Neurizon Therapeutics Limited
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Positive 8-month Interim Data from Open-Label Extension Study in Patients with ALS

Highlights:

- Treatment with NUZ-001 remains well-tolerated, demonstrating encouraging results in slowing disease progression and increasing the life expectancy of patients with ALS
- Key findings compared to untreated matched controls from the PRO-ACT Historical Database were:
  - NUZ-001 significantly increased survival ($\chi 2=11.67$, p=0.00062)
  - NUZ-001 significantly reduced the risk of death by 78.1% (HR=0.219, p=0.0044)
- The mean rate of reduction in disease progression measured by ALSFRS-R from baseline was -0.77 points/month
- Patients are now in their 27th month of continuous treatment with NUZ-001
- There have been no serious adverse events related to treatment with NUZ-001

16 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 provide an interim 8-month update on its ongoing 12-month Open-Label Extension (OLE) study in patients with ALS. The latest results confirm NUZ-001's long-term safety and tolerability, and potential to extend the life of patients with ALS significantly. Treatment continues to be well-tolerated at the recommended 10 mg/kg daily dose, the same dose planned for the upcoming Phase 2/3 HEALEY ALS Platform Trial.

Neurizon Therapeutics CEO & MD Dr. Michael Thurn commented: "The latest data from the OLE study reinforces our commitment to delivering hope for patients with ALS. These findings further highlight the potential of NUZ-001 to positively impact the lives of patients by slowing disease progression and improving their overall survival. They provide further validation of our dose selection and energise our preparations for the HEALEY ALS Platform Trial. We are within days of filing our Investigational New Drug (IND) application with the United States Food and Drug Administration (FDA), which will be an incredible accomplishment for the company and paves the way for the initiation of recruitment in the HEALEY ALS Platform Trial in H1 CY2025. We are proud of the progress made and remain focused on unlocking new possibilities for ALS treatment."

Updated Survival Analysis

Neurizon's statistical partners Berry Consultants have updated the survival probability analysis to quantify the survival benefit of treatment with NUZ-001 compared to untreated matched controls from the PRO-ACT historical control database[1]. As of 13 December 2024, patients have been treated with NUZ-001 for varying durations, ranging from 11.3 to 26.3 months (median of 20.9 months) and at varying dose levels (2 to 10 mg/kg/day). Using disease onset location, pre-baseline ALSFRS-R slope, baseline ALSFRS-R score, and time since disease onset, Berry Consultants matched untreated PRO-ACT controls to each NUZ-001 treatment patient.

Calculated Kaplan-Meier curves displayed below in Figure 1 illustrate the differences in estimated survival probability across 4 different analysis datasets from least (overestimates survival) to most conservative (underestimates survival). Regardless of the dataset used to analyse for a difference in the survival pattern, treatment with NUZ-001 significantly prolonged the survival when compared to untreated matched controls from the PRO-ACT database. The extension in life expectancy was highly statistically significant for each dataset tested (See Table 1). For the most conservative analysis dataset, the $\chi 2$ test statistic was 11.67 with a p value of 0.00062. Under the companion analysis, the Cox proportional hazards model, the estimated hazard ratio was 0.219 (95% CI: (0.077, 0.623), p = 0.0044), indicating that treatment with NUZ-001 significantly reduced the risk of death by 78.1%.

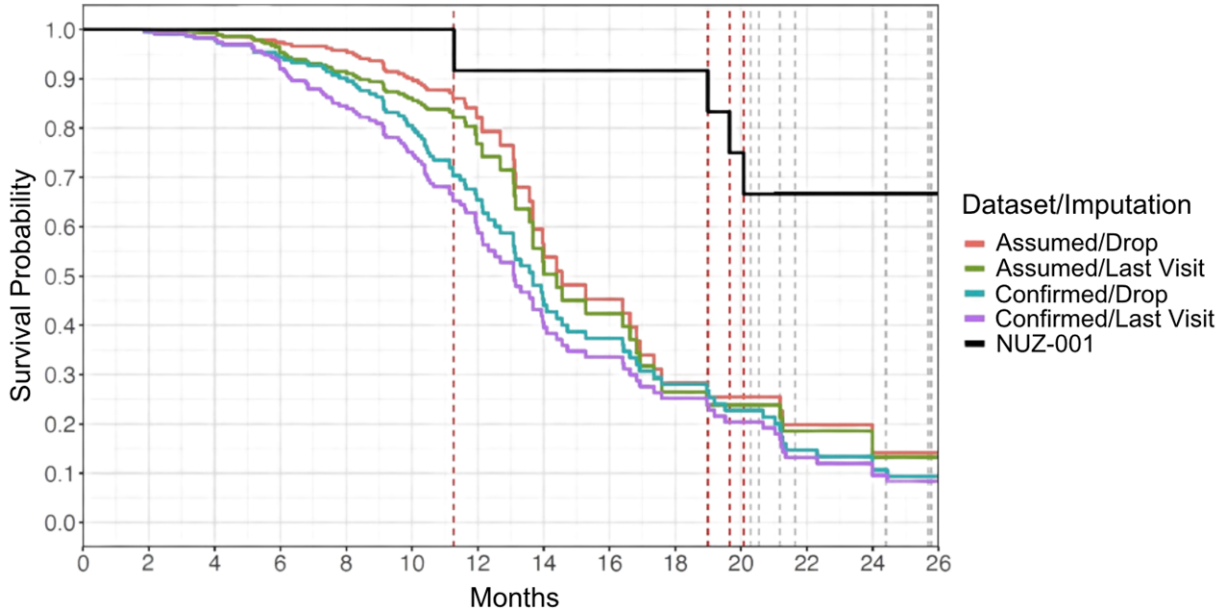

Figure 1: Calculated Kaplan-Meier curves for each of the untreated matched-control PRO-ACT datasets described in Table 1 as well as the NUZ-001 treatment group. Here "Assumed" Dataset assumes that missing death status indicates living status, while "Confirmed" only uses data with non-missing death status. The imputation method "Drop" means that it excludes missing times of death for confirmed dead subjects, while "Last Visit" uses the last visit time as the time of death. Vertical dashed lines represent the exposure time for all patients.

Table 1: Estimated Survival Probability by Analysis Dataset

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**	**11.7**	**0.00062**	**0.219**	**(0.077,0.623)**	**0.0044**
Survival	**Last Visit**	**12.86**	**0.00034**	**0.209**	**(0.074,0.592)**	**0.0032**
Confirmed	**Leave out**	**16.94**	**0.00004**	**0.192**	**(0.07,0.528)**	**0.0014**
Survival	**Last Visit**	**18.89**	**0.00001**	**0.181**	**(0.066,0.495)**	**0.0009**

ALSFRS-R Scores after 8-months in OLE Study

Disease progression in the OLE study is being tracked by assessing each patient's ALSFRS-R score bimonthly. The mean rate of decline over the 8 months for the 9 patients treated daily with 10 mg/kg of NUZ-001 was -0.77 ALSFRS-R points/month. This rate of decline compares favourably with the placebo control groups from the first 5 regimens (A to E) for the HEALEY ALS Platform Trial that had a mean rate of decline of -1.10 ALSFRS-R points/month[2].

About the OLE Study

The OLE study investigates the long-term safety, tolerability, and efficacy of NUZ-001 in ALS patients who completed the Phase 1 MEND Study. Eligible patients receive a daily dose of 10 mg/kg body weight of NUZ-001 for 12 months. The study is conducted at two clinical sites in Australia: Calvary Health Care Bethlehem, led by Associate Professor Susan Mathers, and Macquarie University, led by Professor Dominic Rowe. The study is registered on ClinicalTrials.gov (https://clinicaltrials.gov/study/NCT06177431).

As of this update, 8 of the original 12 patients from the Phase 1 MEND Study continue to receive treatment with NUZ-001 in the OLE study. Since the last interim update, 1 additional patient has died due to respiratory

failure. For this cohort of patients, the mean time since the onset of the disease was 40.3 months (median 40.4), and the total accumulative exposure to NUZ-001 was 15.5 years.

Next Steps

Neurizon Therapeutics is progressing toward the initiation of the HEALEY ALS Platform Trial, expected to commence in early H1 CY2025. These efforts reflect our commitment to ensuring a seamless transition into this critical Phase 2/3 study, providing confidence in our ability to deliver impactful results for the ALS community.

-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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[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]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.