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Neurizon Presents Preclinical Data in Huntington's Disease at ASENT 2026

Highlights:

- **New preclinical data presented at ASENT 2026 expands mechanistic evidence supporting NUZ-001 activity in Huntington's disease (HD) models**
- **NUZ-001 and its major active metabolite NUZ-001 Sulfone demonstrate in vivo biological activity, including disease-dependent restoration of BDNF and enhanced autophagic markers**
- **Ongoing non-clinical studies continue to expand the preclinical evidence base for NUZ-001 across Huntington's disease models**

5 March 2026 – Melbourne Australia: Neurizon® Therapeutics Limited (ASX: NUZ & NUZOA; OTCQB: NUZTF) ("Neurizon" or "the Company"), a clinical-stage biotech company dedicated to advancing innovative treatments for neurodegenerative diseases, announces the presentation of new preclinical data at the 2026 American Society for Experimental NeuroTherapeutics (ASENT) Annual Meeting in Bethesda, Maryland.

The poster presentation expands the mechanistic evidence supporting the activity of NUZ-001 in preclinical models of Huntington's disease (HD). Huntington's disease is caused by a mutation in the HTT gene, which produces a toxic form of the huntingtin protein that damages neurons. The new findings build on previously reported results demonstrating that NUZ-001:

- Prevents phenotypic abnormalities in zebrafish models where huntingtin protein levels are reduced
- Reduces apoptosis
- Restores brain-derived neurotrophic factor (BDNF) levels

The data presented extend prior observations in three important areas:

1. Confirmation of in vivo exposure and metabolite activity
Drug exposure studies confirmed that both NUZ-001 and its major active metabolite NUZ-001 Sulfone are readily taken up in zebrafish. Both compounds demonstrated biological activity in vivo. These findings support that NUZ-001 Sulfone is pharmacologically active and may contribute to the overall therapeutic effect observed with NUZ-001.

2. Disease-dependent restoration of BDNF
The restorative effects of NUZ-001 and its major active metabolite NUZ-001 Sulfone on BDNF levels were shown to be selective to the HTT knockdown condition and were not observed in wild-type animals. This disease-dependent activity suggests a stress-adaptive and pathology-specific mechanism, rather than nonspecific upregulation of neurotrophic signalling.

3. Evidence of enhanced protein clearance pathways in human HD neurons
New cellular data generated in human induced pluripotent stem cell (iPSC)-derived HD neurons demonstrated a reduction in p62 immunoreactivity following treatment with NUZ-001 and NUZ-001 Sulfone. These findings are consistent with enhanced autophagic flux and activation of protein clearance pathways.

Together, these results further support a dual mechanistic framework in HD models involving enhancement of proteostasis and restoration of neurotrophic support under disease-relevant stress conditions.

NUZ-001 is currently being evaluated for the treatment of amyotrophic lateral sclerosis (ALS) as part of the HEALEY ALS Platform Trial. Ongoing preclinical studies are evaluating its activity in additional HD models to further define its translational potential across neurodegenerative disorders characterised by impaired protein homeostasis.

A copy of the poster presented at the ASENT 2026 Annual Meeting is attached to this announcement.

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This announcement has been authorised 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 the potential of NUZ-001 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. NUZ-001 is an investigational product and is not approved for commercial use in any jurisdiction.

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NUZ-001 Enhances Autophagy and Restores Neurotrophic Support in Cellular and Zebrafish Models of Huntington's Disease

13

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INTRODUCTION

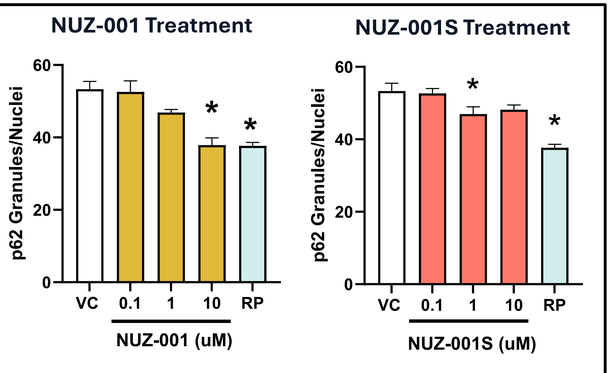
Huntington's disease (HD) is a fatal neurodegenerative disorder caused by a CAG repeat expansion in the HTT gene. Mutant huntingtin (mHTT) drives a dual pathogenic cascade:

1. **Proteostatic collapse** — mHTT misfolds and forms toxic aggregates that overwhelm cellular clearance pathways.
2. **Trophic failure** — reduced brain-derived neurotrophic factor (BDNF) impairs neuronal survival and striatal integrity.

NUZ-001 is a small molecule currently in clinical development for ALS. Preclinical studies support a mechanism centered on enhanced proteostasis, increased clearance of protein aggregates, and modulation of stress-adaptive pathways. Preliminary evidence suggests restoration of neurotrophic signaling.

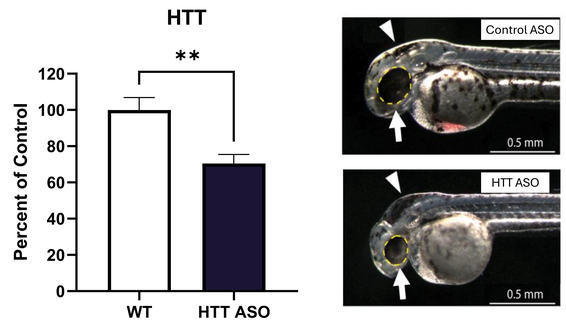
Study Objective: To evaluate the effects of NUZ-001 and its active metabolite, NUZ-001 Sulfone (NUZ-001S), on HD-relevant phenotypes in human iPSC-derived HD neurons and in vivo zebrafish models of HTT reduction.

FIGURE 1: NUZ-001(S) ENHANCES AUTOPHAGY IN HUMAN IPSC-DERIVED HD NEURONS



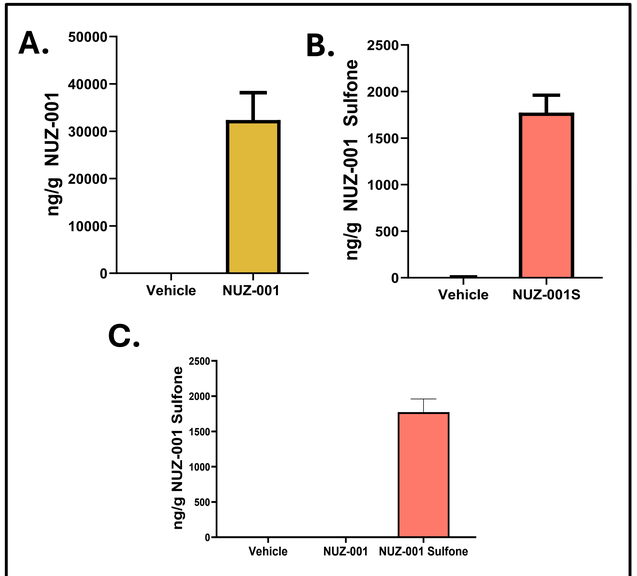
Human iPSC-derived neurons carrying a 50 CAG repeat expansion were treated with increasing concentrations of NUZ-001 or NUZ-001S for 3 days. Rapamycin (RP) served as a positive control for autophagy induction. Both NUZ-001 and NUZ-001S reduced p62 immunoreactivity, consistent with enhanced autophagic flux. *p < 0.05 vs. vehicle.

FIGURE 2: REDUCED HTT EXPRESSION INDUCES DEFICITS IN ZEBRAFISH



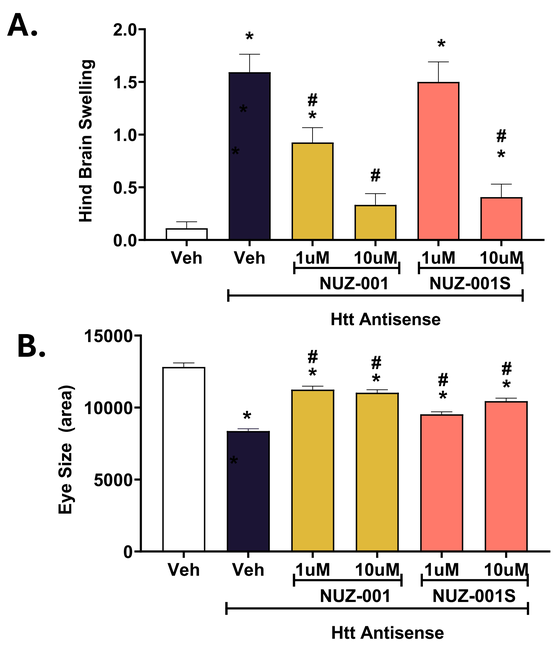
Zebrafish larvae were treated with an antisense oligonucleotide via direct injection. HTT antisense reduced HTT expression by approximately 30%. Reduced HTT expression resulted in phenotypic deficits, including reduced eye size (arrow) and enlarged, swollen hindbrain regions (diamond). HTT reduction also resulted in increased apoptosis (Figure 5) and reduced BDNF expression (Figure 6), leading to both phenotypic and biochemical deficits.

FIGURE 3: NUZ-001 AND NUZ-001S ARE READILY TAKEN UP BY ZEBRAFISH LARVAE



Zebrafish larvae were treated with NUZ-001 or NUZ-001S for 2 days. NUZ-001 **(A)** or NUZ-001S **(B)** levels were quantified following drug treatment using HPLC. **C.** NUZ-001S levels were quantified after NUZ-001 treatment to evaluate the ability of zebrafish to metabolically convert NUZ-001 to NUZ-001S.

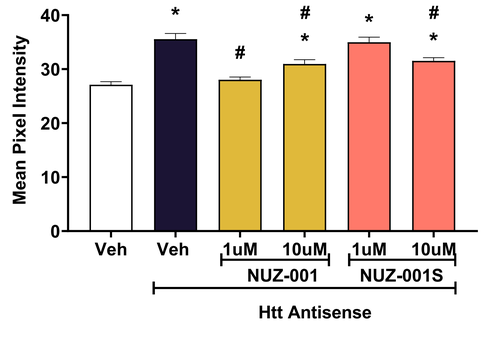
FIGURE 4: NUZ-001(S) PREVENTS PHENOTYPIC DEFICITS FOLLOWING HTT KNOCKDOWN



Zebrafish larvae were treated with NUZ-001 or NUZ-001S for 2 days following HTT ASO administration. HTT reduction induced hindbrain swelling **(A)** and reduced eye size **(B)**. Both compounds significantly prevented these phenotypic abnormalities.

*p < 0.05 vs. vehicle (no ASO); #p < 0.05 vs. vehicle + HTT ASO.

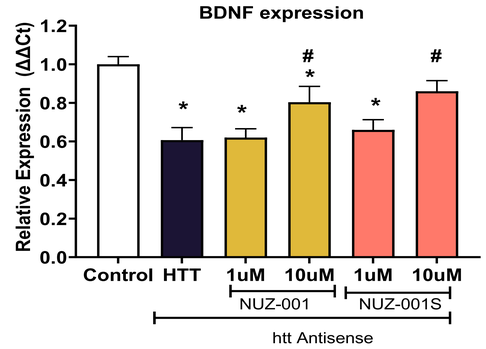
FIGURE 5: NUZ-001(S) PREVENTS APOPTOSIS FOLLOWING HTT KNOCKDOWN



NUZ-001 and NUZ-001S prevented apoptosis induced by HTT knockdown in zebrafish larvae, as measured by apoptotic marker staining.

*p < 0.05 vs. vehicle (no ASO); #p < 0.05 vs. vehicle + HTT ASO

FIGURE 6: NUZ-001(S) RESTORES BDNF FOLLOWING HTT KNOCKDOWN



Zebrafish larvae were treated with NUZ-001 or NUZ-001S for 2 days in the presence of HTT ASO. HTT reduction was associated with decreased BDNF expression. Both compounds prevented the ASO-induced reduction in BDNF levels. Neither compound increased BDNF expression in the absence of HTT ASO (data not shown).

*p < 0.05 vs. vehicle (no ASO); #p < 0.05 vs. vehicle + HTT ASO.

CONCLUSION AND NEXT STEPS

NUZ-001 and its active metabolite, NUZ-001S, enhance autophagic flux in Huntington's disease (HD) neurons, as demonstrated in **Figure 2**, where both compounds reduced p62 immunoreactivity in human iPSC-derived HD neurons in a manner comparable to rapamycin. In vivo, ASO-mediated HTT knockdown induced phenotypic abnormalities and apoptosis in zebrafish **(Figures 2, 4, and 5)**, including hindbrain swelling, reduced eye size, and increased apoptotic markers. Treatment with NUZ-001 or NUZ-001S significantly prevented these deficits and reduced apoptosis. Importantly, HTT reduction also decreased BDNF expression, and both compounds restored BDNF levels toward baseline **(Figure 6)**, supporting recovery of neurotrophic signaling. Drug exposure studies confirmed uptake NUZ-001 to NUZ-001S in zebrafish **(Figure 3)**, supporting target engagement in vivo. Together, these findings demonstrate that NUZ-001 addresses both impaired proteostasis and neurotrophic insufficiency, supporting a dual therapeutic potential in HD. Notably, protective effects were observed selectively under conditions of HTT reduction, consistent with a stress-adaptive mechanism of action.

Ongoing studies are evaluating NUZ-001 in additional human iPSC-derived HD models and rodent models of HD to further strengthen translational validation and mechanistic understanding.