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

Neurizon Presents Company Update and 2025 Outlook

12 December 2024 – 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 latest developments and 2025 Outlook.

The presentation, titled **"Shaping the Future of Neurodegenerative Diseases: Neurizon's Mid-Year Update & Outlook"** outlines the following:

- The Company's strategy and a clear focus on transforming the horizon of neurodegenerative disease treatments and bringing NUZ-001 to market for the treatment of Amyotrophic Lateral Sclerosis (ALS).
- Deep dive into the latest positive preclinical results for NUZ-001, demonstrating the effectiveness in reducing the aggregation of TDP-43, a key pathological feature of ALS.
- Company's regulatory success and future milestones.
- Preparation and key activities for the participation in Phase 2/3 HEALEY ALS Platform Trial.

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.

-ENDS-

This announcement has been authorized for release by 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 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.

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

Neurizon

Shaping the future of neurodegenerative diseases

Neurizon's Mid-Year Update & Outlook

12 December 2024

ASX: NUZ

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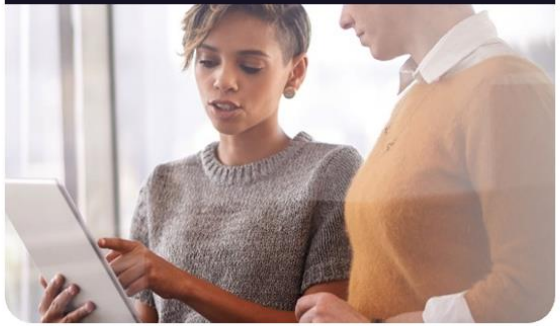
Neurizon Therapeutics' mission is to lead the development of neurodegenerative treatments towards a promising new horizon for patients

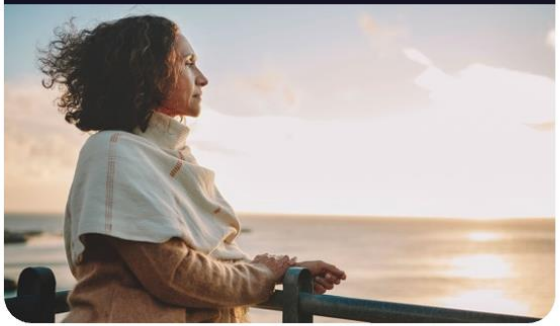
Our success is underpinned by a clear strategic focus on:

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

Long-term safety data
Animal and human safety database accumulating

Positive Phase 1 efficacy data
Animal Efficacy signals

Strong IP Position
Patent protection beyond 2040

Near-term regulatory strategy
Accelerated approval possible across multiple jurisdictions

Additional indications
Pipeline synergies to leverage commercial infrastructure across development programs

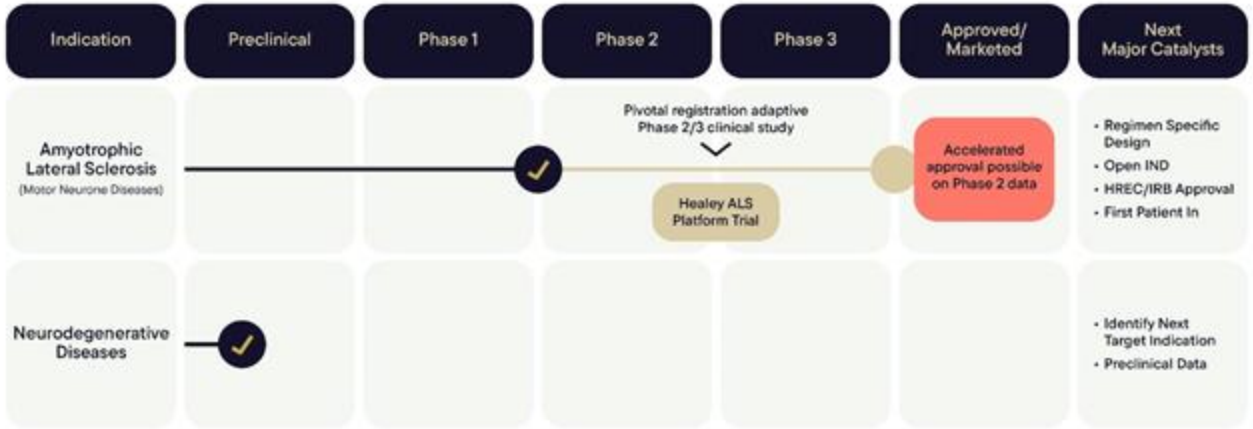
Experienced Management
Experienced world-class Board, SAB and management team

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

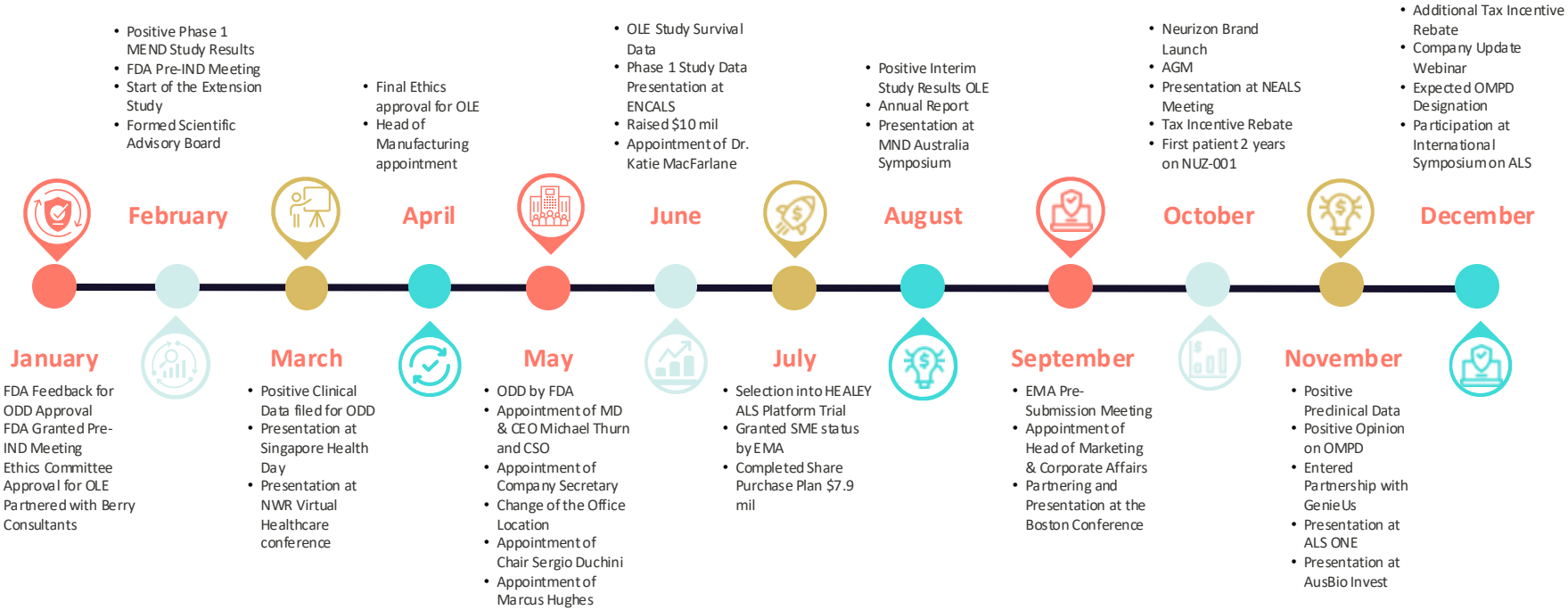
Pipeline

Multiple synergistic product opportunities in neurodegenerative disease

- Single pivotal registration clinical study for ALS
- Targeting accelerated approval from Phase 2 data
- Access to HEALEY ALS Platform Trial reduces study cost and time, and increases patient participation rate



2024 - A Year of Milestones at Neurizon



ALS – Amyotrophic Lateral Sclerosis; EMA – European Medicines Agency; HREC – Human Research Ethics Committee; IND – Investigational New Drug; ODD – Orphan Drug Designation; FDA - Food and Drug Administration, OMPD – Orphan Medicinal Product Designation ; OLE – Open Label Extension; SME – Small and Medium Enterprise.

Meet Our
Board of Directors

Sergio Duchini
Chairman & Non-Executive Director

Sergio serves as a Non-Executive Director and Chair of the Audit Committee at Enlitic Inc. Additionally, he holds the position of Chair at Lymphoma Australia, a leading not-for-profit organization. Sergio previously sat on the AusBiotech Board of Directors for nine years. He also served as a Board Director at Deloitte Australia, overseeing the governance, strategy development, and stewardship of the partnership.

Dr Michael Thurn
Managing Director & Chief Executive

Michael has over 25 years experience in technical, regulatory, commercial and management roles in research organisations and industry, including early stage, fast growing, private and publicly listed biotechnology companies. Michael has led a variety of US IND applications across a range of therapeutic areas and evaluated drugs and vaccines for registration during his engagement at the TGA.

Dr Katie MacFarlane
Non-Executive Director

Katie has over 30 years of experience in the development and commercialisation of pharmaceutical products and devices. She has held senior executive positions at Arkayli Biopharma, Agile Therapeutics, Warner Chilcott, Parke-Davis (now Pfizer). Katie currently serves on the Board of Mayne Pharmaceuticals, an affiliate faculty member of the Purdue University School of Pharmacy and a Founding Member and Advisor to IPhO.

Marcus Hughes
Non-Executive Director

Marcus brings more than 20 years' experience with listed companies. He possesses extensive corporate finance experience, having led project financing and capital raisings in the industrial sector. He has held senior managerial, tax and finance roles with multi-national companies including Lend Lease, Fortescue Metals and Rio Tinto.

Meet Our
Management Team

John Clark
Chief Operating Officer

John has over 20 years of pharmaceutical industry experience in phase I – IV clinical trials across numerous therapeutic areas and multiple geographical regions. John has a thorough knowledge of ICH-GCP and regulatory requirements and held clinical operations leadership roles responsible for implementing global clinical programs.

Dr Nicky Wallis
Chief Scientific Officer

Nicky is a neuroscientist and brings over 12 years of global expertise in clinical development, spanning pre-clinical through to Phase 3 drug and device development. Her extensive experience includes roles such as Clinical Trials Program Specialist at the Australian Clinical Trials Alliance, Vice President of Clinical Operations at Lateral Pharma Biotech, and Clinical Project Manager at Orygen Youth Mental Health Research.

Dr Herbert Brinkman
Head of Manufacturing

Herb has over 30 years of experience in the pharmaceutical industry. He has prepared over 25 Chemistry Manufacturing and Control sections and updates for multiple filings for FDA and EU regulatory agencies. Herb has filed and commercially launched 9 products and contributed to filing 21 ANDAs for various semi-solid and parenteral products. He is also an inventor on 14 patents.

Dr Carol Worth
CMC Operations Manager

Carol brings over 30 years of industry experience and a passion for focusing on quality control and quality assurance. She recently served as Quality Manager at Epichem Pty Ltd as Chief Technical Officer at Suda Pharmaceuticals and Solbec Pharmaceuticals. Carol has also led product development programs at Thermalife International Pty Ltd / Pharmasolv Laboratories Pty Ltd.

Lidija Damjanovic
Head of Marketing and Corporate Affairs

Lidija Damjanovic brings over 15 years of global experience and passion for launching pharmaceutical products and leading corporate communications and affairs in the biotech and pharmaceutical industry. Her extensive leadership experience in driving commercial growth strategies includes marketing and communications roles in companies such as Merck Sharpe and Dohme, Sartorius, Patheon and other global organisations.

Paul Field
Business Development Advisor

Paul brings over 30 years of business development experience across a range of therapeutic areas, including neurodegenerative diseases, and he maintains a deep network in the global biopharmaceutical industry. His experience includes business development roles at Cerecin, Marinova, BioCurate and other companies, and he serves on the Boards of NASDAQ-listed 60 Degrees Pharmaceuticals and Wintermute Biomedical

Meet Our
Scientific Advisory Board

Dr Sabrina Paganoni

Co-Director of the Neurological Clinical Research Institute at the Massachusetts General Hospital, Assistant Professor at Harvard Medical School, and physician investigator at the Sean M. Healey and AMG Center for ALS at Mass General. Dr Paganoni's research focuses on clinical trials and therapy development for ALS. She has served as Principal Investigator of several ALS clinical trials. She is the co-Principal Investigator of the HEALEY ALS Platform Trial, the world's first platform trial for ALS. She has published over 100 peer-reviewed manuscripts and received several awards, including the 2021 Top 10 Clinical Research Achievement Award. She co-chairs the Upper Motor Neuron Task Force, the Technology Committee, and the Recruitment/Retention/Experience Committee at NEALS.

Prof Leonard van den Berg

Professor of Neurology who holds a Chair in Experimental Neurology of motor neuron diseases at the University Medical Center Utrecht in the Netherlands. He also is Director of the centre's Laboratory for Neuromuscular Disease, Director of the Netherlands ALS Center, Chairman of the Neuromuscular Centre the Netherlands, and Chairman of the European Network to Cure ALS (ENCALS), a network of the European ALS Centres. Prof. van den Berg did a fellowship in neuroimmunology at the Neurological Institute at Columbia University in New York and obtained his PhD degree at UMC Utrecht. He has been Professor of Experimental Neurology since 2005 and leads a research group focused on translational research into ALS and other diseases of motor neurons.

Dr Melanie Quintana

Director and Senior Statistical Scientist at Berry Consultants, where she specialises in designing Bayesian adaptive clinical trials across a wide range of therapeutic areas. Her work has included numerous examples in designing platform trials, including the HEALEY ALS Platform Trial and clinical trials in rare and progressive diseases, focusing on developing disease progression models to design better and more powerful clinical trials. Before joining Berry Consultants, Melanie earned her PhD in Statistics from Duke University and pursued a Postdoc in Biostatistics at The University of Southern California.

Dr Christian Freitag

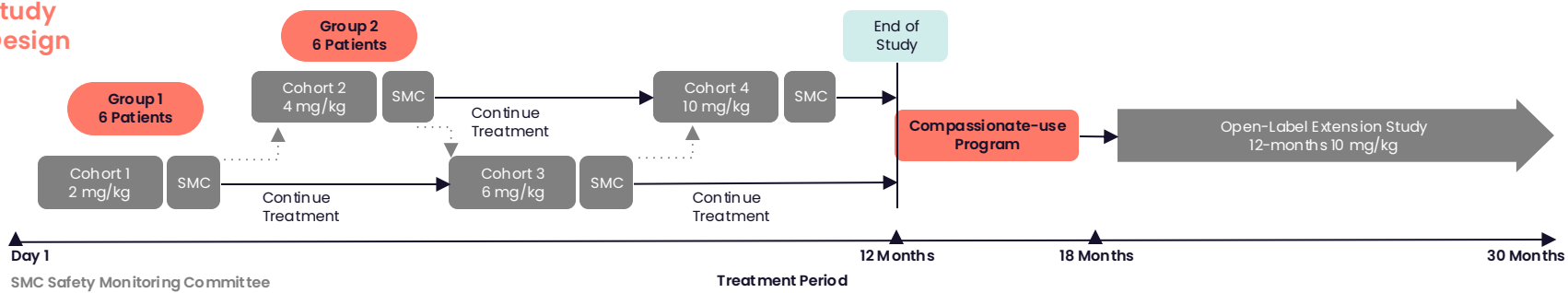
Over 20 years of experience in the pharmaceutical industry with positions in companies including Hoffmann La Roche, Shire, and BTG, where he led global clinical development projects. Dr. Freitag has held the position of Chief Medical Officer at Dynacure and Azafaros, where he was responsible for medical and regulatory strategy, including clinical development of their lead compound in rare diseases. Dr Freitag was the Medical Monitor on Neurizon's Phase 1 MEND study and oversaw medical and clinical activities.

Healey & AMG Center · NEALS · UMC Utrecht · TRICALS · Berry Consultants Statistical Innovation · azafaros · Roche · Shire

Phase 1
ALS MEND Study

The Phase 1 MEND Study was an open label, multicentre study involving 12 patients with ALS with the goal of determining the recommended Phase 2/3 dose based on safety and preliminary efficacy

Study Design



Study Update

- Positive top-line data released in Q1 CY24
- 12 patients continued treatment with NUZ-001 under a compassionate-use program
- 10 patients have rolled-over into 12-month Open-Label Extension Study. Treatment continues to be very well-tolerated
- Updated ALSFRS-R and Survival Analysis to be generated by Berry Consultants.
- First group of 6 patients are entering their 27th month of continuous treatment with NUZ-001
- Phase 1 and baseline OLE data used to design pivotal registration adaptive Phase 2/3 Study, to commence in H2 CY24

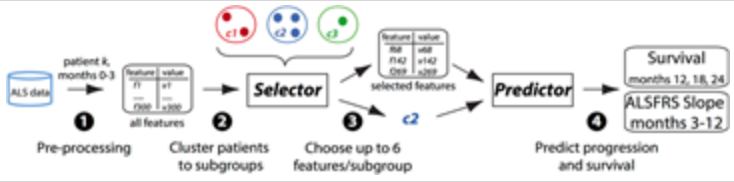
Phase 1
ALS Open Label Extension Study

Compared to matched controls from the PRO-ACT Historical Database, treatment with NUZ-001 results in a significantly (X^2=10.35, p=0.00130) longer survival of patients with ALS

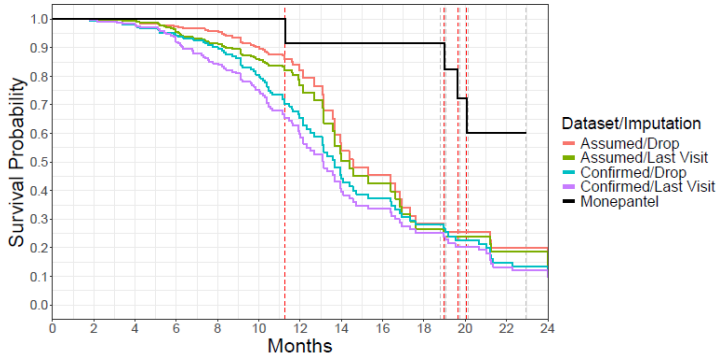
Berry Consultants Statistical Analysis

- Berry's analysis involved comparing patients in the PRO-ACT database with similar characteristics to those in Neurizon's Phase 1 MEND Study adjusting for differing diagnosis durations
- Hazard ratio of 0.237 (95% CI: (0.083,0.674), p = 0.007) indicating that treatment with NUZ-001 reduces the risk of death by 76.3%

Analysis Method		Log-Rank Test		Cox Proportional Hazards Model		
Dataset	Death Time Imputation	χ^2	p-value	Hazard Ratio	95% CI	p-value
Assumed	Leave out	10.35	0.00130	0.237	(0.083, 0.674)	0.007
Survival	Last Visit	11.47	0.00071	0.226	(0.080, 0.638)	0.005
Confirmed	Leave out	14.87	0.00012	0.210	(0.077, 0.576)	0.0024
Survival	Last Visit	16.77	0.00004	0.196	(0.072, 0.537)	0.0015



Overall Survival Probability



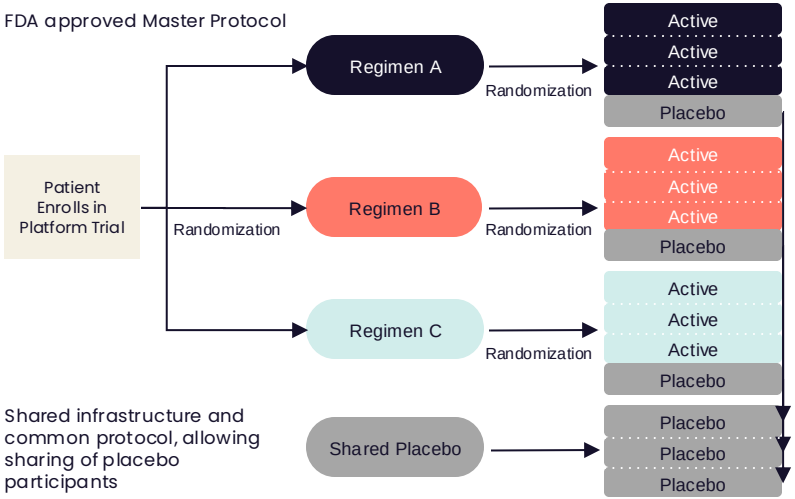
The PRO-ACT database is the largest publicly available repository of merged ALS clinical study data. Data were pooled from 16 completed Phase 2/3 ALS clinical studies and one observational study. Over 8 million de-identified longitudinally collected data points from more than 8,600 persons with ALS, including demographics, family histories, and longitudinal clinical and laboratory data.

[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.

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[1]



Innovative Trial Structure

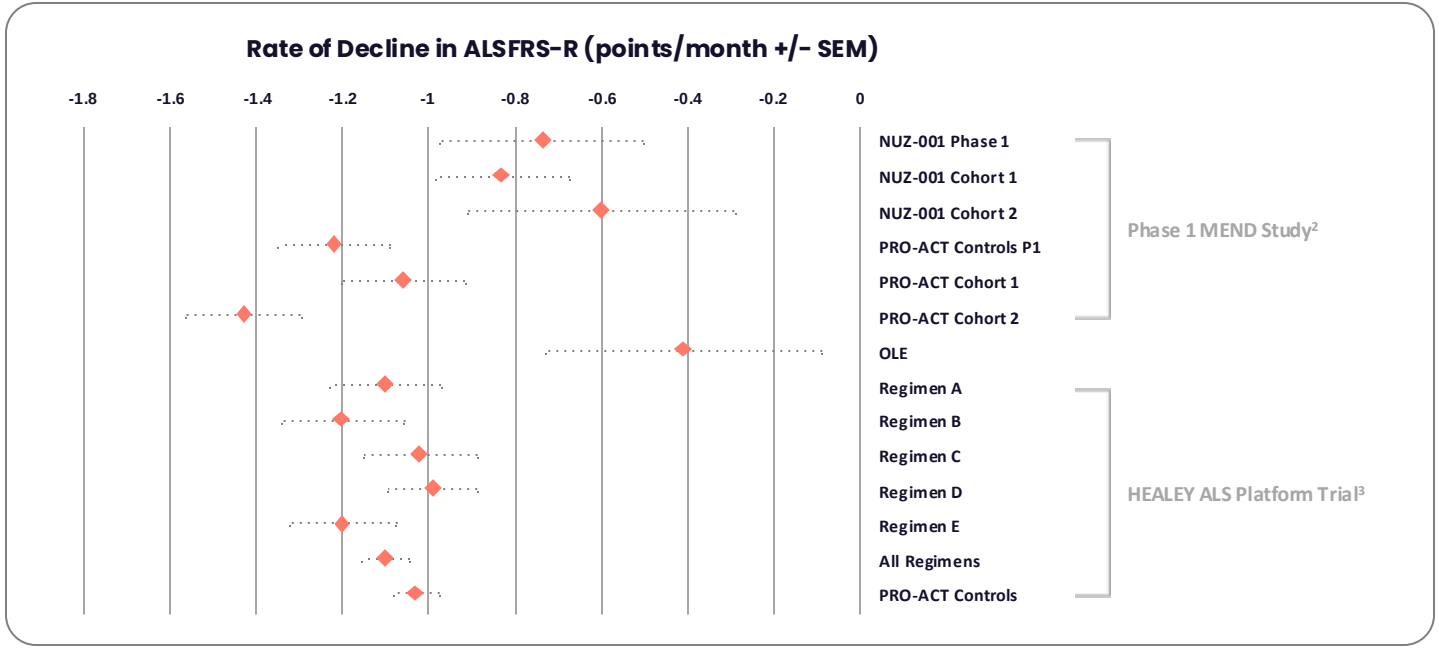
Design
- Shared master protocol
- >70 clinical sites across the US
- 3:1 active drug to placebo ratio
- 160-240 participants per regimen
- 5 regimens completed
- 2 regimens enrolment closed

Next Steps
- Study design phase to create a regimen-specific protocol amendment completed
- File US IND for NUZ-001 – December 2024
- File protocol amendment under MGH's IND – January 2025
- Neurizon to supply NUZ-001 – February 2025
- Commence recruitment Q1 CY 2024

1. HEALEY ALS Platform Trial (https://www.massgeneral.org/neurology/als/research/platform-trial).

Comparisons of ALSFRS-R Rates of Declines Across Studies

Favourable comparisons to the completed regimens in the HEALEY ALS Platform Trial and PRO-ACT Database[1]



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. PharmAust Data on file.
3. Melanie Quintana, Eric Macklin*, Lori Chibnik, Joseph Marion, Anna McGlothlin, Michelle Detry, Matteo Vestrucci, Giorgio Paulon, Jeremy Shefner, Jinsy Andrews, James D. Berry, Marianne Chase, Hong Yu, Alexander Sherman, Sabrina Paganoni, Merit Cudkowicz, for the HEALEY ALS Platform Trial Study Group. Statistical Innovation and Complexities in the HEALEY ALS Platform Trial: Lessons Learned From the First Set of Regimens. Poster Presentation. ENCALS meeting 2024 Stockholm, Sweden June 17-20 2024.

Pre-Clinical Studies

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

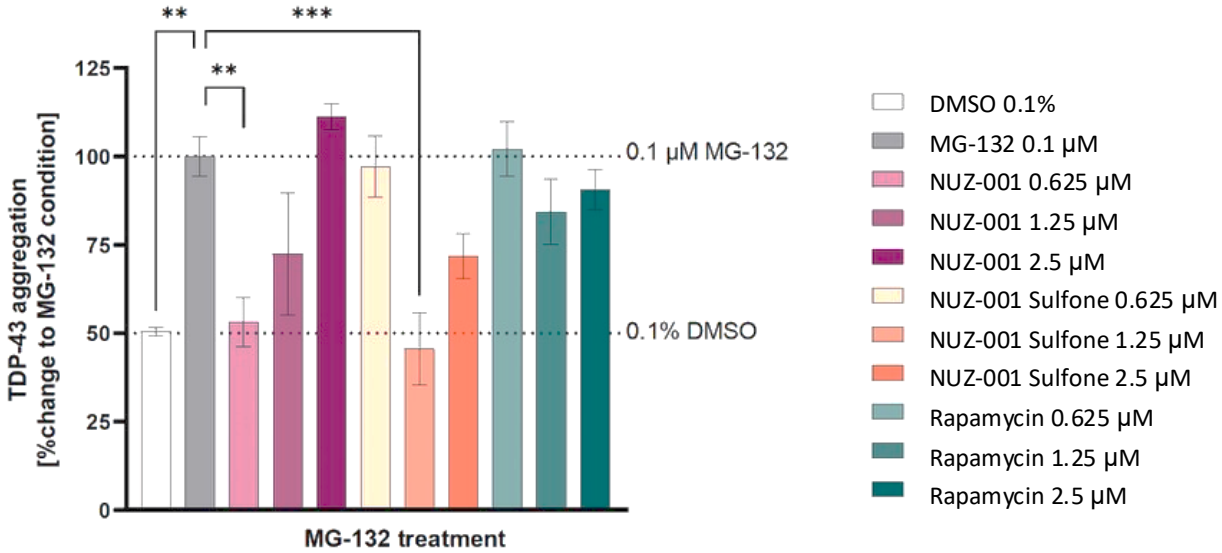
Based on NUZ-001's activity through mTOR inhibition, we are assessing its efficacy in other neurodegenerative diseases with similar underlying pathophysiology

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

Pre-Clinical Data

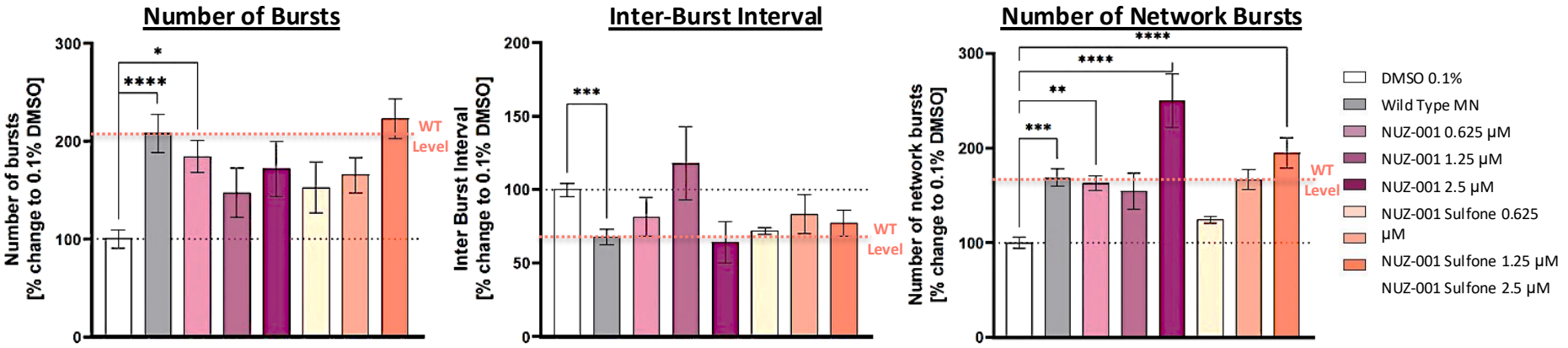
HTRF TDP-43 Aggregation Assay



Dose-dependent effect of treatment was observed on TDP-43 aggregate reduction for:

- **NUZ-001 at 0.625 µM (statistically significant; ~ 50% reduction) and 1.25 µM (~25% reduction)**
- **NUZ-001 Sulfone at 1.25 µM (statistically significant; ~ 55% reduction) and 2.5 µM (~ 25% reduction)**
- **Rapamycin at 3 µM (20% reduction)**

Pre-Clinical Data
Multi-electrode Assay Activity



NUZ-001 and NUZ-001 Sulfone significantly improved the ALS TDP-43 M337V associated phenotype/MEA activity by increasing bursting (NUZ-001 0.625 µM p=<0.05), decreasing inter-burst interval, and increasing network burst activity (NUZ-001 0.625 µM p=<0.005; NUZ-001 2.5 µM p=<0.00005 and NUZ-001 Sulfone 2.5 µM p=<0.00005) at day 18 (corresponding to 4 days of treatment with compound).

Strategic Partnerships
Realising Our Potential

Phase 1

ferrer

US$122 Million ex-US License

VERGE genomics

March 2024

Preclinical

Lilly

US$612 Million License

QurAlis

June 2024

Phase 1

NOVARTIS

US$3 Billion License

PTC THERAPEUTICS

December 2024

Preclinical

Mitsubishi Tanabe Pharma

US$480 Million License

DEWPOINT THERAPEUTICS

December 2024

Chemistry, Manufacturing and Control

Manufacturing partners

- API - Syngene International
- Drug Product - Catalent Pharma Solutions,

Both global leaders in the manufacture and commercial supply of pharmaceutical products.

Syngene is tasked with producing 60 kgs of GMP NUZ-001, which includes an engineering batch of 15 kg and three process validation batches of 15 kg each. These batches are intended to validate the GMP manufacturing process, aid in product registration, and prepare Neurizon for commercial supply.

Syngene
Putting Science to Work

Catalent Pharma Solutions will handle the GMP production of three registration batches, amounting to over 500,000 tablets. These batches will support product registration and facilitate commercial scale-up activities. The manufactured product will be utilized in the forthcoming adaptive Phase 2/3 trial.

Catalent

Current Inventory

- ~100,000 Placebo Tablets
- ~80,000 NUZ-001 Tablets

NUZ-001 Liquid Formulation

- Development of oral liquid formulation of NUZ-001 is in progress
- New formulation development initiated to address administration challenges encountered by subjects that develop swallowing difficulties with late-stage ALS

- New formulation planned to be incorporated into an amended Phase 1 Open Label Extension Study or a Stand-alone PK comparison study in CY25

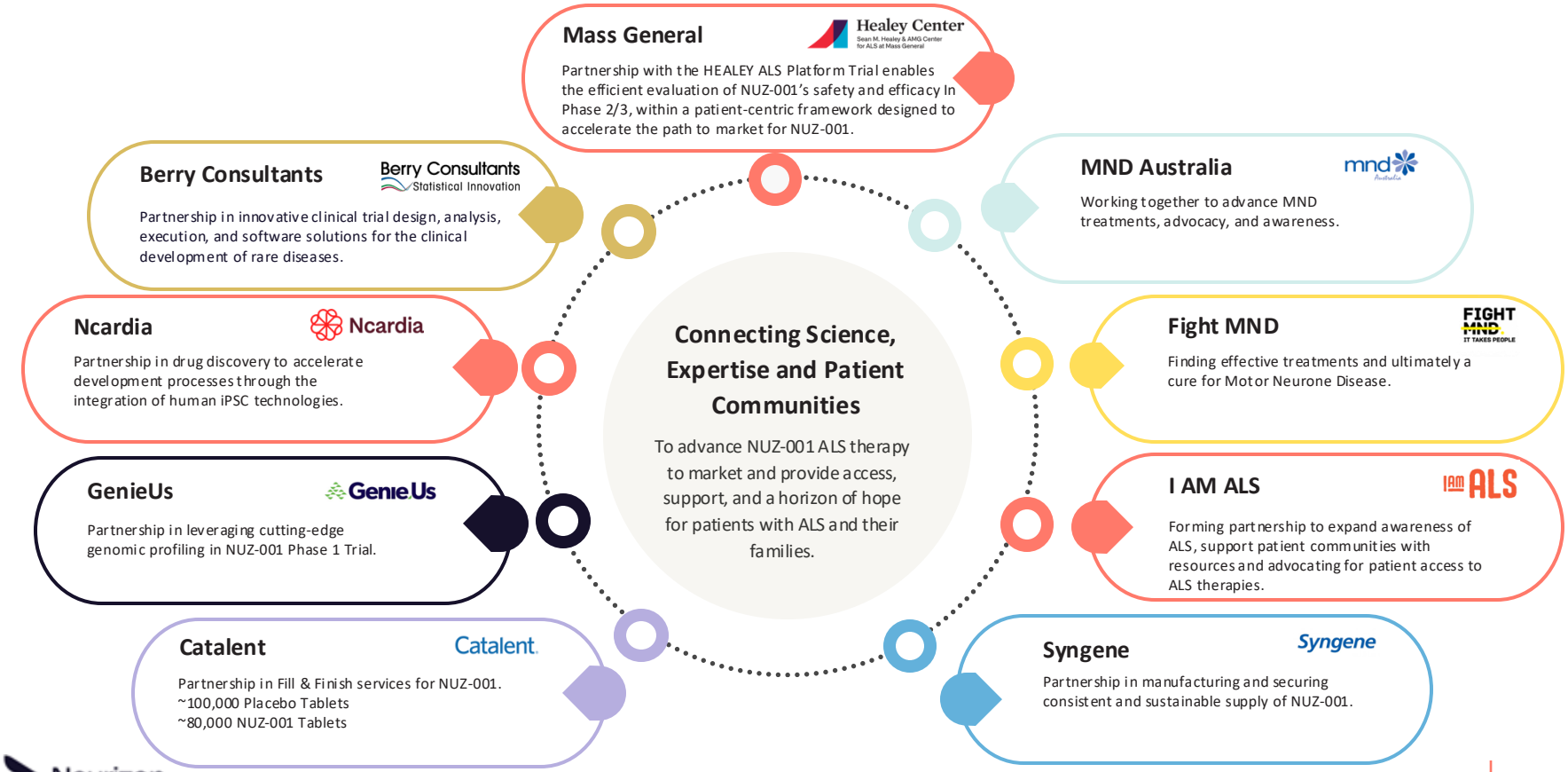
NUZ-001 Regulatory Milestones

- ✓ Pre-IND Meeting
- ✓ Orphan Drug Designation (7 years market exclusivity)
- • IND Submission
- • Fast Track Designation

- ✓ Pre-Submission Meeting
- ✓ Positive Opinion OMPD
- ✓ Formal OMPD Grant (10 years market exclusivity)
- • Scientific Advice

- ✓ Pre-submission Meeting
- • ODD
- • Provisional Determination
- • Provision Approval

Strategic Partnerships & Community Engagement



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
- Notice of Allowance issued by USPTO for US 17,924,537
- Projected patent expiry 2041

Research and Development
Timeline

Derisked lead program in Amyotrophic Lateral Sclerosis (ALS) with multiple near-term catalysts and potential for use in other neurodegenerative diseases

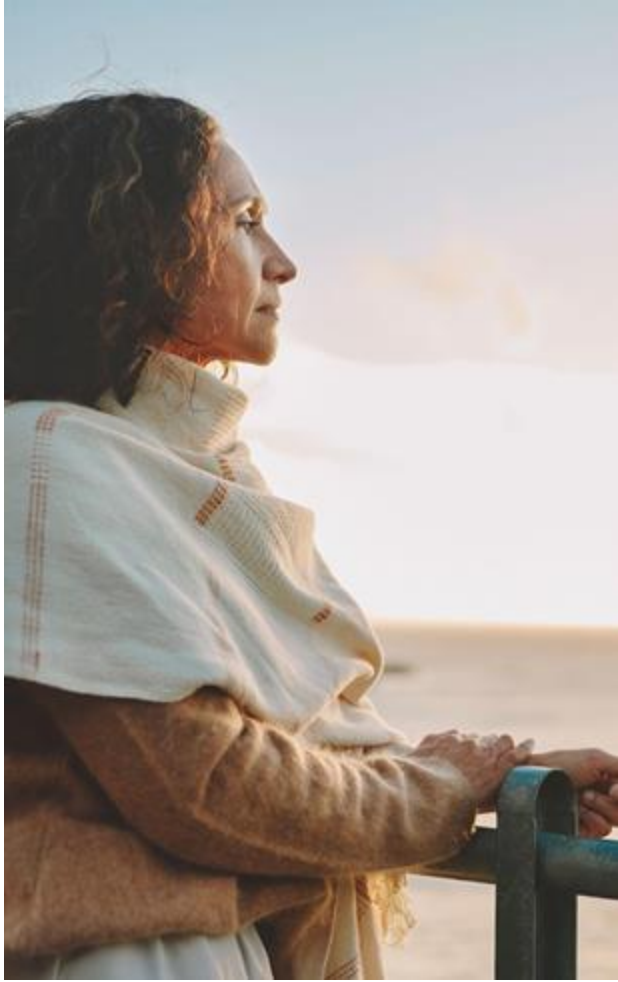
Timeline

H2 CY2024

- OMPD Designation
- OLE Update
- IND Submission

H1 CY2025

- OPEN IND
- HEALEY Protocol Amendment
- Preclinical models update
- Fast track Designation
- CMC Validation Batches
- Enrolment commences HEALEY
- OLE Top-line Results



ALS – Amyotrophic Lateral Sclerosis;; EMA – European Medicines Agency; HREC – Human Research Ethics Committee; IND – Investigational New Drug; OMPD – Orphan Medicinal Product Designation ; OLE – Open Label Extension; SME – Small and Medium Enterprise.

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