

## Neurizon to present Half-Year Results and FDA feedback on NUZ-001 IND Application

**17 February 2025 – Melbourne, Australia:** Neurizon Therapeutics Limited (ASX: NUZ & NUZOA) (“Neurizon” or “the Company”), a clinical-stage biotech company advancing treatments for neurodegenerative diseases, is pleased to announce a presentation by Dr. Michael Thurn, the Company’s Managing Director and CEO, to update the shareholders about the Company’s half-year results and feedback from the United States (U.S.) Food and Drug Administration (FDA) regarding the NUZ-001 IND application.

The presentation will outline the following:

- FDA’s feedback on the NUZ-001 IND Application received on 15 February 2025.
- Neurizon’s strategic focus on bringing NUZ-001 to market as an effective potential treatment for Amyotrophic Lateral Sclerosis (ALS).
- Key regulatory milestones, clinical development progress, and advancements in preclinical research that support the Company’s long-term growth strategy.

Presentation slides are available as an attachment to this announcement. The recording of the presentation will be made available on Neurizon’s website at [www.neurizon.com](http://www.neurizon.com).

-ENDS-

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

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### About Neurizon Therapeutics Limited

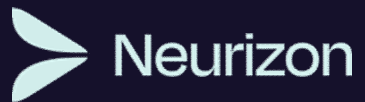
Neurizon Therapeutics Limited (ASX: NUZ) is a clinical-stage biotechnology company dedicated to advancing treatments for neurodegenerative diseases. Neurizon is developing its lead drug candidate, NUZ-001, for the treatment of ALS, which is the most common form of motor neurone disease. Neurizon's strategy is to accelerate access to effective ALS treatments for patients while exploring NUZ-001's potential 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.

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## Half Year Update: Key Developments and Future Outlook

February 2025

ASX: NUZ



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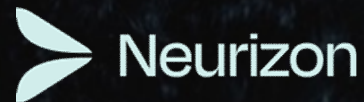
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Our mission is to lead the development of neurodegenerative treatments towards a promising new horizon for patients



# FDA Guidance on the NUZ-001 IND Application

**FDA response received on Saturday, 15<sup>th</sup> February 2025**

## **Key Points:**

- A single request for additional animal exposure data to reinforce safety margins for clinical development
- This gives the FDA greater confidence in bridging the gap between veterinary and human use of NUZ-001
- Strengthens our path through to the market approval

## **Next Steps:**

- Initiatives underway to generate additional exposure data to address the FDA's request
- Collaboration among Board, management, advisors, scientific, and regulatory teams
- Further updates will be provided as developments occur and the final response timeline is established

**There were no safety concerns identified from previous clinical studies using NUZ-001**

## **Our Commitment Remains:**

- Advancing NUZ-001 as a potential treatment for ALS and other neurodegenerative diseases

## Our success is underpinned by a clear strategic focus on:

**Advancing patient access**  
to innovative ALS treatments



**Accelerating hope by**  
**partnering** with the world's  
leading Neurologists and Mass  
General's HEALEY ALS Platform  
Trial



**Unlocking the potential**  
**of NUZ-001**  
to treat a range of  
neurodegenerative diseases





# Investment credentials for NUZ-001



## Orally Bioavailable

Ease of delivery



## Crosses blood brain barrier

Centrally acting drug



## Solid scientific foundation

Reduces TDP-43 accumulation (50-55%) and partially rescues electrophysiological function



## Long-term safety data

Animal and human safety database accumulating



## Positive Phase 1 efficacy data

Promising efficacy signals



## Strong IP Position

Patent protection runway until 2039



## Near-term regulatory strategy

Accelerated approval possible across multiple jurisdictions



## Additional indications

Pipeline synergies to leverage commercial infrastructure across development programs



## Experienced Management

Experienced world-class Board, SAB and management team



## High deal flow

Neurology assets in demand with 4 ALS deals over the last year alone



# Pipeline

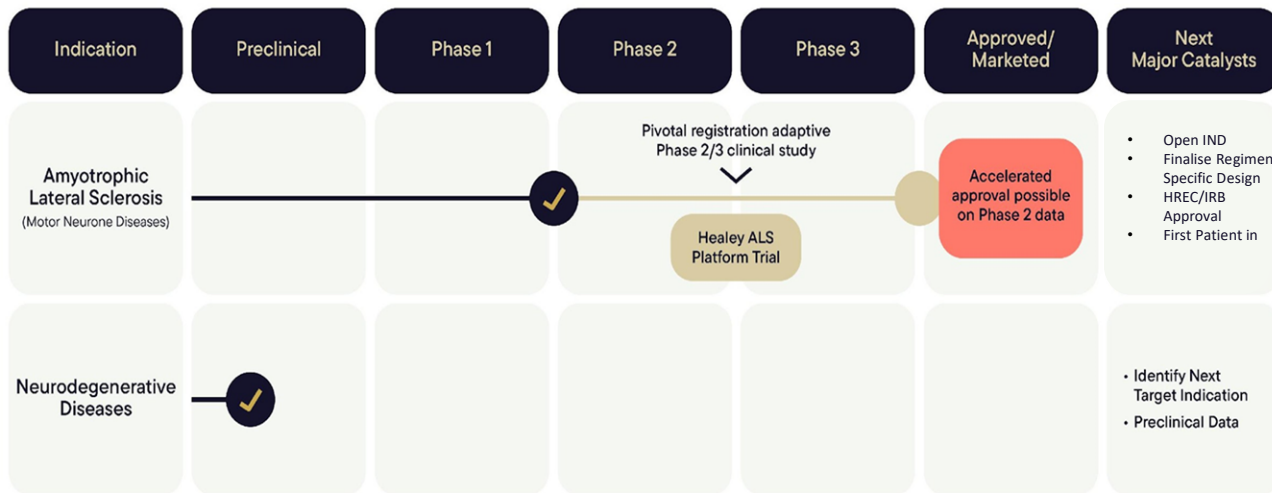
## Multiple synergistic product opportunities in neurodegenerative disease

- Single pivotal registration clinical study for ALS
- Targeting accelerated approval from Phase 2 data

### NUZ-001 ((S)-Monepantel) is an mTOR inhibitor

Nat Cell Biol (2019) Kim J et al./  
J Mol Biol (2020) Djajadikerta  
A et al./Int J Molec Sci (2019)  
Thelling S et al.

- mTOR pathway is central to normal protein homeostasis in cells
- mTOR inhibition leads to reduced de novo net protein production and increased recycling of existing excessive or misprocessed cellular proteins
- Reduced phosphorylation of RPS6KB1 in PBMCs is a marker of mTOR inhibition

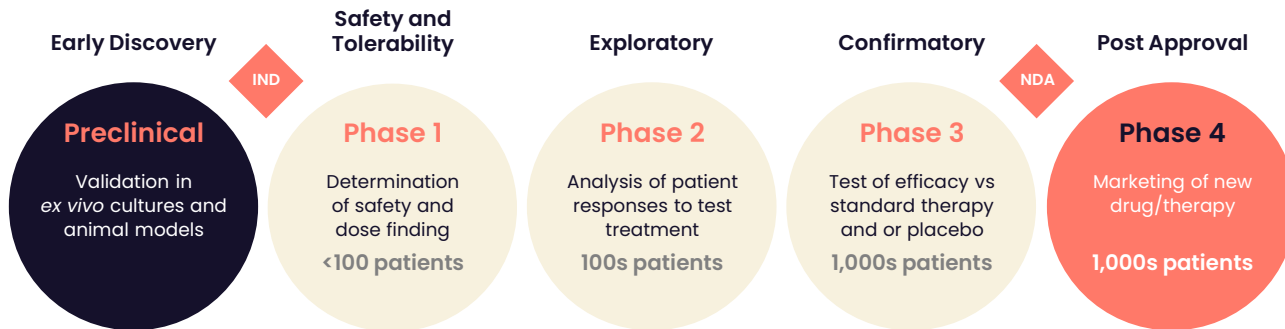


# Accelerating Access - Faster, More Efficient Development for NUZ-001

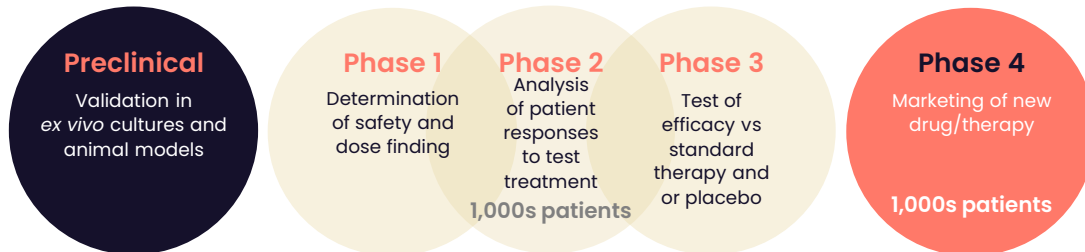
**Rare diseases** have the advantages of accelerated development timelines and lower development costs

Access to the **HEALEY ALS Platform Trial** increases patient participation rate and reduces study cost and time, enabling wider and earlier patient access.

## Standard Drug Development & Trial

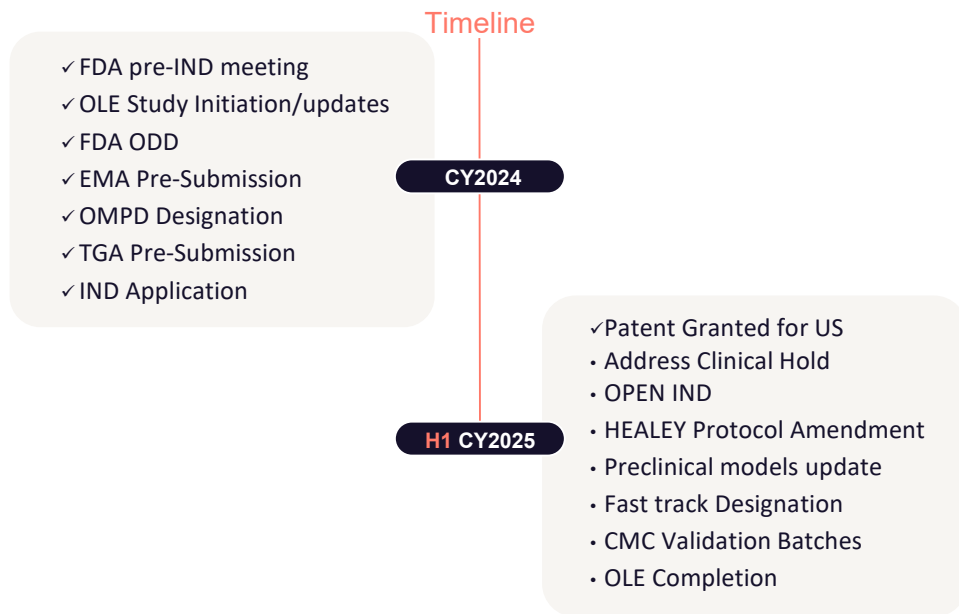


## Rare Disease & HEALEY Access

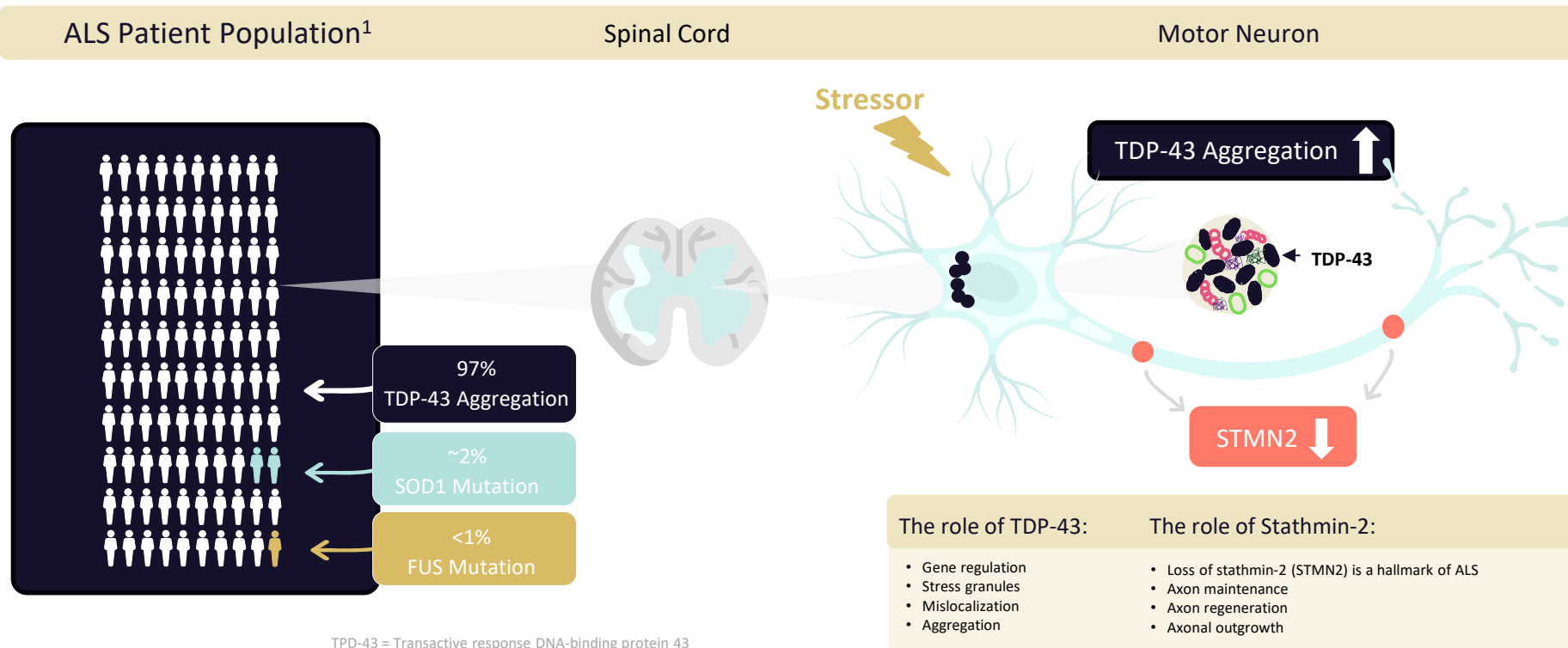


# Development Milestones

Derisked lead program in ALS with multiple near-term catalysts and potential for use in other neurodegenerative diseases



# TDP-43 aggregates are a hallmark of ALS pathology



TPD-43 = Transactive response DNA-binding protein 43

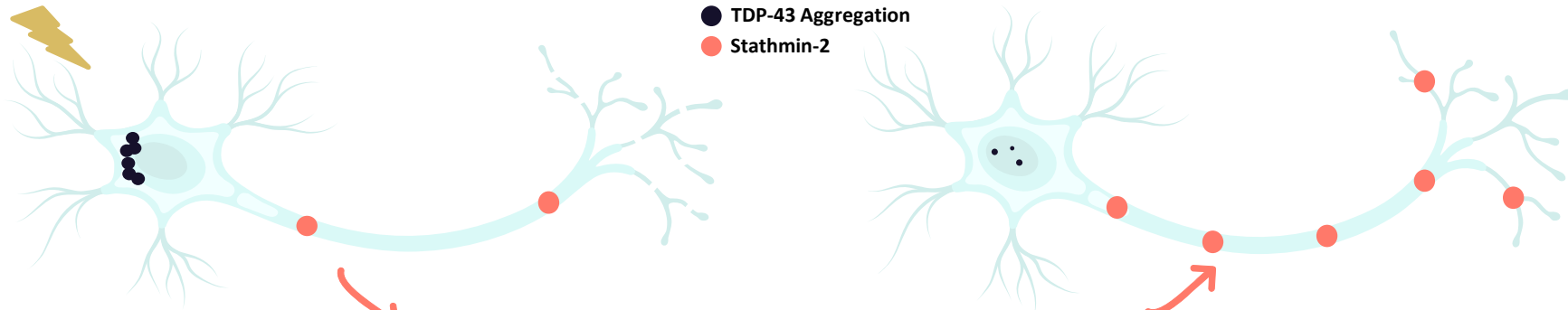
STMN2 – Stathmin-2

<sup>1</sup>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. PMID: 23931993; PMCID: PMC4411085

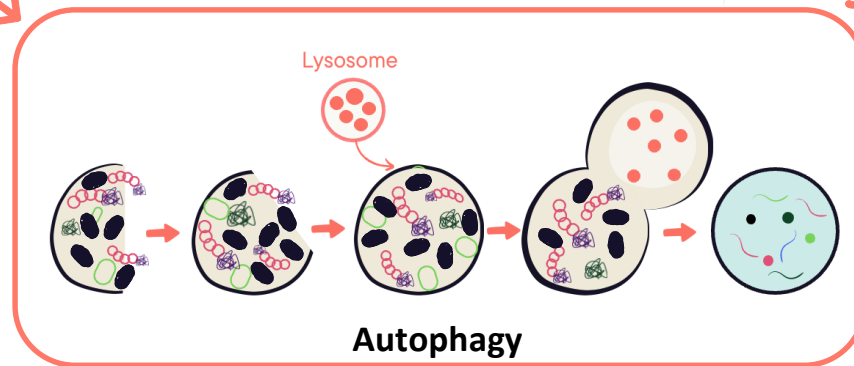
# NUZ-001 Mechanism of Action

## Stressor

- TDP-43
- TDP-43 Aggregation
- Stathmin-2



NUZ-001 and NUZ-001 Sulfone dose-dependent reduced the aggregation of TDP-43 and help restore functional activity in M337V Motor Neurons derived from hiPSCs in co-cultured in response to a stressor



Investigating the effects of NUZ-001 and NUZ-001 Sulfone on autophagic flux and their ability to restore STMN2 loss in M337V Motor Neurons derived from hiPSCs in co-cultured in response to a stressor

# Phase 1 & OLE Study Highlights

No deaths, no Serious Adverse Events related to treatment and a very low incidence of Adverse Events

## Phase 1 Study

- Only 3 Adverse Events (mild in severity) possibly related to treatment
- NUZ-001 and its active metabolite, NUZ-001 Sulfone, detectable in cerebrospinal fluid
- Slows the rate of progression by 58% (Cohort 2 High Dose)
- Marked decreased biomarker NfL CSF levels in 3 patients
- Optimal dose selected for pivotal Phase 2/3 clinical study

## OLE Study

- 8 patients continue on treatment
- Mean time since onset = 40.17 months
- Total drug exposure = 22.3 years
- Progression 0.77 ALFRS-R points per month after 8 months
- Patients want to stay on drug following completion of OLE
- Projected increase in life expectancy >8 months

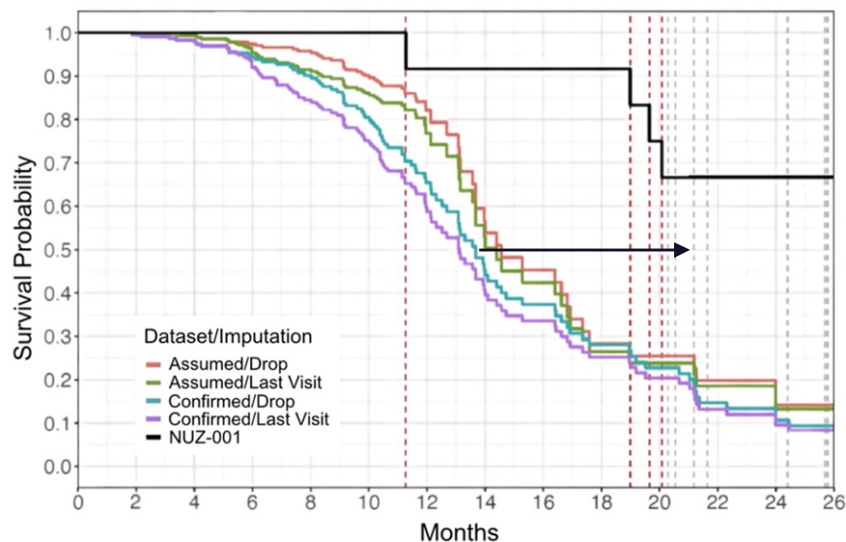


# Phase 1

## ALS Open Label Extension Study

Compared to matched controls from the PRO-ACT Historical Database, treatment with NUZ-001 results in a significantly ( $\chi^2=10.35$ ,  $p=0.00130$ ) longer survival of patients with ALS reducing the risk of death by 76.3%

### Overall Survival Probability



### Approved Drugs Life Expectancy



**Radicava™ (edaravone)**  
The FDA approved Radicava™ in 2017, making it the first new treatment specifically for ALS in 22 years.

Prolongs life ~6 months

List price US\$171,000



**Rilutek (riluzole)**  
This was the first FDA-approved drug available to treat ALS — in 1995. It inhibits glutamate release.

Prolongs life ~3 months

List price US\$5,360

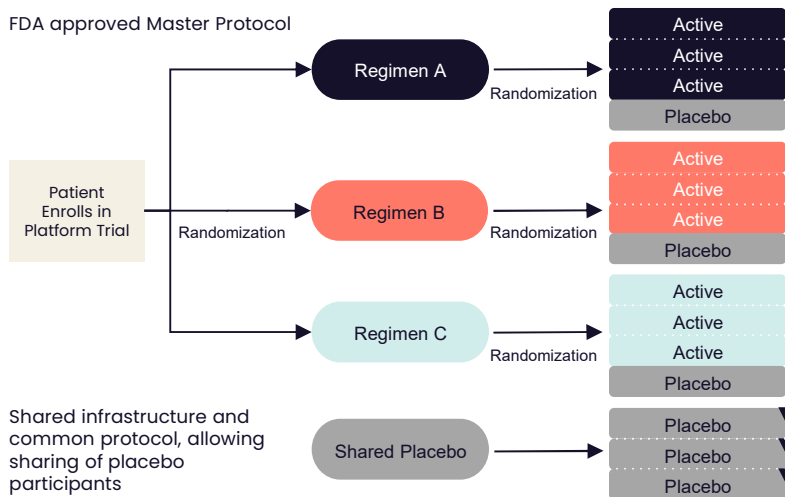




# NUZ-001 selected for entry into the HEALEY ALS Platform Trial

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

- Address FDA's clinical hold concerns
- Finalise regimen-specific protocol amendment (Regimen H)
- File protocol amendment under MGH's Investigator-initiated IND
- Commence recruitment CY 2025

# NUZ-001 Significant Global Opportunity

The Neurodegenerative Disease Market is estimated to be USD 55.12 billion in 2024, and is expected to reach USD 77.82 billion by 2029, growing at a CAGR of 7.14%<sup>1</sup>

## Motor Neurone Disease

ALS, the most common type of MND

- > 268,000 ALS patients globally
- no cure, always fatal

**ALS sales > \$1B globally by 2029<sup>2</sup>**

## Parkinson's Disease

2nd most common neurodegenerative disorder

- > 8.5m PD patients globally
- only symptomatic treatments

**PD sales > \$6B globally by 2029<sup>3</sup>**

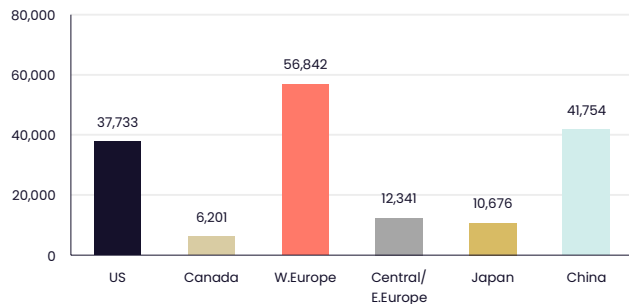
## Dementias

Alzheimer's disease – the most common dementia & neurodegenerative disorder

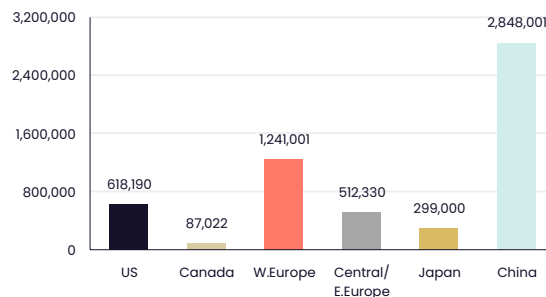
- > 57m dementia patients globally
- very limited treatment options

**AD sales > \$9B globally by 2029<sup>4</sup>**

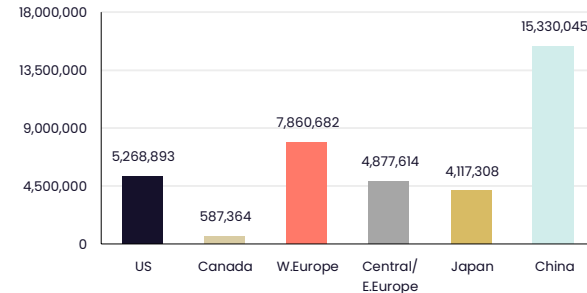
Est. Diagnosed MND Patients by Region<sup>5</sup>



Est. Diagnosed PD Patients by Region<sup>6</sup>



Est. Diagnosed Dementias Patients by Region<sup>7</sup>



# Pre-Clinical Studies



MoA studies are ongoing, employing gold standard *in vitro* models of MND



Based on NUZ-001's activity through mTOR inhibition, we are assessing its efficacy in other neurodegenerative diseases with similar underlying pathophysiology



Our current areas of focus include Alzheimer's Disease (AD), Parkinson's Disease (PD), and Huntington's Disease (HD)

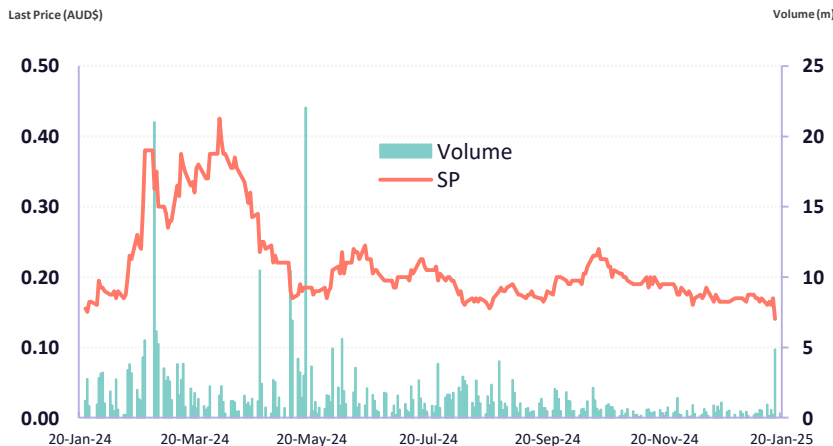


We are employing a suite of *in vitro* models of disease to assess its efficacy

# Corporate Overview

Mid-stage biotechnology company targeting human neurodegenerative diseases

## Share Price Performance



## Board & Management

<b>Mr Sergio Duchini</b>	Chairman & Non-Executive Director
<b>Dr Michael Thurn</b>	Chief Executive Officer & Managing Director
<b>Mr Marcus Hughes</b>	Non-Executive Director
<b>Dr Katie MacFarlane</b>	Non-Executive Director
<b>Mr Stefan Ross</b>	Company Secretary

## Capital Structure (AUD\$)

14 February 2025

Current Share Price (NUZ/NUZOA)	\$0.13 / \$0.050
52 Week Low / High (NUZ)	\$0.115 / \$0.535
No. of Shares (NUZ)	492,305,766
Listed Options (NUZOA)	116,315,955
<b>Market Capitalisation</b>	<b>\$64.00m</b>
Cash (as at 31-Dec-24)	\$14.13 m
Debt (as at 31-Dec-24)	Nil
<b>Net Cash</b>	<b>\$14.13m</b>
<b>Enterprise Value</b>	<b>\$49.87m</b>
Unlisted Options (10c/15c/17.5c/20c/26c/33.25c)	24.08m
<b>Enterprise Value (fully diluted)</b>	<b>\$68.12m</b>

## Top Shareholders\*

Hybrid Holdings Pty Ltd <Darcy Family Super Fund A/C>	4.52%
Mr GJ & Mrs G Van Blommestein <Van Blommestein S/F A/C>	3.76%
Dr Roger Aston	3.06%
Mr Chek Loon Tan	1.97%
Board & Management	4.03%

\* As at 14 February 2025

February 2025

# Patent Portfolio



- 6 patent families
- Portfolio of 62 granted patents with 8 patent applications under examination



- Covers key jurisdictions (United States, Canada, Europe (validated in 11 countries), Australia, New Zealand, Japan, Korea, China, and Hong Kong)



- Broad protection over the method of use of NUZ-001, and related compounds for mTOR pathway-related diseases



- Covers neurodegenerative diseases specifically Amyotrophic Lateral Sclerosis, Alzheimer's Disease, Parkinson's Disease & Huntington's Disease



- Key patent granted in the US (US 9,790,176) for "Compounds For The Treatment of mTOR Pathway Related Diseases".
- Projected expiry for these patents is August 2033.



- Provisional application filed for new process of manufacture of NUZ-001
- **Patent issued by USPTO for US 17,924,537**
- Projected patent expiry 2039

# Upcoming Events and Conferences



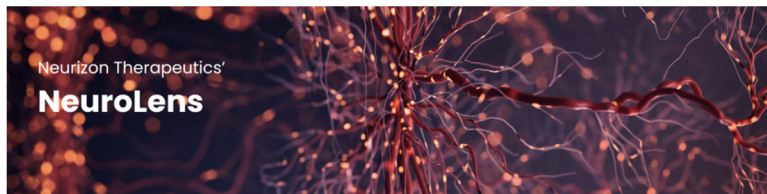
## Events – First half of CY 2025

08 Feb	<b>MND Relay</b>	Melbourne, VIC
19-21 Feb	<b>TRICALS Masterclass</b>	Amsterdam, The Netherlands
20 Feb	<b>Fierce Biotech Webinar w Ncardia – Breaking New Ground in ALS Research</b>	Online
25-27 Feb	<b>Bio-Neuroscience</b>	Amsterdam, The Netherlands
20 Mar	<b>NEALS Clinical Trial Workshop</b>	Boston, MA, USA
1-2 Apr	<b>BioTrinity</b>	London, UK
1-5 Apr	<b>AD/PD - International Conference on Alzheimer's and Parkinson's Diseases</b>	Vienna, AU
5-9 Apr	<b>American Academy of Neurology</b>	San Diego, CA, USA
12-14 May	<b>4<sup>th</sup> ALS Drug Development Summit</b>	Boston, MA, USA
16-19 June	<b>BIO International</b>	Boston, MA, USA

### Register at:

<https://www.fiercepharma.com/premium/webinar/breaking-new-ground-als-research>

# Introducing Quarterly e-newsletter “NeuroLens”



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NeuroLens is our exclusive newsletter, delivering the latest **company milestones, upcoming events, and scientific breakthroughs** in ALS research. Stay informed with **insights from our CEO, key industry updates, and powerful NeuroFacts** that bring us closer to new hope for patients.

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