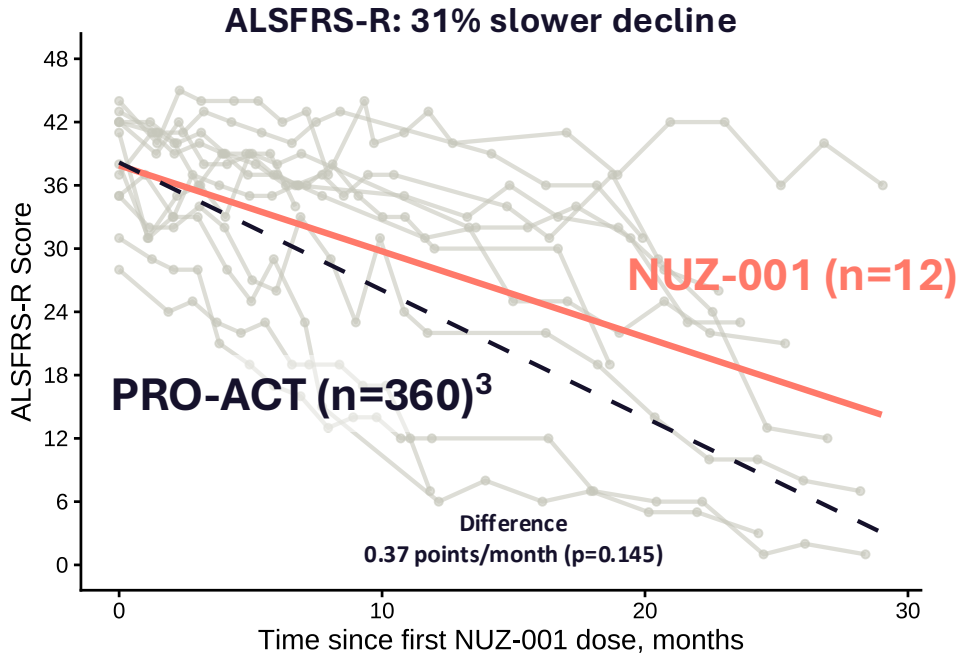


Phase 1 Open Label Extension

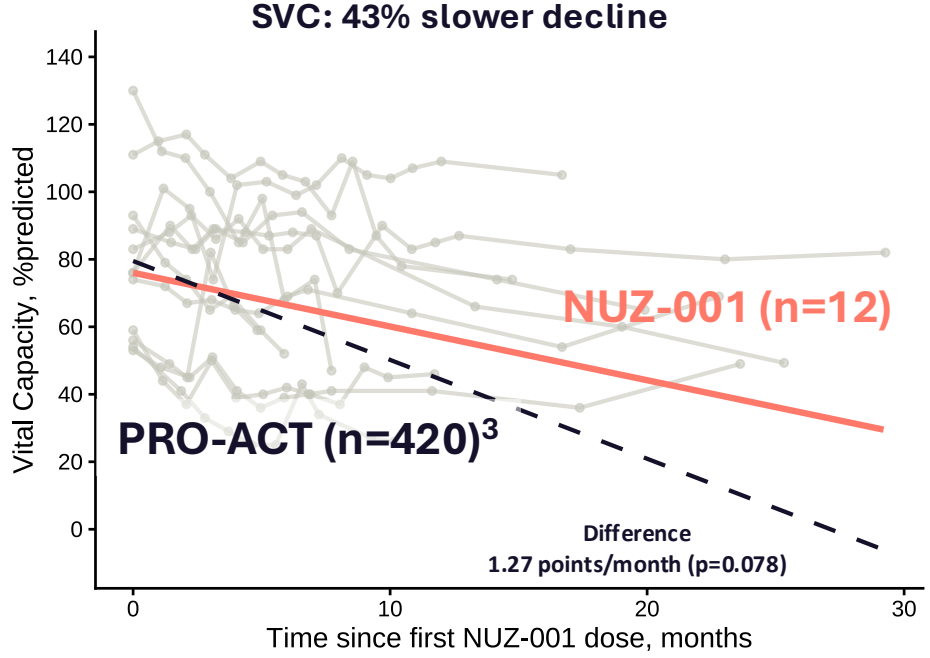
Preliminary Efficacy ALSFRS-R and SVC

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. Independently matched by Berry Consultants on time since onset, baseline ALSFRS-R, pre-baseline ALSFRS-R slope, and disease onset location

Phase 1 Open Label Extension

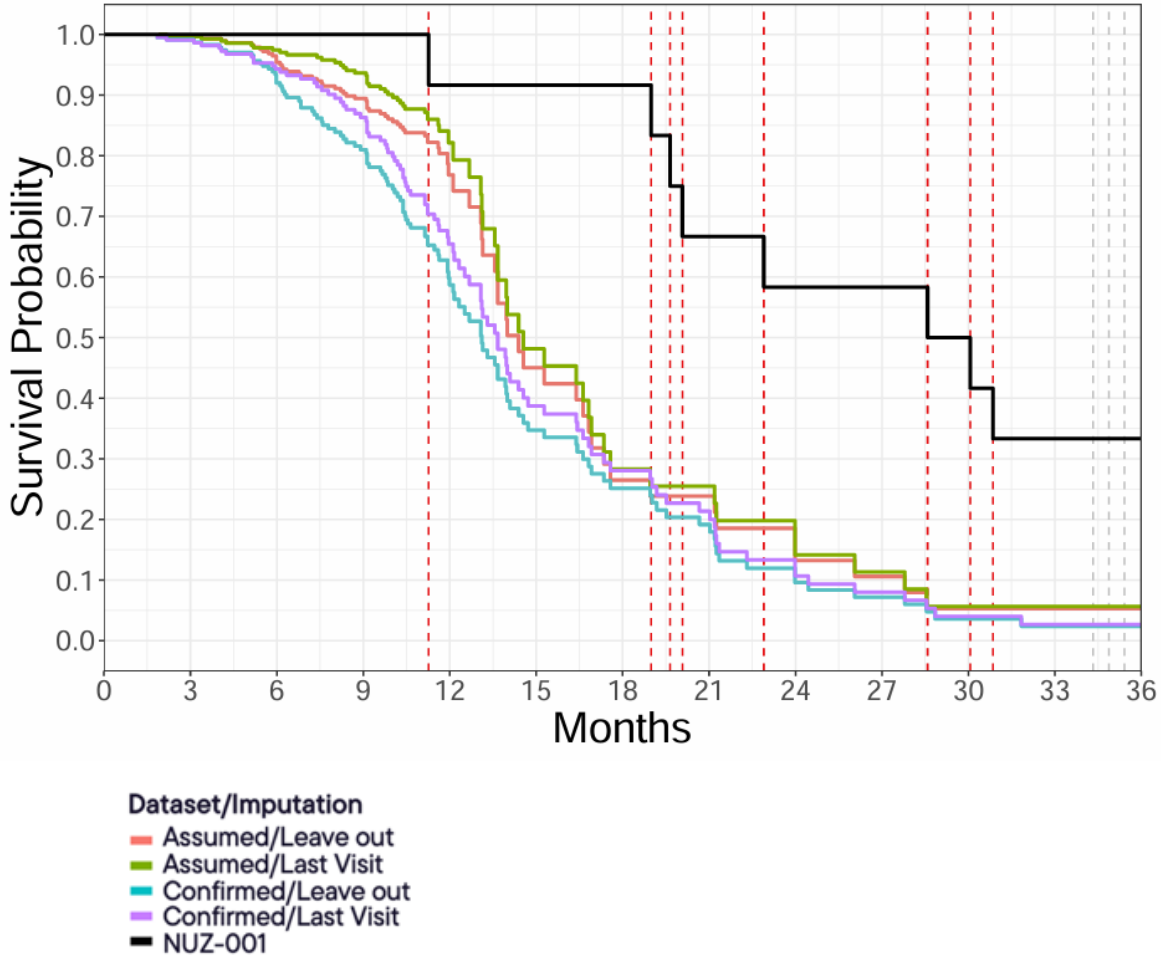
Survival Probability Analysis

Treatment with NUZ-001 resulted in significantly longer survival of participants with ALS, (X^2=11.35, p=0.00075), when compared to matched controls[1] from the PRO-ACT database[2]

71% reduction in risk of death in Phase 1b

Hazard ratio: 0.29 (95% CI: 0.131, 0.644, p=0.0024)

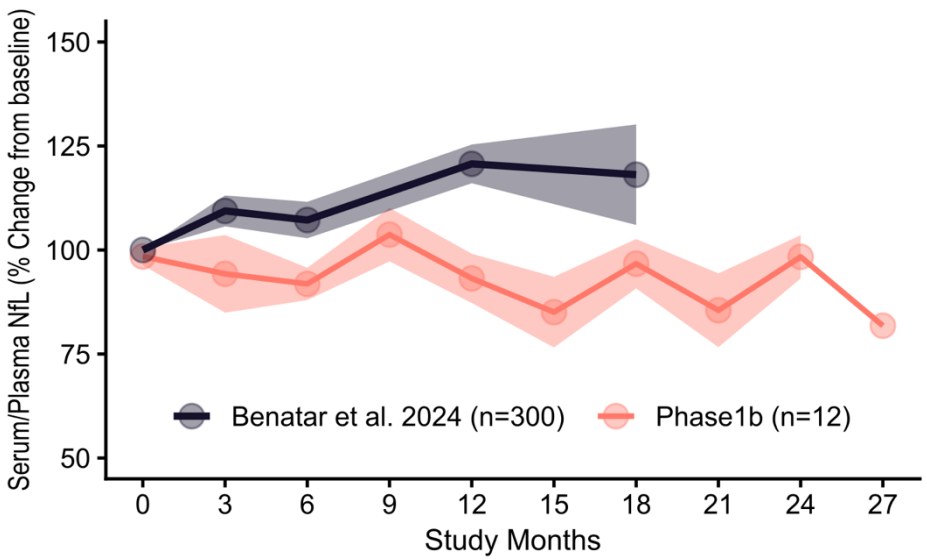
NUZ-001 vs matched PRO-ACT controls (n=12 vs matched cohort)

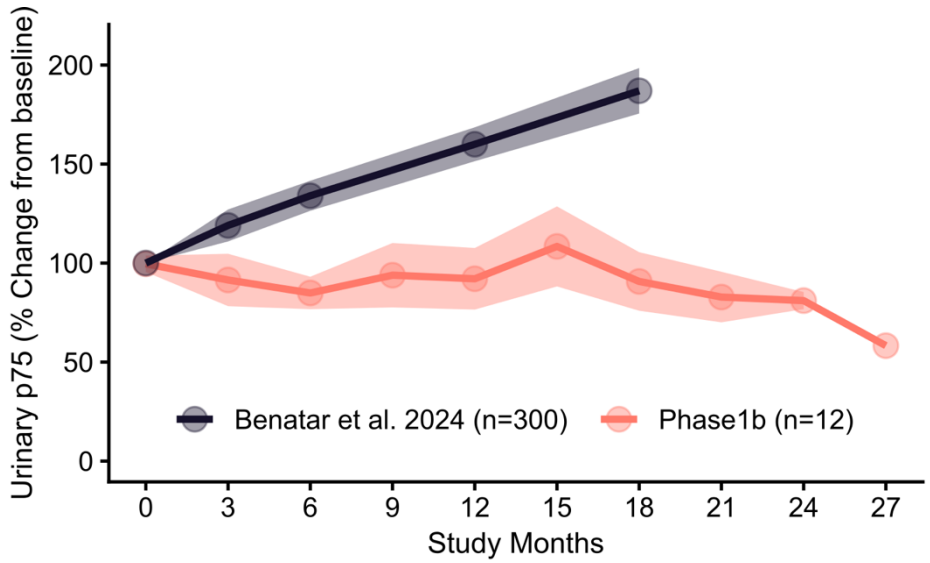


1. Matched on time since onset, baseline ALSFRS-R, pre-baseline ALSFRS-R slope, and disease onset location
2. Atassi N, Berry J, Shui A, Zach N, Sherman A, Sinani E, Walker J, Katsovskiy I, Schoenfeld D, Cudkowicz M, Leitner M. The PRO-ACT database: design, initial analyses, and predictive features. Neurology. 2014 Nov 4;83(19):1719-25. doi: 10.1212/WNL.0000000000000951.Epub 2014 Oct 8. PMID: 25298304; PMCID: PMC4239834

NUZ-001 demonstrates encouraging Biomarker trajectory compared with ALS natural history

- Neurizon established **Biomarker strategy** for pathophysiology monitoring during Phase 1b
- **Stable neurofilament** (NfL) and p75 concentrations during NUZ-001 treatment suggest reduced disease pathology progression
- Contrasting reference ALS data using standard of care (Benatar et al. 2024 "**Prognostic Clinical and Biological Markers for Amyotrophic Lateral Sclerosis Disease Progression: Validation and Implications for Clinical Trial Design and Analysis.**" *eBioMedicine* 108: 105323. https://doi.org/10.1016/j.ebiom.2024.105323.)





Benatar et al. (2024): serum NfL; Neurizon Phase 1: plasma NfL. Absolute values are not directly comparable due to matrix and assay differences. Data shown for contextual purposes only.

NUZ-001 Phase 2/3 registrational trial underway — HEALEY ALS Platform Trial

NUZ-001 independently selected for inclusion in the HEALEY ALS Platform Trial; world's leading platform trial for ALS

Topline data readout expected early Q3 2027

Strong IP and regulatory position established

- Formulation and method of use patents granted: USA IP protection to 2041, EU & JP Pending
- Orphan Drug Designation granted by both FDA (United States) and EMA (European Union)
- Active regulatory engagement with FDA, EMA, and PMDA (Japan)

GMP manufacturing and supply chain established

- Established GMP manufacturing process: supply secured for Phase 2/3 and potential commercial launch
- Oral *tablet* formulation: established manufacturing process & supply agreement
- Oral *liquid* formulation: Phase 1 PK study Q3 2026, expanding patient access

NUZ-001 is dosing now in the HEALEY ALS Platform Phase 2/3 Trial across the U.S.

78 Activated Sites

201 Regiment Assignment

164 Dosed Participants (Target: 240)

IND Amendment Submission
Platform Trial IND submitted to regulatory authorities

FDA Clearance
NUZ-001 entry accepted

First Patient Screened
First patient screened for eligibility

First Patient Dosed
First participant dosed in Regimen I

Enrollment Complete
240 patients enrolled in the trial

Last Patient Dosed
Last participant receives final dose

Database Lock
Clinical trial database locked for analysis

Topline Data Released
Topline results of the trial announced

- **Primary** endpoint: Change from baseline to Week 36 in disease severity, measured by the ALSFRS-R total score and survival
- **Secondary**: respiratory function, Survival through Week 36 (death or equivalent endpoint)
- **Biomarker**: Protein panel, mtDNA, Digital biomarker of Speech

Neurizon

Numbers referred to above are as of 16 June 2026.

NUZ-001: a de-risked, late-clinical stage asset addressing a significant unmet need in ALS

NUZ-001 addresses TDP-43 pathology, a central pathological feature observed in 97% of ALS cases, with encouraging Phase 1b signals across function, survival and disease biomarker measures.

NUZ-001 is de-risked

- First-in-class oral small molecule
- Validated **blood brain barrier penetration**
- Favourable safety profile observed over 3.5 years

NUZ-001 Opportunity

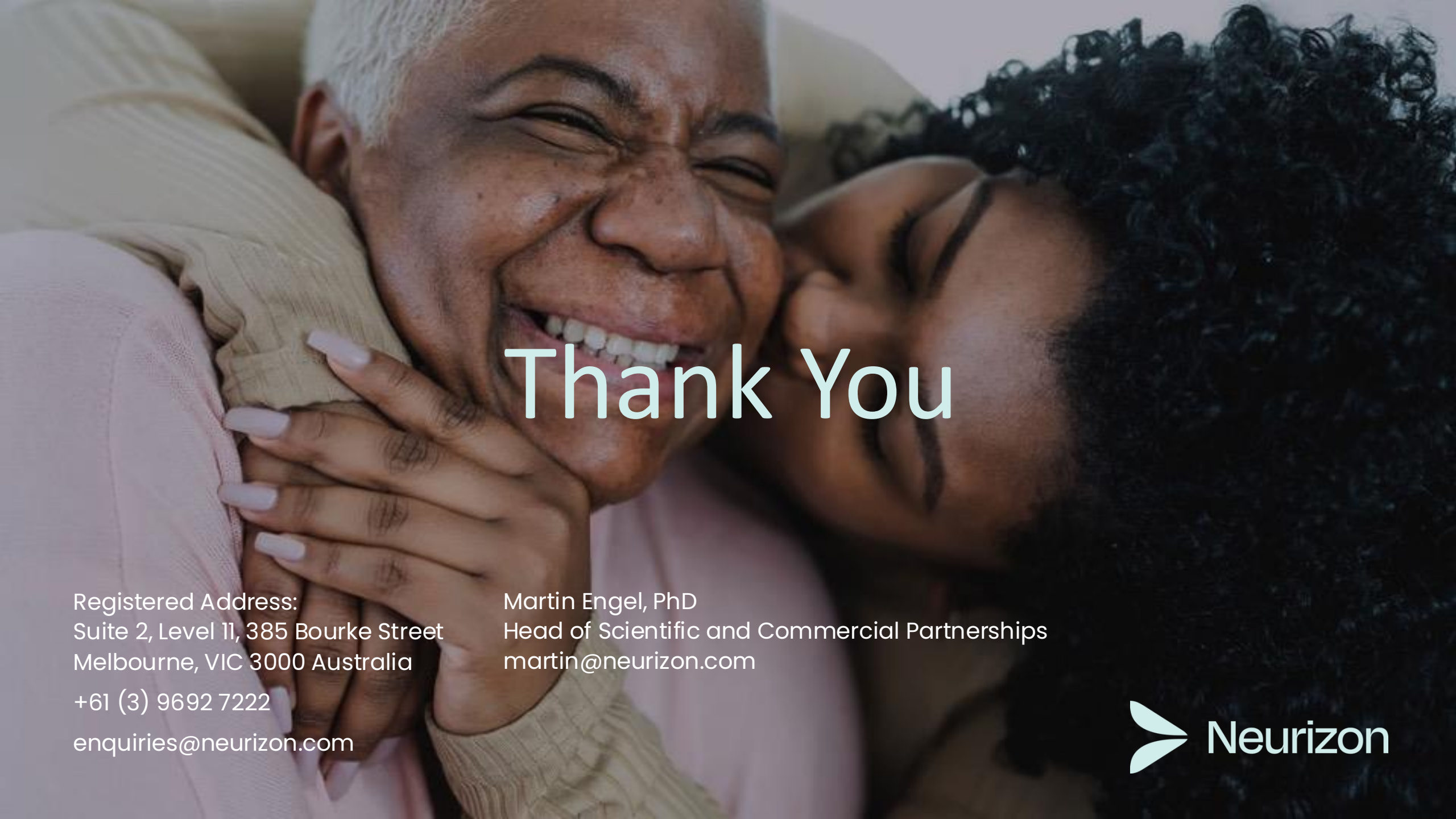
- **Engaging global and regional partners for licensing and strategic investment**
- 15% annual sales growth rate of ALS market, US$1.28B by 2029

Phase 2/3 Clinical Trial

- Independent HEALEY trial selection with 240 participants to be enrolled within ~6 months
- Topline readout early Q3 2027

Strong Market Readiness

- Patent protection in USA and AU out to 2041, EU and JP pending
- Orphan Drug Designation FDA & EMA
- GMP supply agreement & process in place



Thank You

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