Neurizon Therapeutics Limited
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NUZ-001 promotes survival in mouse NSC-34 motor neuron TDP-43 challenge model

Highlights:

- **Independent study completed in collaboration with The University of Queensland to explore NUZ-001's effect on survival and autophagy in NSC-34 motor neuron cell line**
- **NUZ-001 had a small but significant survival effect on TDP-43-mediated cell death following acute treatment for only 24 hours**
- **The survival effect was independent of the activation of autophagy, suggesting that an additional pharmacological process may be at play**
- **Future studies will evaluate the effects of NUZ-001 following chronic treatment to further elucidate the biological mechanism(s) of action**
- **Findings to be presented at the AD/PD 2025 Advances in Sciences & Therapy conference in Vienna, by University of Queensland representative, Mr Austin Read**
- **Highlights second presentation of NUZ-001's potential benefits at AD/PD conference into a range of specific indications**

4 April 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 announce results from an additional independent study carried out in partnership with Professor Trent Woodruff and Dr John Lee's research group at The University of Queensland ("UQ"). Mr Austin Read will present a poster entitled "Investigating the Pharmacological Activity of NUZ-001 on Autophagy in the NSC-34 Motor Neuron Cell Line" at the AD/PD 2025 Advances in Sciences & Therapy conference on 4-5 April (local time). AD/PD is the leading international conference on Alzheimer's and Parkinson's diseases and related neurological disorders held in Vienna, Austria between 1 and 5 April.

The aim of the study was to investigate the acute effects of NUZ-001 on the survival of mouse NSC-34 motor neurons following exposure to TDP-43 aggregates and link any changes in viability to enhanced autophagy. Autophagy is a critical process for maintaining neural homeostasis, which is increasingly recognised as a key therapeutic target in neurodegenerative diseases, including Amyotrophic Lateral Sclerosis (ALS). Mouse NSC-34 motor neuron cells are a lab-grown model of motor neurons used to study ALS. The aggregation of TDP-43 is the key underlying pathological feature in 97% of ALS cases.

UQ researchers treated NSC-34 cells with various concentrations of NUZ-001 (1 µM, 10 µM and 50 µM) and compared it to Rapamycin, a known autophagy activator over a 24-hour period. Key markers of autophagy activation, LC3-II and Beclin-1 were then analysed using immunoblotting techniques, while cell viability assays were performed to further determine if NUZ-001 promoted survival.

Preliminary data suggest that NUZ-001 had a small but significant effect on TDP-43-mediated cell death in the mouse MSC-34 motor neuron cell line. Despite enhancing survival, acute treatment with NUZ-001 showed no effect on autophagy markers, suggesting that an additional pharmacological process may be at play. These data also suggest that the neuroprotective effects of NUZ-001 may require repeated exposure providing further insight into its overall biological effects. Future studies will evaluate the effects of NUZ-001 under specific treatment conditions to further elucidate the biological mechanism of action.

A copy of results poster being presented by Mr Austin Read is attached to this ASX release for further reference.

Managing Director and Chief Executive Officer Dr. Michael Thurn commented: "The presentation in collaboration with UQ represents the second set of independent results presented at AD/PD, highlighting the potential benefits of NUZ-001 across a range of indications (refer to ASX announcement: 1 April 2025). These presentations are expected to provide Neurizon with increased international visibility and robust additional data to support ongoing partnering discussions and the clinical development pathway for NUZ-001.

We are indebted to Dr Lee's team for performing and assembling the data in time for the conference, considering the challenges posed by the recent tropical cyclone threat in Queensland. We look forward to our continued collaboration and await with excitement the near-term readouts from the mouse model of Parkinson's disease."

UQ's Dr John Lee commented: "We are pleased to collaborate with Neurizon Therapeutics in exploring the pharmacological activity of NUZ-001 in neurodegenerative disease models. Understanding the cellular mechanisms at play in TDP-43 mediated pathology is critical for advancing potential therapeutic approaches. We look forward to continuing our research to further investigate the biological effects of NUZ-001 and its implications for ALS."

Studies were designed to look at the acute effects of NUZ-001 on TDP-43 mediated cell death and activation of autophagy markers.

-ENDS-

This announcement has been authorized for release by the Board of Neurizon Therapeutics Limited.
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Our partners range from startups and small businesses to governments and global companies. Our world-class researchers work with partners to understand their challenges and find creative solutions that deliver impact. UQ has more highly cited researchers than any other Australian university.

The University currently has more than 3,400 active research projects, with many seeking to address the national and global challenges of climate change and energy transition, food and water security, biodiversity conservation, defence and space, minerals and resources, and disease prevention and treatment.

Discover more about partnering with UQ: research.uq.edu.au/partner

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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Investigating the Pharmacological Activity of NUZ-001 on Autophagy in the NSC-34 Motor Neuron Cell Line

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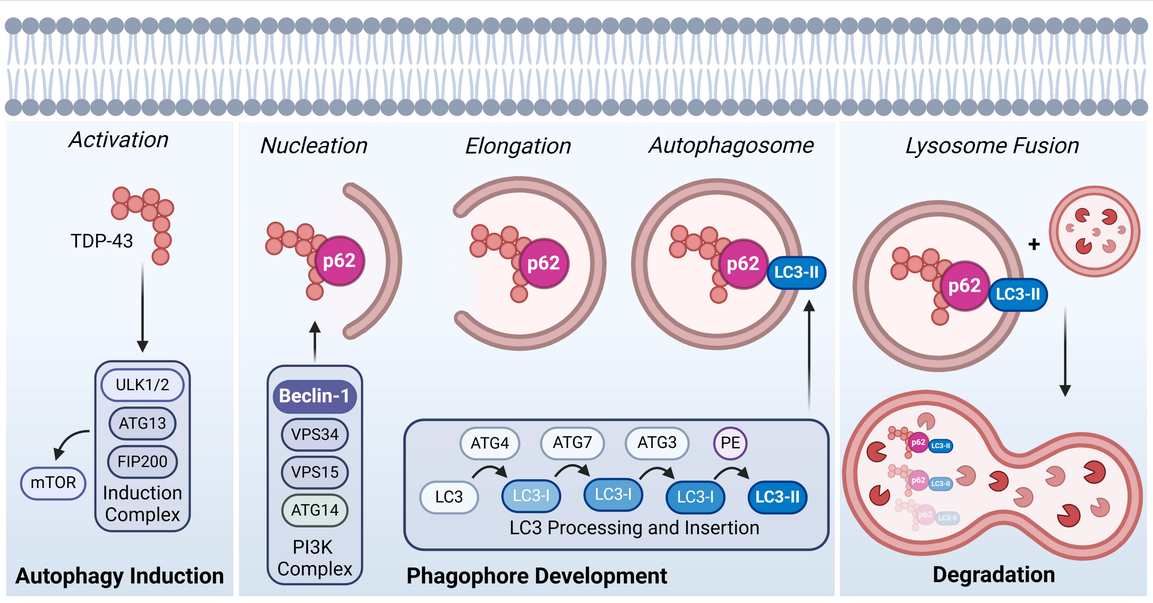
Background

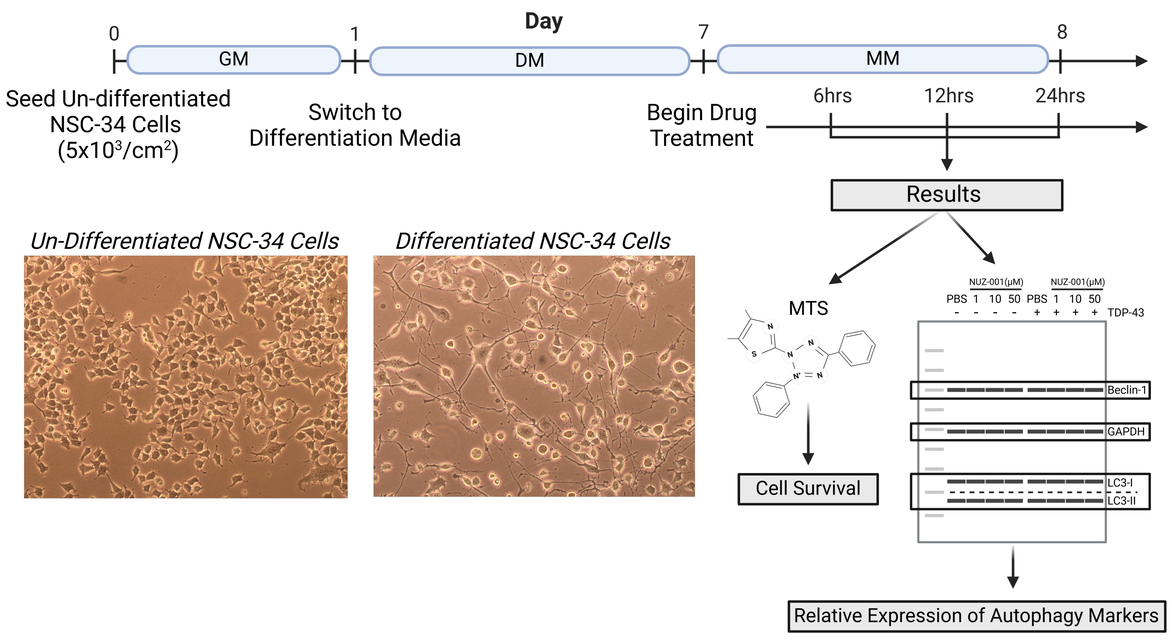


Objective

To assess the effect of NUZ-001 on the survival of NSC-34 motor neurons following exposure to TDP-43 aggregates and link any changes in viability to enhanced autophagy.

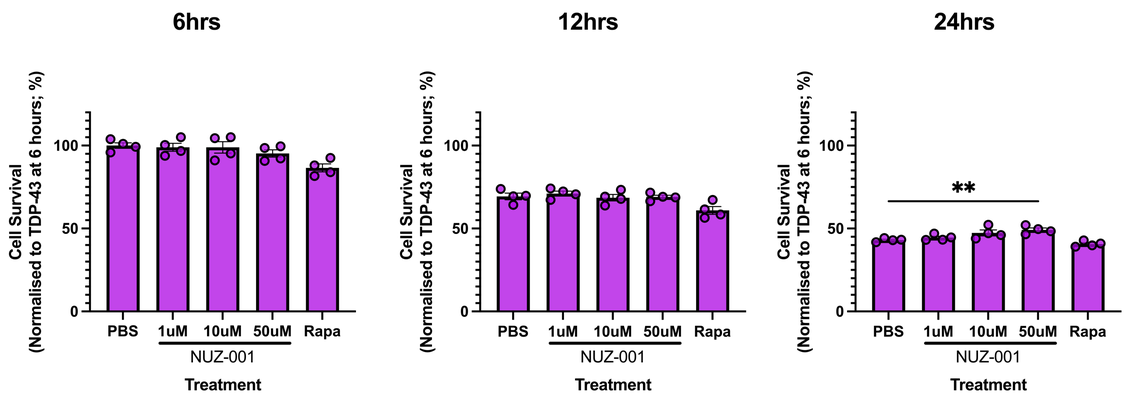
Methods

Growth Media (GM):
DMEM (High Glucose) + 10% FCS +1% Pen/Strep
Differentiation Media (DM):
DMEM:F12 (1:1) + 1% FCS + 1% Non-Essential Amino Acids + 1% Pen/Strep + 10µM All-Trans Retinoic Acid
Maintenance Media (MM):
DMEM:F12 (1:1) + 1% FCS + 1% Non-Essential Amino Acids + 1% Pen/Strep

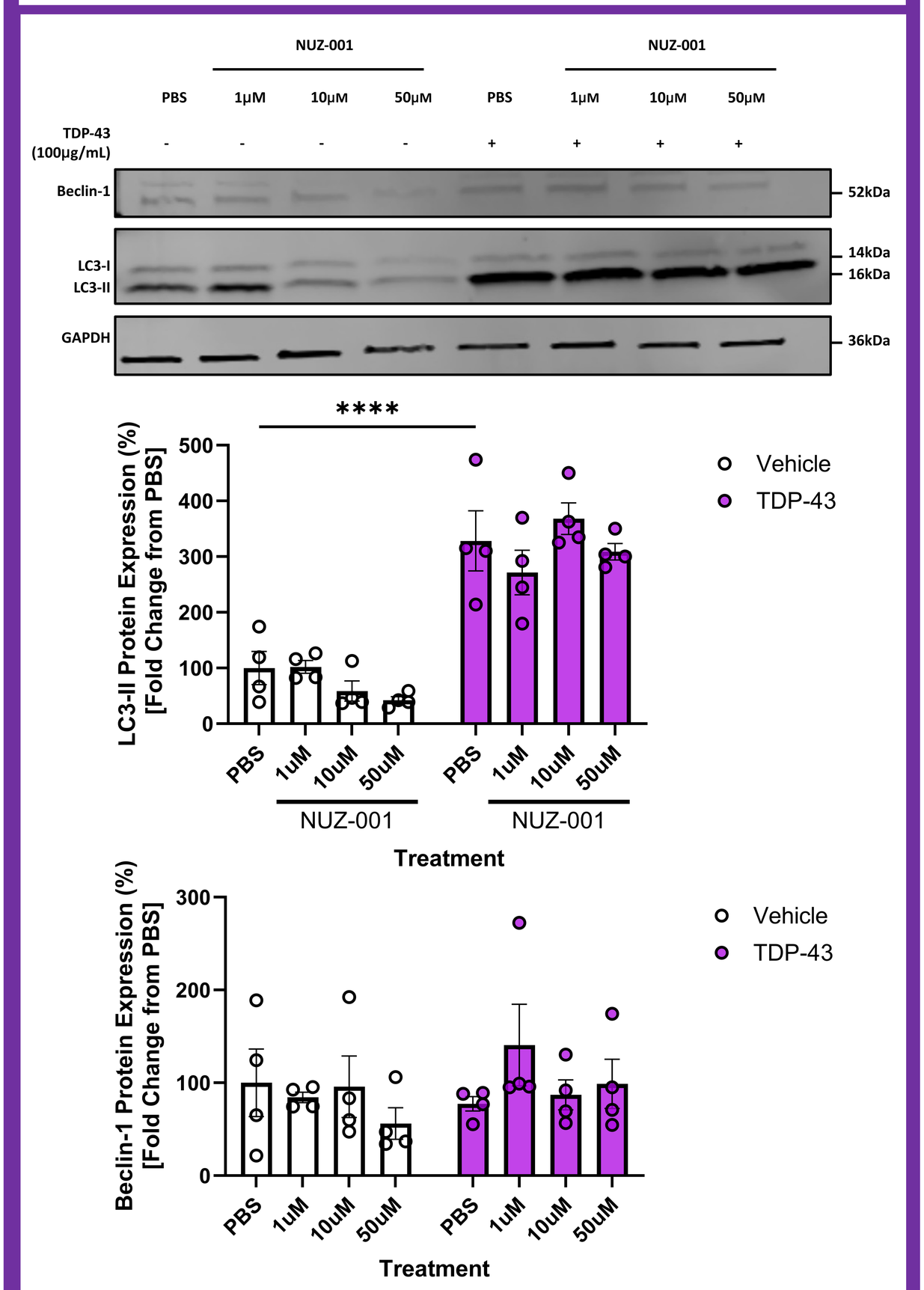


Results

1. NUZ-001 increases the survival of NSC-34 motor neurons treated with TDP-43 aggregates after 24 hours.



2. TDP-43 increases LC3-II levels in NSC-34 Motor Neurons



Summary

Key Points:

- **NUZ-001 treatment increased the viability of NSC-34 motor neurons exposed to TDP-43 aggregates.**
- **TDP-43 aggregates significantly increased LC3-II expression in NSC-34 cells, indicating an autophagic response to proteotoxic stress.**
- **NUZ-001 treatment did not alter LC3-II or Beclin-1 levels in response to TDP-43 at 24 hours.**

Future Direction

- **Autophagy-related protein expression should be assessed at earlier time points to determine whether NUZ-001 transiently modulates autophagic flux prior to the onset of cell death.**
- **Additional functional assays will help clarify the mechanisms underlying NUZ-001's protective effects in TDP-43-induced neurotoxicity.**

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