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HEALEY ALS Platform Trial Preparation Shows Positive Respiratory Outcome of NUZ-001

Highlights:

- **Updates to HEALEY ALS Platform Trial Master Protocol have been made to enhance the potential of establishing a clinically meaningful outcome for patients, including;**
  - **Treatment period extended from 24 to 36 weeks to allow longer evaluation of treatment effects**
  - **Inclusion Criteria modified for time since symptom onset from 36 to 24 months to enrich the study population for fast progressors**
  - **peripheral blood mononuclear cell (PBMC) collection has been added to aid future research and therapy development**
- **New PRO-ACT data analysis undertaken by Berry Consultants confirms Slow Vital Capacity (SVC), a measure of respiratory function, as a key secondary endpoint for NUZ-001**
- **Compared to untreated matched controls, treatment with NUZ-001 resulted in a 48% slowing in the loss of respiratory function for all 12 patients in the Phase 1 MEND Study**
- **Neurizon to finalise its Regimen Specific Appendix (RSA) under the Master Protocol for submission to the FDA as soon as the clinical hold on NUZ-001 has been lifted**
- **Neurizon remains well placed for trial entry in H2 CY2025**

24 March 2025 – Melbourne, Australia: Neurizon Therapeutics Limited (ASX: NUZ & NUZOA) ("Neurizon" or "the Company"), a clinical-stage biotech company dedicated to advancing treatments for neurodegenerative diseases, is pleased to provide the following update on preparations for entry into the HEALEY ALS Platform Trial, along with encouraging new data showing that NUZ-001 slows the decline in slow vital capacity (SVC), a key respiratory function and survival metric in Amyotrophic Lateral Sclerosis (ALS).

Updates to HEALEY ALS Platform Trial Master Protocol:

The HEALEY ALS Platform Trial is the first of its kind clinical trial for ALS. The trial is a multicenter, double-blind, placebo-controlled, perpetual and adaptive study evaluating the safety and efficacy of multiple investigational products for ALS treatment. As previously advised, Neurizon expects entry into the trial in H2 CY2025 and advises of the following changes to the Master Protocol from the Healey & AMG Center.

The platform trial features a perpetual and adaptive design facilitating integration of new information from experience, data analysis, and participant feedback. Initial regimens tested in the trial have subsequently undergone thorough testing and analysis by a suite of project experts including lead medical investigators, biostatisticians, the United States (US) Food and Drug Administration (FDA) and industry partners.

Following the latest round of testing, updates to the Master Protocol have been included to enhance and optimise future learning within the trial based on data collected from the first 5 regimens. The changes include:

- The Randomized Controlled Trial (RCT) period has been extended from 24 to 36 weeks to allow for a longer evaluation of treatment effects and increase the power to detect positive treatment outcomes, especially for therapies that take longer to show effects
- The Inclusion Criteria for the trial have also been modified, setting the time since symptom onset from 36 to 24 months to enrich the study population for fast progressors
- Peripheral blood mononuclear cell (PBMC) collection has been added to be banked for future generation of induced pluripotent stem cells (iPSCs), aiding research and therapy development

- In addition, patient-centric aspects of the trial have been refined, with a more streamlined and flexible visit schedule.

In connection with efforts to improve the patient experience, increased opportunities for remote visits are now available in the Active Treatment Extension (ATE) program.

The Company believes that these changes further reduce the risks associated with NUZ-001's clinical development program and enhance the potential to establish a clinically meaningful outcome for patients with ALS. These modifications allow Neurizon to finalise its Regimen Specific Appendix (RSA) under the Master Protocol for submission to the FDA as soon as the clinical hold on NUZ-001 has been lifted. Further information on the RSA for NUZ-001 will be provided following FDA acceptance in H2 CY2025.

New data analysis confirms SVC as a key secondary endpoint for NUZ-001:

As part of finalising the RSA for NUZ-001's new data analysis of SVC results captured from the completed Phase 1 MEND study last year, the Company has confirmed the selection of SVC as a key secondary endpoint in the HEALEY ALS Platform Trial.

SVC is a pulmonary function test that measures the maximum volume of air a person can exhale slowly after a full inhalation. It is a key respiratory function metric in ALS because respiratory muscle weakness is a major cause of morbidity and mortality in patients with ALS. Research has shown a strong correlation in the rate of decline between percent predicted SVC and ALSFRS-R scores.

To aid confirmation of secondary endpoints for the HEALEY ALS Platform Trial, a comparative analysis was performed by Berry Consultants against 35 matched controls from the Pooled Resource Open-Access ALS Clinical Trials (PRO-ACT) database for SVC decline against the 12 patients treated with NUZ-001 in the Phase 1 MEND Study.

The estimated rate of decline for all 12 patients treated with NUZ-001 was -1.51 VC percent predicted (PP) points per month compared to -2.93 VC PP points per month (difference 1.42; p=0.058) for untreated matched controls (see Figure 1). This new data represents a 48% slowing in VC PP decline for patients treated with NUZ-001 and correlates closely with the 39% slowing in the ALS Functional Rating Scale-Revised (ALSFRS-R) rate of decline seen in these patients compared to untreated matched controls as announced on February 27th 2024.

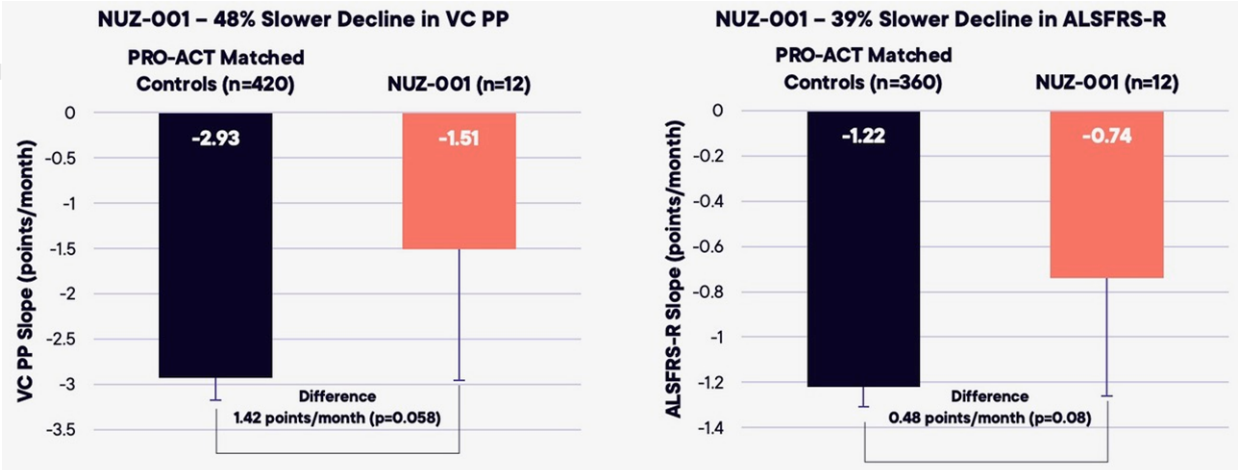

Figure 1: The difference in the rate of decline (mean +/- 95% CI) for respiration (VC PP) and fine and gross motor function (ALSFRS-R) between untreated matched controls in the PRO-ACT database and patients treated with NUZ-001.

SVC has been selected as a key secondary endpoint for the trial, alongside the targeted primary endpoint of overall function (ALSFRS-R) and survival in the patient population.

The PRO-ACT database is one of the largest repositories of clinical trial data for ALS. It is often considered for use as an external control arm in clinical trials. Over 8 million de-identified longitudinally collected data points from more than 8,600 persons with ALS were standardised across studies and merged to create the PRO-ACT database.

This database includes demographics, family histories, and longitudinal clinical and laboratory data. Matching is a procedure that finds treatment and control subjects with similar baseline characteristics to enable treatment effect estimation. In this case patients were matched based on ALSFRS pre-baseline slope, onset location, baseline ALSFRS, time since onset and baseline VC PP.

Managing Director and Chief Executive Officer, Dr Michael Thurn commented: "Following a comprehensive review of the data from the first 5 completed regimens, HEALEY has implemented improvements to the HEALEY Master Protocol to maximise the potential for a positive outcome. We were excited to learn about the strong correlation between reducing the respiratory function decline rate in patients treated with NUZ-001 and overall functional decline as measured by ALSFRS-R. Having supporting positive secondary endpoints greatly increases the likelihood of receiving accelerated approval.

"Over the coming months, the Company will continue to work towards finalising participation in the HEALEY trial, with entry expected during H2 CY2025, which will include completing the two short-term pharmacokinetic studies required to lift the FDA's clinical hold."

-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.

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