

## NUZ-001 OLE Study Demonstrates Long-Term Safety and Efficacy Signals

### Highlights:

- The OLE study met its primary endpoint, confirming long-term treatment with NUZ-001 at the recommended Phase 2 dose was safe and well-tolerated
- Treatment during the OLE was associated with a durable functional benefit (ALSFRS-R decline  $-0.88$  points/month), minimal respiratory decline (stable SVC), and supportive biomarker trends (stable plasma NfL and decreased ( $-17\%$ ) urinary p75<sup>ECD</sup>)
- Preliminary efficacy was assessed by comparing NUZ-001-treated patients to matched, untreated historical controls from the PRO-ACT database from the start of the Phase 1 MEND Study:
  - NUZ-001 significantly increased survival ( $\chi^2=13.75$ ,  $p=0.00021$ )
  - NUZ-001 significantly reduced the risk of death by 76.7% ( $HR=0.233$ ,  $p=0.0013$ )
  - Treatment with NUZ-001 showed an estimated median survival extension of  $\sim 16$  months
  - NUZ-001 slowed the rate of functional decline by 31% ( $-0.83$  vs  $-1.21$  ALSFRS-R points/month;  $p=0.145$ )
  - NUZ-001 reduced the rate of respiratory decline by 43% ( $-1.65$  vs  $-2.93$  VC PP points/month;  $p=0.078$ )
- NUZ-001 has been safely used for more than 2.5 years, with five patients still receiving treatment under the TGA's Special Access Scheme
- These encouraging results reinforce the rationale for the planned pivotal HEALEY ALS Platform Trial, expected to commence in Q4 CY2025

**20 August 2025 – Melbourne, Australia:** Neurizon® Therapeutics Limited (ASX: NUZ & NUZOA) ("Neurizon" or "the Company"), a clinical-stage biotech company dedicated to advancing innovative treatments for neurodegenerative diseases, is pleased to report positive topline results from the Open-Label Extension (OLE) study of its lead candidate NUZ-001, for the treatment of amyotrophic lateral sclerosis (ALS), the major form of motor neurone disease (MND).

Long-term treatment with NUZ-001 at the recommended Phase 2 dose was safe and well-tolerated. Importantly, preliminary efficacy findings demonstrated that treatment with NUZ-001, compared to matched historical controls from the Pooled Resource Open-Access ALS Clinical Trials (PRO-ACT) database, was associated with a significant survival advantage, sustained slowing of global functional decline, a reduced rate of respiratory decline, and a stable or downward trend in key disease biomarkers.

These encouraging 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.

**Managing Director and Chief Executive Officer, Dr. Michael Thurn, commented:** "We are very encouraged by these long-term treatment results, which reinforce the potential of NUZ-001 to deliver meaningful clinical benefits for people living with ALS. Importantly, the therapy has been shown to be safe and well-tolerated, even with extended use. For too long, patients and families have faced this devastating disease with very few treatment options, and the field has struggled to find truly viable new options. To see sustained functional and respiratory benefits, a clear survival advantage, and supportive biomarker trends after nearly three years of treatment gives us additional confidence as we finalise preparations for entry into the HEALEY ALS Platform Trial. I would like to thank Associate Professor Susan Mathers at Calvary Health Care Bethlehem and Professor Dominic Rowe at Macquarie University, as well as their clinical teams and the incredible patients, families, and caregivers who made this study possible."

## Study Overview and Results

The OLE study was an open-label, safety, tolerability, and preliminary efficacy study of NUZ-001 in 10 patients with ALS who completed the Phase 1 MEND Study, at the recommended Phase 2 dose of 10 mg/kg administered orally daily for 12-months.

Daily treatment with NUZ-001 was safe and well-tolerated, with no treatment-related deaths observed. Eight patients completed the study, while two patients died during the OLE due to respiratory failure and pneumonia. Throughout the study, a total of 25 treatment-emergent adverse events (AEs) were reported, of which only 3 were considered possibly treatment-related (mild to moderate dry mouth at night, increased hair growth, and elevated liver enzymes). Notably, there were no treatment-related severe AEs and no discontinuations due to AEs.

Five patients continue to access NUZ-001 via the Therapeutic Goods Administration (TGA) Special Access Scheme (SAS). Since the Phase 1 MEND Study started in October 2022, the initial patients enrolled have now been on daily treatment with NUZ-001 for over 2.5 years, providing strong evidence of the excellent long-term safety profile of NUZ-001.

During the OLE study, disease progression was assessed using the FDA-accepted primary endpoint for ALS trials, the ALS Functional Rating Scale-Revised (ALSFRS-R). Among the 10 patients, the estimated mean rate of decline was -0.88 points/month (CI: -1.58, 0.10), compared with -0.74 points/month (CI: -1.26, -0.23) observed in the Phase 1 MEND Study. These comparable results indicate a stable and durable treatment effect with long-term NUZ-001 therapy.

Slow Vital Capacity (SVC) decline is a validated marker of disease progression and survival in ALS. In the OLE study, the mean Vital Capacity Percent Predicted (VC PP) at baseline was 72.4% (CI: 54.41, 90.45), decreasing gradually to 62.33% (CI: 36.69, 87.96) at month 12. This 12-month value was not statistically different from the baseline value in the Phase 1 MEND Study of 84.40% (CI: 67.94, 100.86;  $p = 0.3616$ ) despite long-term treatment. These findings are consistent with a durable treatment effect and support the potential disease-modifying activity of NUZ-001 in ALS.

The results of the additional exploratory efficacy measures of ALSSQOL-R quality of life scores and ECAS further supported a durable treatment effect despite long-term treatment with NUZ-001. In addition, plasma NfL levels remained broadly stable over the 12-month OLE, with a transient reduction observed at Month 6 before returning to baseline levels by Month 12 ( $n=7$ ), while urinary p75<sup>ECD</sup> decreased by ~17% ( $n=3$ ). These stable and downward biomarker trends over the OLE period provide additional evidence supporting the potential disease-modifying effect of NUZ-001.

## Integrated Preliminary Efficacy Comparator Analysis to the PRO-ACT Database

The PRO-ACT database is the largest publicly available dataset for ALS clinical trial data worldwide. The richness of the PRO-ACT lies in its longitudinal clinical, laboratory, and outcome data. Because of its size and breadth, PRO-ACT has become a critical external control resource for ALS drug development. In early-phase studies patient trajectories from PRO-ACT can serve as a virtual placebo or reference group, against which the observed treatment (ALSFRS-R slope, SVC decline, and survival) effect can be benchmarked.

A comparative analysis against the PRO-ACT database was conducted for the entire treatment period encompassing both the Phase 1 MEND and OLE studies, reflecting continuous NUZ-001 administration. Figures 1 and 2 present the ALSFRS-R and SVC decline, respectively, for all 12 patients. The matching protocol model used months since onset, pre-baseline slope, onset site, and baseline ALSFRS-R as fixed effects to align historical control patients with those treated with NUZ-001.

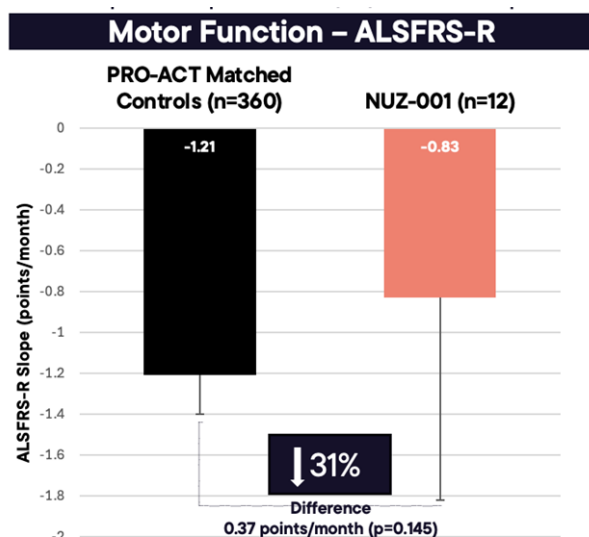


Figure 1: Slowing in ALSFRS-R Decline

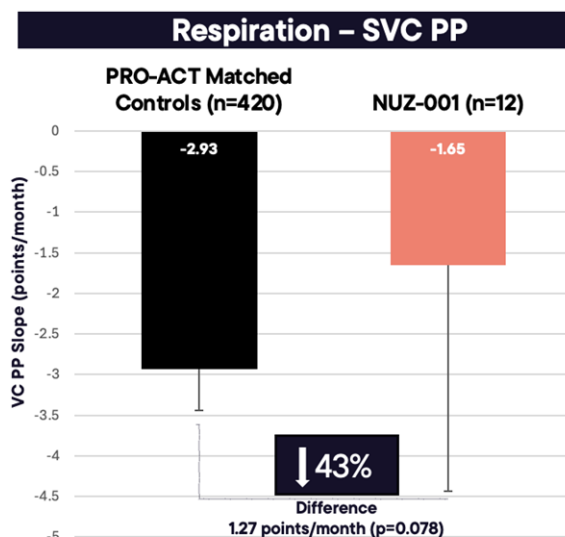


Figure 2: Slowing in VC PP Decline

As shown in Figure 1, compared with untreated matched historical controls from the PRO-ACT database, patients treated with NUZ-001 exhibited a 0.37 points/month slower decline in ALSFRS-R, corresponding to a 31% reduction in disease progression ( $-0.83$  vs  $-1.21$  points/month;  $p = 0.145$ ). The estimated rate of decline in VC PP for all 12 NUZ-001-treated patients was  $-1.65$  points/month, compared with  $-2.93$  points/month for untreated matched controls (difference: 1.27;  $p = 0.078$ ; see Figure 2). This represents a 43% slowing in VC PP decline, which aligns closely with the 31% slowing observed in ALSFRS-R, further supporting the potential disease-modifying effect of NUZ-001.

### Survival Analysis

As of 15 August 2025, 6 of the 12 patients who participated in the initial Phase 1 MEND study remain alive. Treatment durations range from 11.3 to 34.4 months (median 28.9 months). In the most conservative dataset, the log-rank test shows a significant survival benefit ( $\chi^2 = 13.75$ ,  $p = 0.00021$ ). The Cox proportional hazards analysis estimated a hazard ratio of 0.233 (95% CI: 0.096, 0.566,  $p = 0.0013$ ), corresponding to a 76% reduction in the risk of death versus untreated matched controls and an estimated median survival extension of ~16 months.

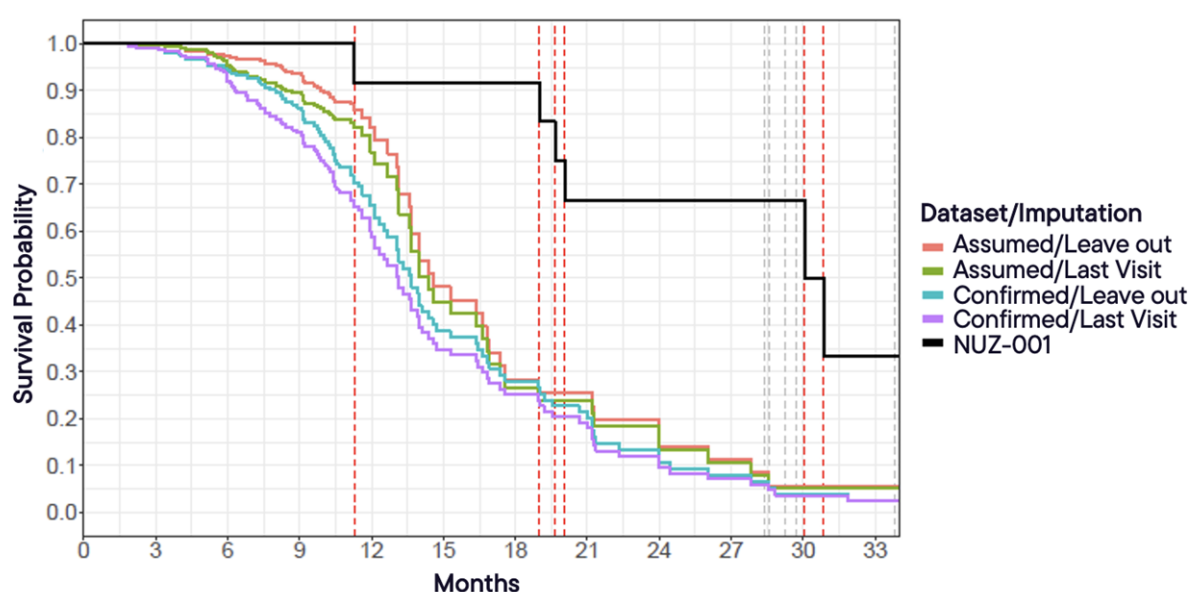


Figure 3: Survival Probability Analysis

In Figure 3, estimated Kaplan-Meier curves are shown for the NUZ-001 treatment group and each of the matched PRO-ACT control datasets described in Table 2. In these analyses, the “Assumed” Dataset treats missing death status

as indicating survival, whereas the “Confirmed” dataset includes only patients’ non-missing death data. The imputation method “Leave out” excludes missing times of death for confirmed deceased patients, while “Last Visit” assigns the last visit date as the time of death. Grey vertical dashed lines indicate exposure time, and the red vertical dashed lines represent death events.

This figure highlights how estimated survival probabilities vary depending on the dataset and imputation method, with the “Assumed” dataset using “Leave out” producing higher survival estimates.

Analysis Method		Log-Rank Test		Cox Proportional Hazards Model		
Dataset	Death Time Imputation	$\chi^2$	p-value	Hazard Ratio	95% CI	p-value
Assumed Survival	Leave out	13.75	0.00021	0.233	(0.096, 0.566)	0.0013
	Last Visit	14.88	0.00011	0.225	(0.093, 0.544)	0.0009
Confirmed Survival	Leave out	20.87	0.00000	0.203	(0.087, 0.472)	0.0002
	Last Visit	22.79	0.00000	0.194	(0.083, 0.450)	0.0001

**Table 1. Estimated Survival Probability by Analysis Dataset.** The left column details the 4 analysis datasets considered. The middle column reports the  $\chi^2$  statistic (with  $df = 1$ ) and corresponding p-value from the log-rank test. The right column provides the estimated hazard ratio with 95% confidence interval and two-sided p-value.

**Associate Professor Susan Mathers, Principal Investigator at Calvary Health Care Bethlehem, commented:** “It has been a pleasure to be part of the development of NUZ-001 as a potential drug treatment for people living with ALS, and to work with Prof Rowe’s team at Macquarie University, Neurizon Therapeutics and especially our participants, their families and the research team at Calvary Health Care Bethlehem. NUZ-001 has been a well-tolerated therapy and we hope that the future phase 2/3 study will confirm its potential to benefit the wider ALS community.”

## Study Results Presentation

A detailed study presentation of the top-line results is enclosed with this release.

A recorded results presentation can also be accessed in the Announcements section of Neurizon’s Investor Hub, featuring John Clark, Chief Operating Officer, Neurizon Therapeutics, and Melanie Quintana, Ph.D., Director & Senior Statistical Scientist, Berry Consultants.

## Next Steps

Encouraged by these results, Neurizon will advance NUZ-001 to the pivotal Phase 2/3 HEALEY ALS Platform Trial in Q4 CY2025, pending FDA clinical hold clearance, to confirm the observed benefits in a larger, placebo-controlled setting. The OLE findings reinforce the Company’s confidence in its clinical development strategy for NUZ-001 and validate the selected dosing regimen for the HEALEY ALS Platform Trial. Neurizon remains dedicated to developing NUZ-001 as a potential treatment capable of delivering meaningful clinical impact for people living with ALS.

The Company will continue to provide updates to the market as key milestones are achieved in the lead-up to anticipated trial participation in Q4 CY2025.

-ENDS-

This announcement has been authorized for release by the Board of Neurizon Therapeutics Limited.  
For further information, please contact:

**Dr. Michael Thurn**

Managing Director and Chief Executive Officer  
Neurizon Therapeutics Limited  
[enquiries@neurizon.com](mailto:enquiries@neurizon.com)  
+61 (3) 9692 7222

**Lidija Damjanovic**

Head of Marketing and Corporate Affairs  
Neurizon Therapeutics Limited  
[lidija@neurizon.com](mailto:lidija@neurizon.com)  
+61 (0) 425 700 504

**Released through:** Henry Jordan, Six Degrees Investor Relations, +61 (0) 431 271 538

**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.

**Neurizon Investor Hub**

We encourage you to utilise our Investor Hub for any enquiries regarding this announcement or other aspects concerning Neurizon. This platform offers an opportunity to submit questions, share comments, and view video summaries of key announcements.

To access Neurizon Investor Hub please scan the QR code or visit  
<https://investorhub.neurizon.com>



Neurizon® is a registered trademark of Neurizon Therapeutics Limited



---

# Phase 1 Open-Label Extension Study Top-Line Results

20 August 2025

John Clark, Chief Operating Officer

Melanie Quintana, Berry Consultants





# Disclaimer

This disclaimer applies to this presentation and the information contained in it (This presentation has been prepared by Neurizon Therapeutics Limited (ASX: NUZ) (the “Company”). It does not purport to contain all the information that a prospective investor may require in connection with any potential investment in the Company. You should not treat the contents of this presentation, or any information provided in connection with it, as financial advice, financial product advice or advice relating to legal, taxation or investment matters.

No representation or warranty (whether express or implied) is made by the Company or any of its officers, advisers, agents or employees as to the accuracy, completeness or reasonableness of the information, statements, opinions or matters (express or implied) arising out of, contained in or derived from this presentation or provided in connection with it, or any omission from this presentation, nor as to the attainability of any estimates, forecasts or projections set out in this presentation.

This presentation is provided expressly on the basis that you will carry out your own independent inquiries into the matters contained in the presentation and make your own independent decisions about the affairs, financial position or prospects of the Company.

The Company reserves the right to update, amend or supplement the information at any time in its absolute discretion (without incurring any obligation to do so).

Neither the Company, nor its related bodies corporate, officers, their advisers, agents and employees accept any responsibility or liability to you or to any other person or entity arising out of this presentation including pursuant to the general law (whether for negligence, under statute or otherwise), or under the Australian Securities and Investments Commission Act 2001, Corporations Act 2001, Competition and Consumer Act 2010 or any corresponding provision of any Australian state or territory legislation (or the law of any similar legislation in any other jurisdiction), or similar provision under any applicable law. Any such responsibility or liability is, to the maximum extent permitted by law, expressly disclaimed and excluded.

Nothing in this material should be construed as either an offer to sell or a solicitation of an offer to buy or sell securities. It does not include all available information and should not be used in isolation as a basis to invest in the Company.

## Future Matters

This presentation contains reference to certain intentions, expectations, future plans, strategy and prospects of the Company. Those intentions, expectations, future plans, strategy and prospects may or may not be achieved. They are based on certain assumptions, which may not be met or on which views may differ and may be affected by known and unknown risks. The performance and operations of the Company may be influenced by a number of factors, many of which are outside the control of the Company. No representation or warranty, express or implied, is made by the Company, or any of its directors, officers, employees, advisers or agents that any intentions, expectations or plans will be achieved either totally or partially or that any particular rate of return will be achieved.

Given the risks and uncertainties that may cause the Company’s actual future results, performance or achievements to be materially different from those expected, planned or intended, recipients should not place undue reliance on these intentions, expectations, future plans, strategy and prospects. The Company does not warrant or represent that the actual results, performance or achievements will be as expected, planned or intended.

## US Disclosure

This document does not constitute any part of any offer to sell, or the solicitation of an offer to buy, any securities in the United States or to, or for the account or benefit of any “US person” as defined in Regulation S under the US Securities Act of 1993 (“Securities Act”). The Company’s shares have not been, and will not be, registered under the Securities Act or the securities laws of any state or other jurisdiction of the United States, and may not be offered or sold in the United States or to any US person without being so registered or pursuant to an exemption from registration including an exemption for qualified institutional buyers.

# Phase 1 Open Label Extension

## Executive Summary

Positive Phase 1 OLE study results demonstrating durable long-term safety and efficacy signals at the recommended Phase 2 dose

Open-Label Extension Key Findings	
Primary Objectives	<ul style="list-style-type: none"><li>Primary outcome met</li><li>Long-term treatment with NUZ-001 at the recommended Phase 2 dose was safe and well-tolerated</li></ul>
Preliminary Efficacy Signals	<ul style="list-style-type: none"><li>Durable functional benefit, stable respiration, and supportive biomarker trends with NUZ-001</li></ul>
Integrated Preliminary Efficacy Comparator Analysis to the PRO-ACT Database	
Survival Advantage	<ul style="list-style-type: none"><li>NUZ-001 significantly increased survival (<math>\chi^2=13.75</math>, <math>p=0.00021</math>)</li><li>NUZ-001 significantly reduced the risk of death by 76.7% (HR=0.233, <math>p=0.0013</math>)</li><li>NUZ-001 showed an estimated median survival extension of ~16 months</li></ul>
Functional Decline	<ul style="list-style-type: none"><li>NUZ-001 slowed the rate of functional decline by 31% (<math>-0.83</math> vs <math>-1.21</math> ALSFRS-R points/month; <math>p=0.145</math>)</li></ul>
Slow Vital Capacity	<ul style="list-style-type: none"><li>NUZ-001 reduced the rate of respiratory decline by 43% (<math>-1.65</math> vs <math>-2.93</math> VC PP points/month; <math>p=0.078</math>)</li></ul>
Next Steps	<ul style="list-style-type: none"><li>NUZ-001 has been safely used for more than 2.5 years, with 5 patients still receiving treatment under the TGA's Special Access Scheme</li><li>These encouraging results reinforce the rationale for the planned pivotal HEALEY ALS Platform Trial, expected to commence in Q4 CY2025</li></ul>





# Phase 1 Open Label Extension

## ALS Study Design



### Study Design:

This was an open-label, safety, tolerability, and preliminary efficacy study of NUZ-001 in 10 patients with ALS who completed the Phase 1 MEND Study, at the recommended Phase 2 dose of 10 mg/kg administered orally daily for 12-months.



### Patient Population: 9 Men, 1 Woman

- Adults with Familial or Sporadic ALS
- Completed Phase 1 MEND Study
- Adequate bone marrow reserve, renal & liver function
- All patients were on a stable dose of riluzole
- **Median Age: 67 (48 – 79) years**
- **Median Disease Duration: 28.1 (16.7 – 48.7) months**



### Intervention: 10 patients enrolled

- Oral tablets
- Eligible patients received recommended Phase 2 dose of 10 mg/kg daily for 12-months
- **Median OLE treatment duration:**
  - **12.0 months (range: 1.5–12.3 months)**
- **Median OLE follow-up:**
  - **13.2 months (range: 3.7–13.3 months)**



### Locations:

#### Two Centres in Australia

- Calvary Hospital Bethlehem, Melbourne
- Macquarie University, Sydney



### Primary & Exploratory Outcomes:

#### OLE Study

- Safety and tolerability
- ALS Functional Rating Scale–Revised (ALSFRS-R)
- Slow Vital Capacity (SVC)
- ALS Quality of Life Questionnaire (ALSSQOL-R)
- Edinburgh Cognitive and Behavioural ALS Screen (ECAS)
- Biomarkers
  - Plasma neurofilament light chain (NfL)
  - Urinary p75<sup>ECD</sup>/Creatinine

#### Integrated Preliminary Efficacy Comparator Analysis to the PRO-ACT Database (Combined studies)

- ALSFRS-R
- SVC
- Survival probability
- Median life extension

# Phase 1 Open Label Extension

## ALS: Demographics, Baseline Characteristics, ALS History, and Treatment Duration

- Most patients were male (90%)
- Median age was 67.0 years
- The most common site for the 1st disease onset was the Upper Limb region (60%)
- ALS diagnosis was considered Probable (70%) in most cases
- Median Phase 1 Baseline ALSFRS-R was 39.5
- Median OLE Baseline ALSFRS-R was 31.5
- Median Phase 1 Pre-Baseline ALSFRS-R Slope was 0.739 p/mth
- Median ALS duration (Date of Onset to 1<sup>st</sup> OLE Dose) was 28.1 months
- Median Treatment Duration from first Phase 1 dose to last OLE dose was 28.9 months
- Median Treatment Duration from first OLE dose to last OLE dose was 12 months

Gender, n (%)	
Female	1 (10.0)
Male	9 (90.0)
Age (years)	
Mean (SD)	64.8 (9.9)
Median (Min, Max)	67.0 (48,79)
Site of First Disease Onset, n (%)	
Lower Limb	2 (20.0)
Upper Limb	6 (60.0)
Limb Onset	1 (10.0)
Bulbar	1 (10.0)
ALS Diagnosis, n (%)	
Definite	3 (30.0)
Probable	7 (70.0)
Time since Onset (Months)	
Mean (SD)	28.7 (9.60)
Median (Min, Max)	28.1 (16.7, 48.7)

Phase 1 Baseline ALSFRS-R	
Mean (SD)	38.8 (4.26)
Median (Min, Max)	39.5 (31, 44)
OLE Baseline ALSFRS-R	
Mean (SD)	28.2 (11.45)
Median (Min, Max)	31.5 (6, 41)
Phase 1 Pre-Baseline Slope	
Mean (SD)	0.792 (0.463)
Median (Min, Max)	0.739 (0.210, 1.478)
Treatment Duration (months)	
First Phase 1 Dose to Last OLE Dose, Median (Min, Max)	28.9 (11.3, 34.4)
First OLE Dose to Last OLE Dose, Median (Min, Max)	12.0 (1.5, 12.3)

# 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 TEAEs 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
- Two (20%) deaths, both unrelated to study drug
  - Pneumonia, Respiratory Failure
- No unexpected safety findings observed in the OLE compared with Phase 1 MEND.
- 5 patients still receiving treatment under the TGA's Special Access Scheme.

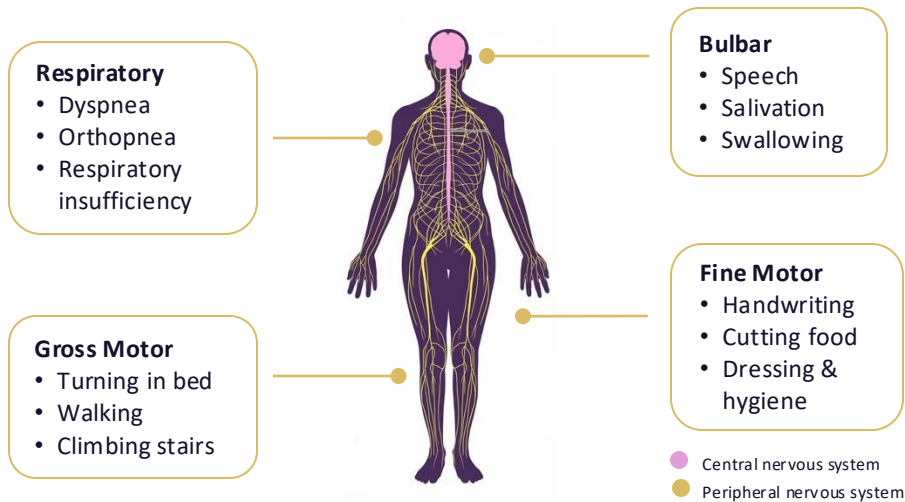


# Phase 1 Open Label Extension

## Preliminary Efficacy Amyotrophic Lateral Sclerosis Function Rating Scale – Revised (ALSFRS-R)

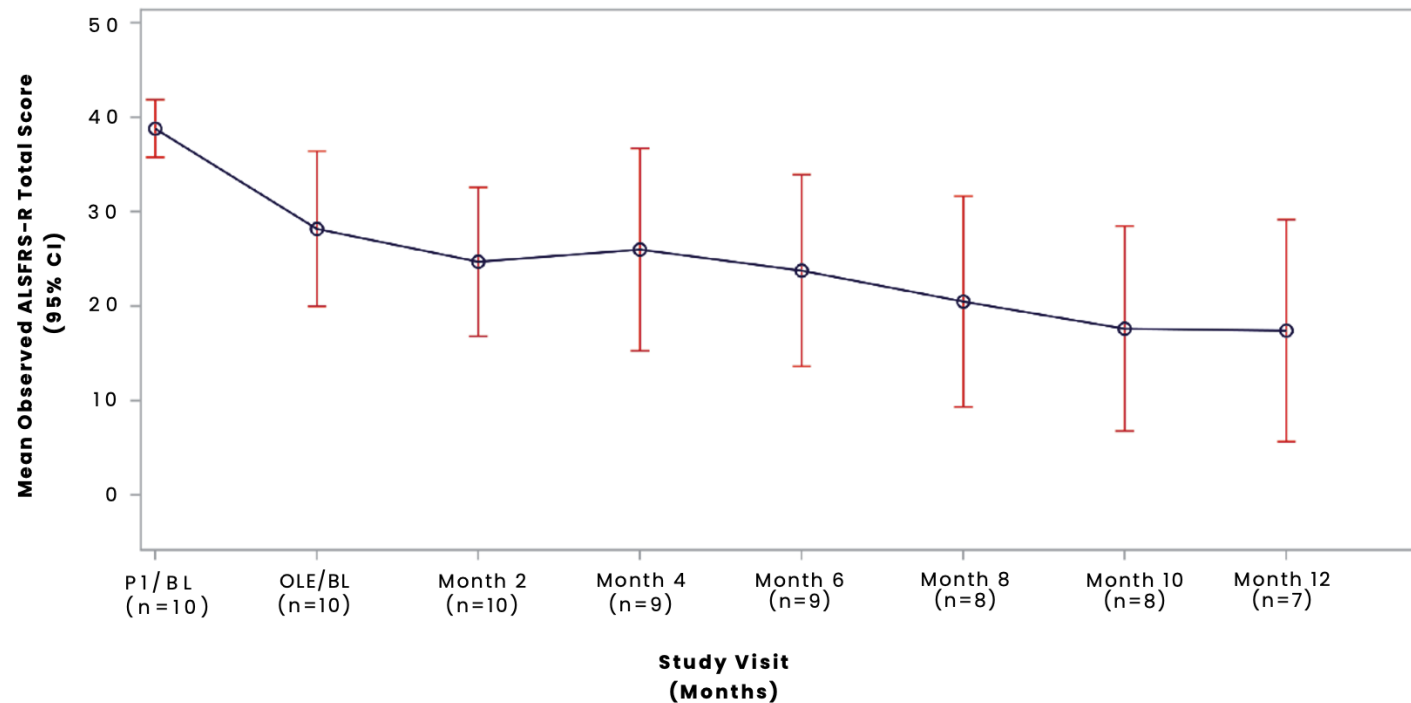
Estimated mean rate of decline was -0.88 pts/month (CI: -1.58, 0.10) in the OLE, compared with -0.74 pts/month (CI: -1.26, -0.23) in the MEND Study. These comparable results indicate a stable & durable treatment effect with long-term NUZ-001 therapy.

### ALSFRS-R Domains Assessed



Each task is rated on a five-point scale from 0 = can't do, to 4 = normal ability. Individual item scores are summed to produce a reported score of between 0=worst and 48=best.

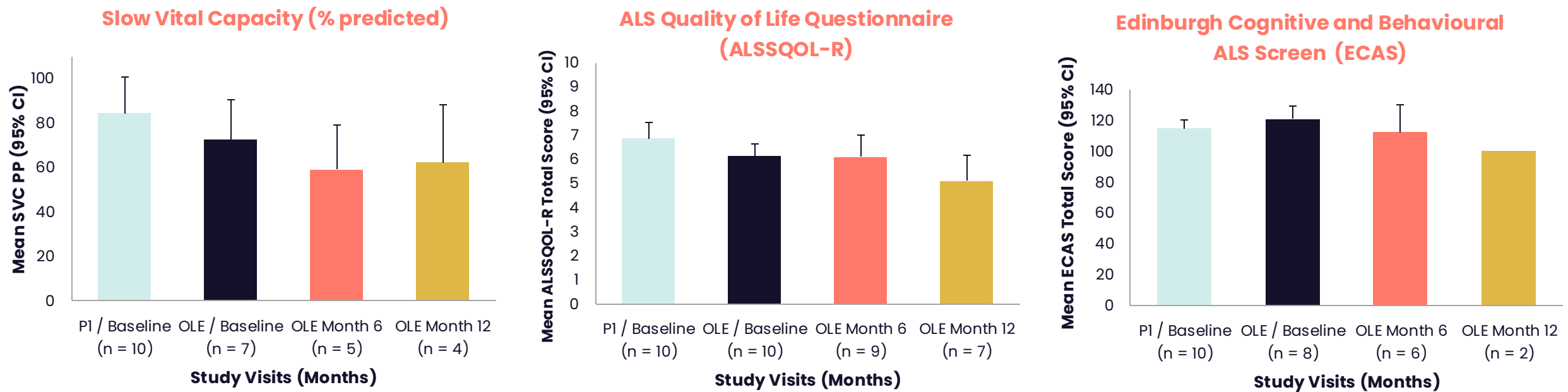
### Observed ALSFRS-R Total Score





# Phase 1 Open Label Extension


## Exploratory Endpoints

Slow Vital Capacity PP, ALS Quality of Life Questionnaire, and Edinburgh Cognitive and Behavioural ALS Screen declined to Month 12, consistent with ALS progression. No unexpected effects or signal of accelerated decline due to NUZ-001 were observed.



 A lung function test that measures how much air can be exhaled in a relaxed manner until the lungs are completely empty.

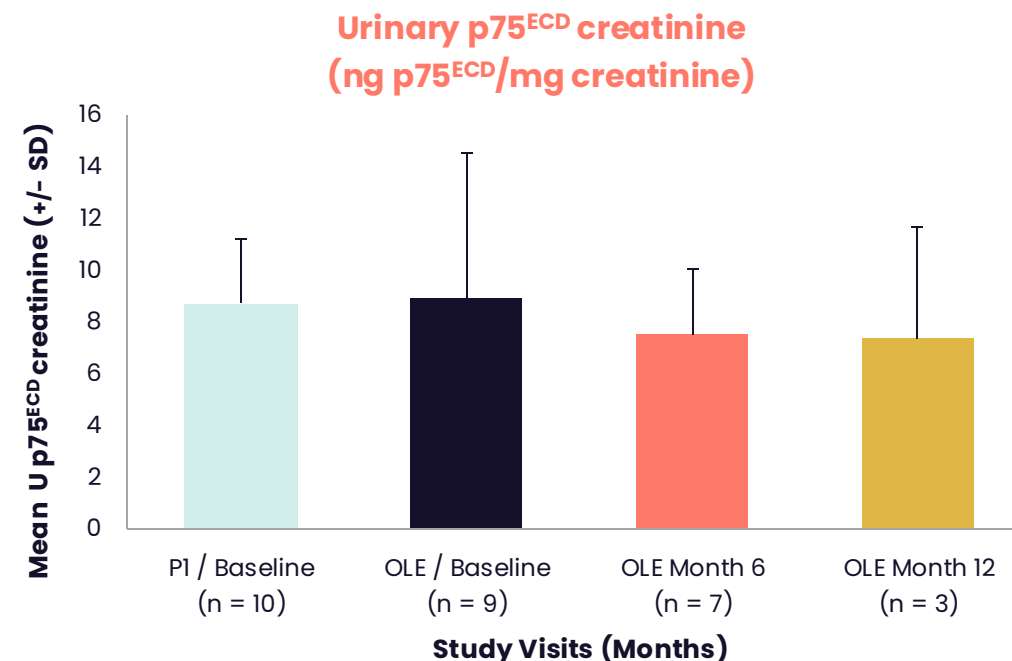
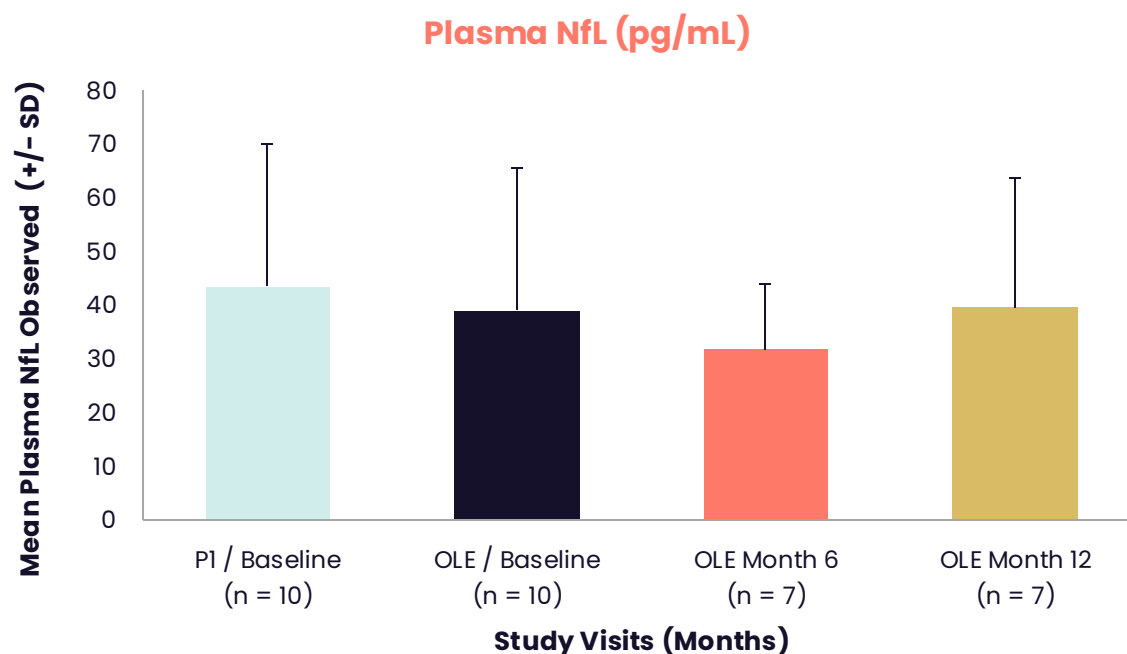
 50-item questionnaire rated on a 10-point scale, across 6 domain scores (negative emotion, interaction with people and environment, intimacy, religiosity, physical symptoms, and bulbar function).

 Cognitive screening tool. Includes assessment of fluency, executive functions, language, memory, and visuospatial functions. The total score is 136 points.

# Phase 1 Open Label Extension

## Exploratory Biomarkers Assessment – Plasma NfL & Urinary p75<sup>ECD</sup>

Over the 12-month OLE, plasma NfL levels remained stable with a transient dip at M6, while Urinary p75<sup>ECD</sup>/Creatinine decreased by ~17%. Together, these biomarker trends provide supportive evidence for a potential disease-modifying effect of NUZ-001.



Neurofilament light (NfL) levels correlate with disease progression rate in ALS and higher levels of neurofilament are associated with faster/greater decline of ALSFRS-R over time<sup>1</sup>. NfL levels are strongly prognostic of survival in ALS.

Urinary p75<sup>ECD</sup>/Creatinine levels are elevated in ALS and correlate with disease severity and progression. Higher levels are associated with faster functional decline and shorter survival<sup>2</sup>.

<sup>1</sup>Brodovitch A, Boucraut J, Delmont E, Parlanti A, Grapperon A-M, Attarian S, et al. Combination of serum and CSF neurofilament-light and neuroinflammatory biomarkers to evaluate ALS. Sci Rep. 2021;11(1):703. doi: 10.1038/s41598-020-80370-6.

<sup>2</sup>Shepherd SR, Chataway T, Schultz DW, Rush RA, Rogers ML. Urinary p75<sup>ECD</sup>: a prognostic, disease progression, and pharmacodynamic biomarker in ALS. Neurology. 2017;88(12):1137-1144. doi:10.1212/WNL.0000000000003739



# ALS PRO-ACT Clinical Trial Database



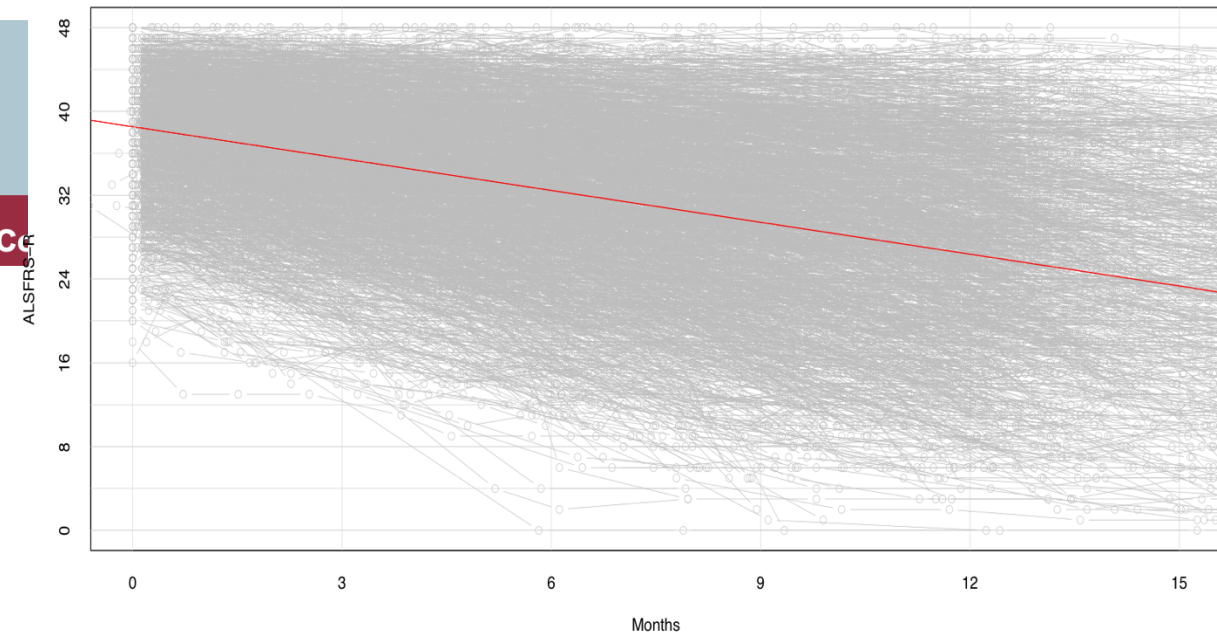
Welcome to the  
**P**ooled **R**esource **O**pen-Access **A**LS **C**linical **T**rials Database

[Home](#) [Data](#) [How to Use PRO-ACT](#) [ALS Prize](#) [ALS Links](#) [About Us](#) [Contact](#)

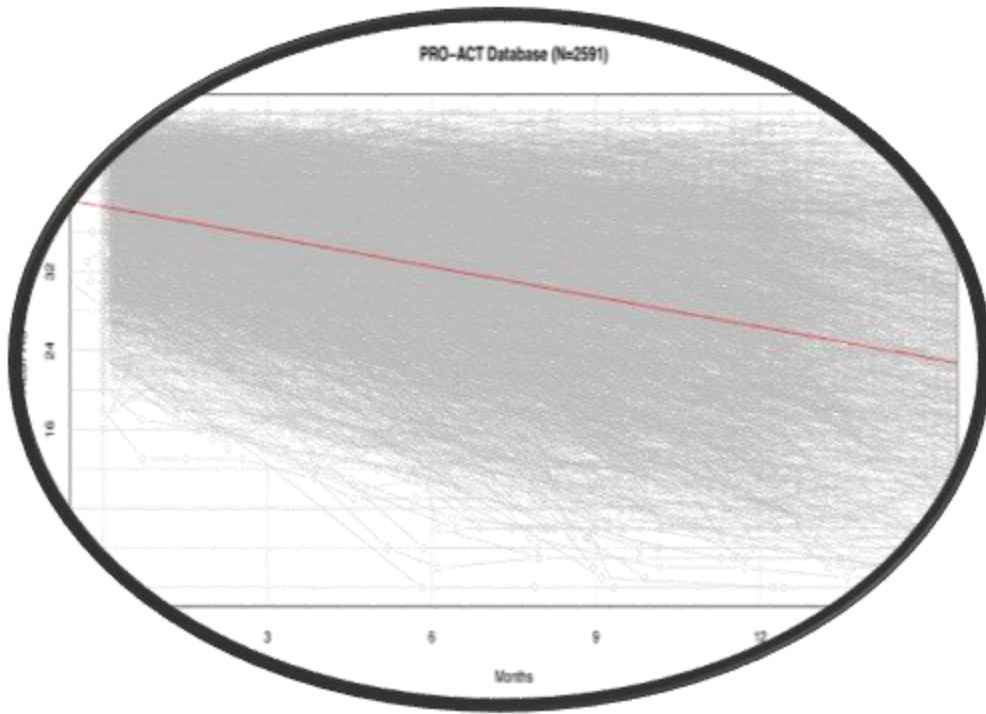
**PRO-ACT** provides users with easy access to:

- Over 11,600 fully de-identified clinical patient records
- Placebo and treatment-arm data from 29 Phase II/III clinical trials
- Demographic, lab, medical and family history, and other data elements
- More than 10 million longitudinally collected data points

PRO-ACT Database (N=2591)



# Use of PRO-ACT in ALS Clinical Trials



Historical Control  
Comparisons using  
Matched participant-  
level data

Evidence-based  
Clinical Trial Design  
and Optimization

# Exploratory Analysis: Disease progression compared to Historical Controls

## PRO-ACT Matching Algorithm

- Subset PRO-ACT to those participants meeting major inclusion/exclusion criteria from Phase 1 study
- Calculate propensity scores (PS) based on pre-specified known prognostic factors of disease progression
- Match each participant who received NUZ-001 to 30 participants in PRO-ACT based on PS and baseline covariates

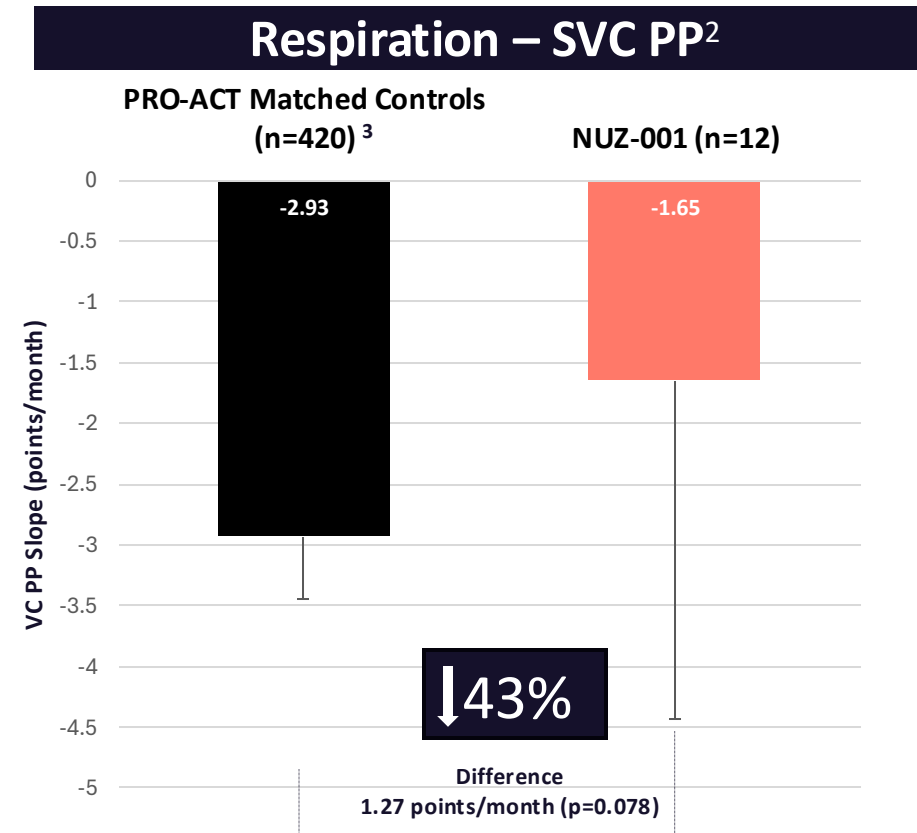
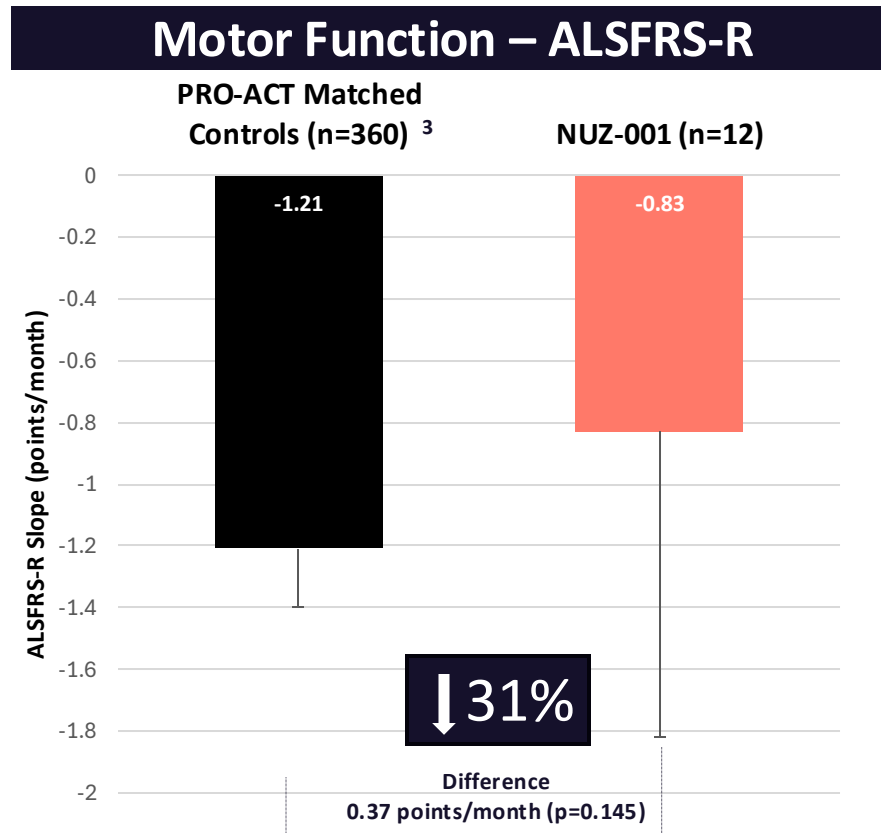
## Matching Results in Balanced Baseline Covariates

	PRO-ACT Controls (N = 360)	NUZ-001 (N = 12)
<b>Time since Onset (Months)</b>		
Mean (SD)	15.3 (7.27)	14.7 (8.38)
Median [Min,Max]	14.5 [3.8, 35.8]	13.9 [3.6, 34.0]
<b>Baseline ALSFRS-R</b>		
Mean (SD)	37.9 (4.64)	38.2 (5.10)
Median [Min,Max]	38.0 [24.0, 46.0]	39.5 [28.0, 44.0]
<b>Pre-Baseline Slope</b>		
Mean (SD)	0.786 (0.438)	0.826 (0.461)
Median [Min,Max]	0.733 [0.11, 2.14]	0.739 [0.21, 1.48]
<b>Onset Location</b>		
Bulbar	60 (16.7%)	2 (16.7%)
Other	300 (83.3%)	10 (83.3%)

# Phase 1 Open Label Extension

## Preliminary Efficacy ALSFRS-R and SVC

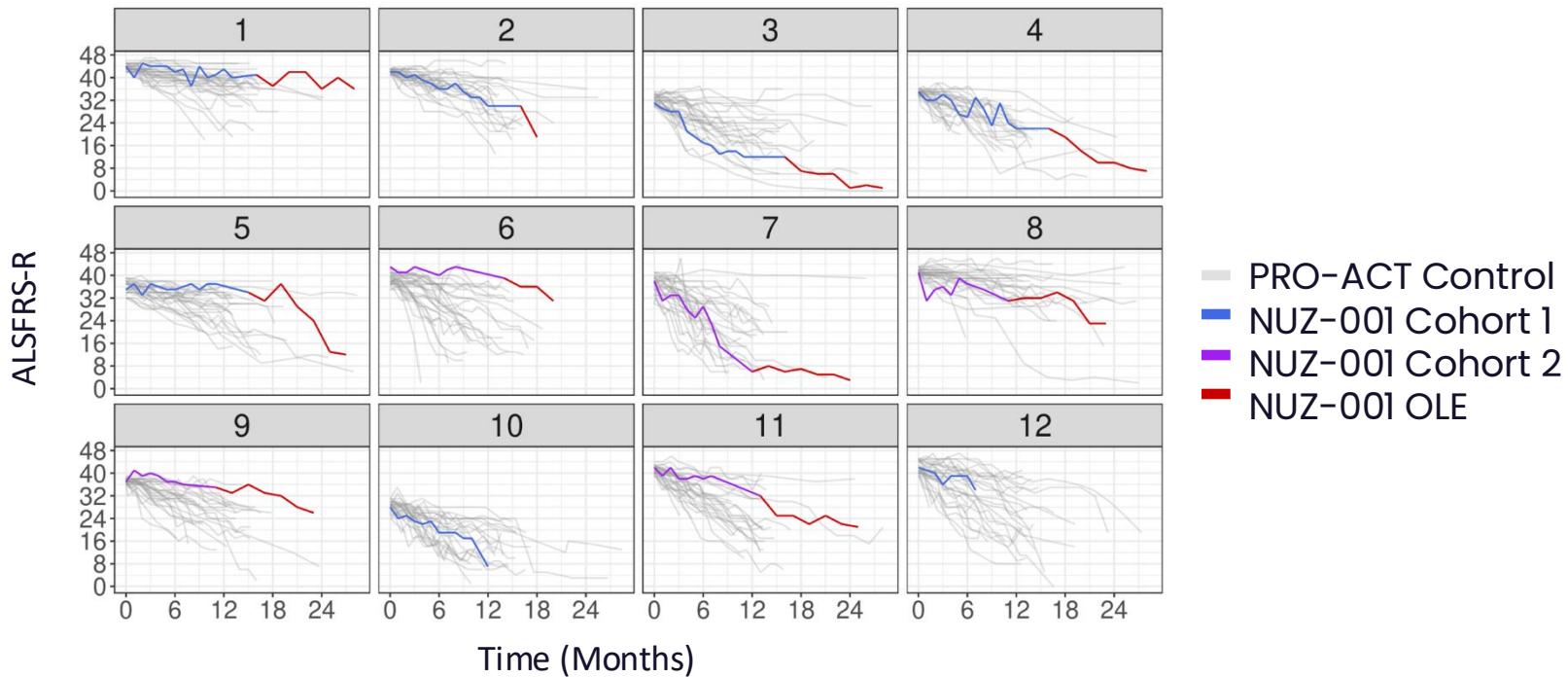
Treatment with NUZ-001 across combined Phase 1 and OLE studies slowed the progression of ALS in all patients by 31% for ALSFRS-R and 43% for SVC percent predicted (PP) when compared to matched controls from the PRO-ACT historical database<sup>1</sup>



# Phase 1 Open Label Extension

## Preliminary Efficacy ALSFRS-R

Compared to matched controls from the PRO-ACT, treatment with NUZ-001 showed a 31% reduction in disease progression



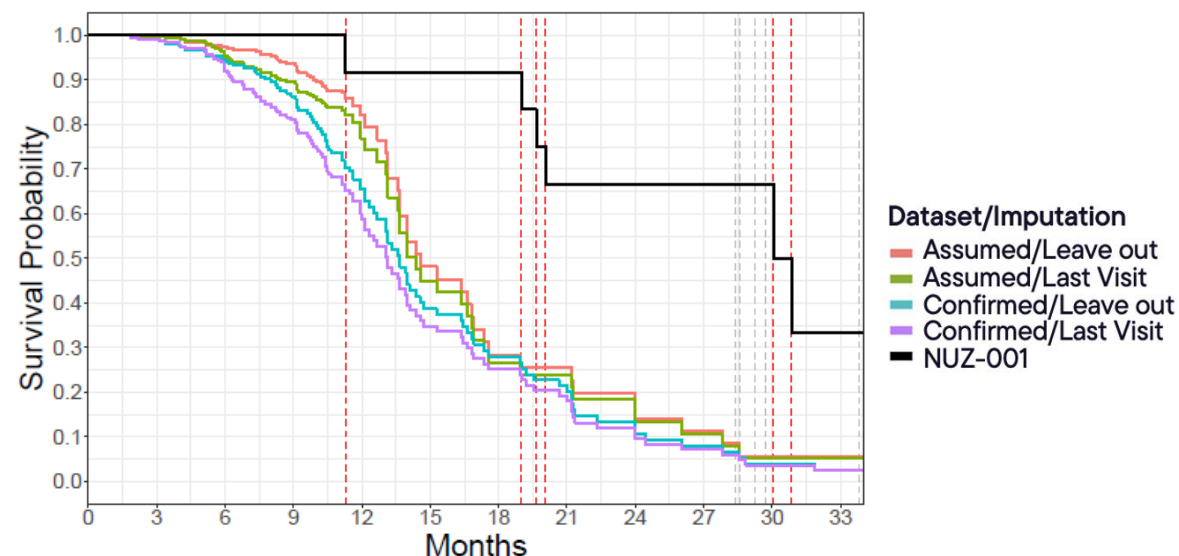
Efficacy Endpoint	PRO-ACT Control (n=360)	NUZ-001 (n=12)	Between-group Differences
ALSFRS-R Slope Estimate	-1.21	-0.83	0.37
95% CI	(-1.3, -1.1)	(-1.33, -0.34)	(-0.13, 0.88)
p-value	-	-	0.145

# Phase 1 Open Label Extension

## Survival Probability Analysis

Compared to matched controls from the PRO-ACT, treatment with NUZ-001 results in a significantly ( $\chi^2=13.75$ ,  $p=0.00021$ ) longer survival of patients with ALS

Analysis Method		Log-Rank Test		Cox Proportional Hazards Model		
Dataset	Death Time Imputation	$\chi^2$	p-value	Hazard Ratio	95% CI	p-value
Assumed Survival	Leave out	13.75	0.00021	0.233	(0.096, 0.566)	0.0013
	Last Visit	14.88	0.00011	0.225	(0.093, 0.544)	0.0009
Confirmed Survival	Leave out	20.87	0.00000	0.203	(0.087, 0.472)	0.0002
	Last Visit	22.79	0.00000	0.194	(0.083, 0.450)	0.0001



Hazard ratio of 0.233 (95% CI: (0.096, 0.566),  $p = 0.0013$ ) indicating that treatment with NUZ-001 reduces the risk of death by 76.7%



# Phase 1 Open Label Extension

## Conclusion

These encouraging 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

### Highlights (Based on a small study population of 12 patients)



#### Primary Objectives

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



#### Slowed Functional Decline

- Sustained slowing in disease progression by 31% compared to PRO-ACT matched controls



#### Respiratory Stabilisation

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



#### Survival\*

- Reduction in the risk of death by 76.7% compared to PRO-ACT matched controls
- Estimated life extension of ~16 months



#### Biomarker Trends

- Stable plasma NfL and decreased (–17%) urinary p75<sup>ECD</sup>



#### Patient Satisfaction

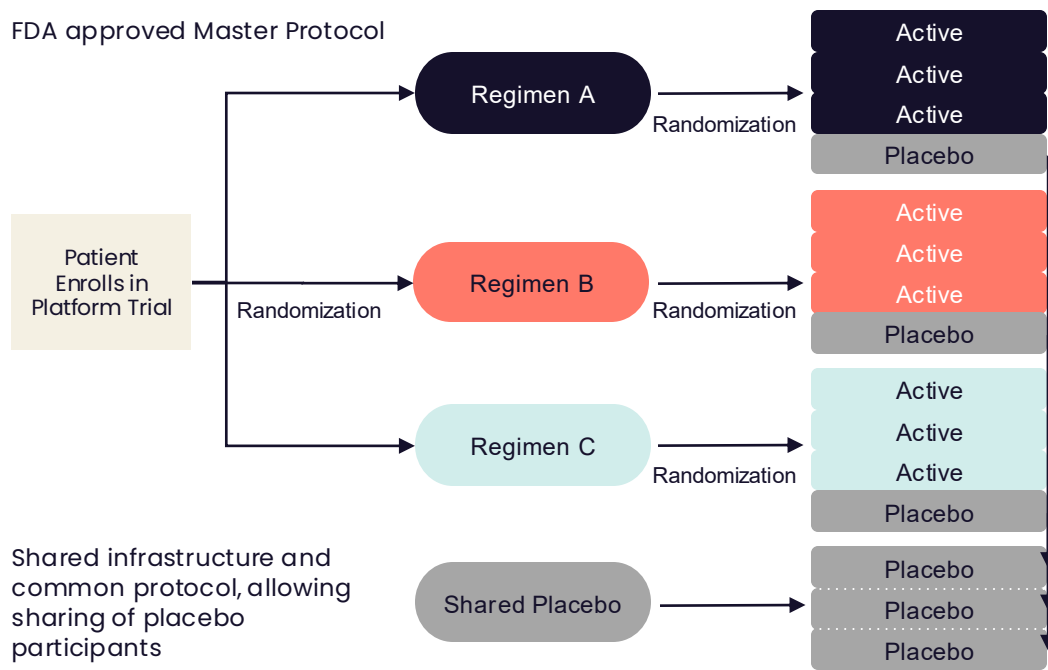
- No study discontinuations; 5 of the 6 remaining patients accessing NUZ-001 under the TGA's Special Access Scheme

\* Data cut 15 Aug 2025

# NUZ-001 selected for entry into the HEALEY ALS Platform Trial

The HEALEY ALS Platform Trial is a competitive process led by a group of expert ALS scientists and members of the Healey & AMG Center Science Advisory Committee

## HEALEY ALS Platform Trial Design<sup>1</sup>



## Innovative Trial Structure

### Design

- Shared master protocol
- >70 clinical sites across the US
- 3:1 active drug to placebo ratio
- 160–240 participants per regimen
- 7 regimens completed
- 2 regimens progressing to Phase 3



### Next Steps

- Lift the FDA's clinical hold
- File protocol amendment under MGH's Investigator-initiated IND
- Commence participation Q4 CY25

# We extend our sincere thanks to the Participants, Investigators, Site Staff and Partners



The OLE participants, their families, and caregivers



Calvary Health Care Bethlehem, A/Prof Susan Mathers, Emma Windebank, and Nicole Panerio



Centre for Motor Neurone Disease Research Faculty of Medicine & Health Research, Macquarie University, Prof Dominic Rowe, Richard Gan and Paula Bayeh



Motor Neurone Disease & Neurotrophic Research Laboratory, Flinders University, A/Prof Mary-Louise Rogers



Wicking Dementia Research and Education Centre, University of Tasmania, A/Prof Anna King




Alithia Life Sciences, A/Prof Tina Soulis, Mary Hayek, and Taryn Lowe



Berry Consultants, Melanie Quintana and Matteo Vestrucci



Clinical Data Management, Anna Dellas and Samantha Matias



Registered Address:  
Suite 2, Level 11, 385 Bourke Street,  
Melbourne, VIC 3000, Australia  
+61 (3) 9692 7222  
[enquiries@neurizon.com](mailto:enquiries@neurizon.com)

