

NUZ-001 Shows Positive Results in Human 3D Brain Model

Highlights:

- Completion of independent study with Tessara Therapeutics to assess the effect of NUZ-001 in Tessara's RealBrain® 3D human micro-tissues model
- Results showed that NUZ-001 and NUZ-001 Sulfone exhibited strong safety characteristics in the ArtiBrain™ model (healthy human brain) and suggested short-term treatment:
 - promotes health and viability of brain tissues
 - has neuroprotective properties against neurotoxic insult
 - may promote neuroplasticity by boosting neuronal branching
- Results to be presented by Tessara Therapeutics' Principal Scientist, Dr Mark Greenough, at the AD/PD 2025 Advances in Sciences & Therapy Conference
- AD/PD is the preeminent international conference on Alzheimer's and Parkinson's diseases in Vienna, Austria
- Additional study underway to explore the therapeutic potential of NUZ-001 Tessara's ADBrain™ model for sporadic Alzheimer's disease with results expected this quarter

1 April 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 advise that results from an independent study undertaken in collaboration with Tessara Therapeutics ("Tessara") will be presented by the group's Principal Scientist and Alzheimer's Disease expert, Dr Mark Greenough at the AD/PD 2025 Advances in Sciences & Therapy conference on April 2nd to 3rd. AD/PD is the preeminent international conference on Alzheimer's and Parkinson's diseases and related neurological disorders in Vienna, Austria, from 1 to 5 April.

The results are part of a study in ongoing collaboration with Tessara, a leading biotechnology company pioneering a new approach in 3D cell-based models of the brain, having developed its RealBrain® 3D human micro-tissues technology that replicates the biological complexity of the human brain in a scalable and reproducible manner. Tessara has validated and recently launched two brain models: the ArtiBrain™ model (healthy human brain) and the ADBrain™ model (Alzheimer's disease). Tessara has leveraged these models to explore the effect of Neurizon's lead candidate, NUZ-001.

During the study, NUZ-001 and NUZ-001 Sulfone (major active metabolite) were tested in the ArtiBrain™ model over a three-day period at doses ranging from 5 µM to 50 µM. NUZ-001 demonstrated an excellent safety profile in Tessara's RealBrain® micro-tissues. The compounds offered protection against a newly identified form of cell death, ferroptosis (induced by RSL3 exposure). This unique type of programmed cell death is mechanistically different from apoptosis, autophagy, or necrosis and has been implicated in diseases where lipid peroxidation is a mechanism of neurodegeneration, such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis.

Confocal imaging and subsequent neuronal network analysis, using Tessara's algorithms, further revealed that NUZ-001 and NUZ-001 Sulfone increased neuronal (B3-tubulin+) branching. This suggests an effect on neural connectivity and plasticity, with longer-term drug treatments potentially being required to elicit an overall effect on network and synaptic density.

Tessara's Managing Director and Chief Executive Officer, Dr Christos Papadimitriou commented: "We are delighted for Neurizon on the results they have generated in our ArtiBrain™ model. These findings indicate that short-term treatment with NUZ-001 and NUZ-001 Sulfone maintains an excellent safety profile in Tessara's RealBrain® micro-tissues. In addition, the compounds appear to offer neuroprotective effects against ferroptosis and encourage neural branching, potentially boosting plasticity by enabling neurons to form additional

connections. While further research is needed to clarify the mechanisms responsible for these benefits, current data suggest that longer-term treatment may enhance network density and overall plasticity. In humans, this could translate into tangible benefits in cognition, learning, memory, or resilience to neurodegenerative processes involved in diseases such as Alzheimer's disease, Parkinson's disease and Amyotrophic Lateral Sclerosis (ALS).

As part of ongoing initiatives with Tessara, the therapeutic efficacy of NUZ-001 is now being assessed through other screening modalities, including Tessara's ADBrain™ platform, for sporadic Alzheimer's disease. Results from further testing are anticipated this quarter and will be used to assess the potential for NUZ to expand its lead asset into a broader range of indications.

A copy of the poster presentation by Dr Greenough at AD/PD is attached to this ASX release for further reference.

Managing Director and Chief Executive Officer, Dr Michael Thurn commented: "These results provide initial validation of the broader potential use of NUZ-001 in other neurodegenerative diseases, highlighting its safety and efficacy in ArtiBrain™ 3D human micro-tissues model. The presentation of the study results at the world's leading Alzheimer's and Parkinson's diseases and related neurological disorder conference in Vienna, is also a major milestone for the Company, which will provide strong independent support for our lead asset.

"I would like to take this opportunity to thank Tessara Therapeutics for the excellent collaboration to date, which will continue as we assess NUZ-001's potential as a treatment of Alzheimer's disease in the ADBrain™ model. These additional results are expected to materialise this quarter and have the potential to highlight NUZ-001's potential in another widespread and debilitating condition."

-ENDS-

This announcement has been authorized for release by the Board of Neurizon Therapeutics Limited.

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About Tessara Therapeutics:

Tessara Therapeutics is a Melbourne-based biotechnology company pioneering novel drug discovery technologies for neurological and neurodegenerative diseases. Through its proprietary RealBrain® platform, Tessara has developed the first scalable, reproducible 3D human brain micro-tissue models that closely replicate both healthy and diseased neural physiology. These models include ArtiBrain, representing the healthy brain, and ADBrain, capturing sporadic Alzheimer's disease cases. By enabling cost-effective, high-throughput screening and delivering predictive, human-relevant data, Tessara's approach accelerates discovery timelines, enhances the likelihood of successful clinical trials, and supports the industry-wide shift to non-animal research.

For more information about Tessara, please visit www.tessaratherapeutics.com.

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>



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1. Abstract (#787)

The advent of 3D human culture models has provided a more physiologically relevant alternative to classical drug testing approaches that rely on *in vitro* 2D cultures and *in vivo* rodent models. Tessara Therapeutics have developed the RealBrain® 3D neuronal micro-tissue platform for industry-level high throughput compound screening.

Objectives: To utilise Tessara's platform to assess the safety and toxicity of compounds from Neurizon Therapeutics.

Methods: Initial assays have focussed on cytotoxicity (lactate dehydrogenase (LDH)) and cell viability (Resazurin) assays following a three-day exposure of RealBrain® micro-tissues to a dose range (0.5µM – 50µM) of NUZ-001 and its major active metabolite NUZ-001 sulfone.

Results: No loss of cell viability (Resazurin) or elevation in LDH release (a proxy for cytotoxicity) was detected relative to vehicle control. NUZ-001 exhibited a significant elevation in Resazurin signal from 5-50 µM and its major active metabolite exhibited a trend to an elevation, relative to vehicle-only control.

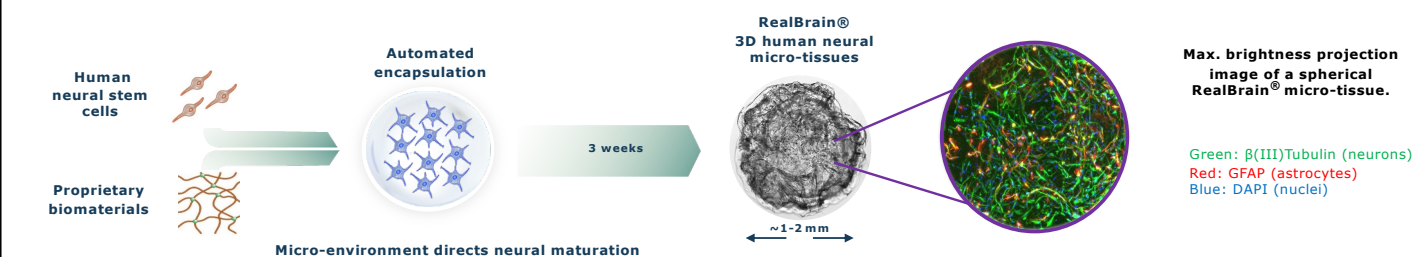
Conclusions: The tested compounds were safe and non-toxic in Tessara's 3D human cell-based micro-tissue platform, with data suggestive of a small proliferative/positive effect on cells within the micro-tissue. The therapeutic efficacy of the compounds is now being assessed through other screening modalities, including ADBrain™, Tessara's 3D model of sporadic Alzheimer's disease.

2. Neurizon Therapeutics

Neurizon Therapeutics 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.

3. Tessara Therapeutics - Automated RealBrain® production

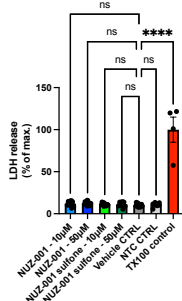
Tessara is a leader in 3D cell-based models of the brain, having developed its RealBrain technology that replicates the biological complexity of the human brain in a scalable and reproducible manner. Tessara has validated and recently launched two brain models: the ArtiBrain™ model (healthy human brain) and the ADBrain™ model (Alzheimer's disease). Tessara has leveraged these models to explore the effect of Neurizon's lead candidate, NUZ-001.



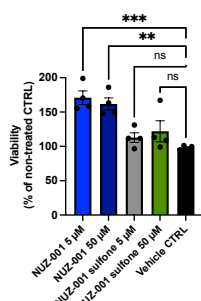
Schematic: the pipeline for production of Tessara's RealBrain® 3D models of the human brain.

4. Results

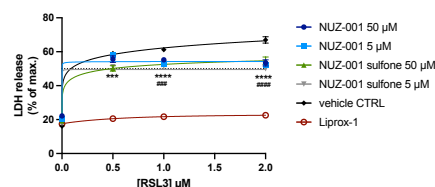
NUZ-001 and NUZ-001 sulfone are not cytotoxic



NUZ-001 increases baseline viability



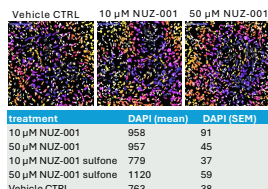
NUZ-001 and NUZ-001 sulfone offer protection from ferroptotic cell death



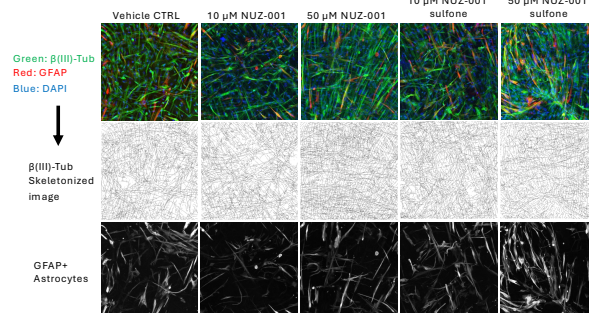
NUZ-001 demonstrated an excellent safety profile in Tessara's RealBrain® micro-tissues. The compounds offered protection against a newly identified form of cell death, ferroptosis (induced by RSL3 exposure in Tessara's ArtiBrain™ ferroptosis assay). This is a unique form of programmed cell death that is mechanistically different from apoptosis, autophagy or necrosis and has been implicated in diseases where lipid peroxidation is a mechanism of neurodegeneration eg. Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis.

Non treated control (NTC); TritonX100 (TX100) positive control; Not significant (NS); liproxstatin-1 (Liprox-1) suppresses the accumulation of lipid hydroperoxides and is a potent inhibitor of ferroptosis; RSL3 is a potent ferroptosis-triggering agent that inhibits the activity of glutathione peroxidase 4.

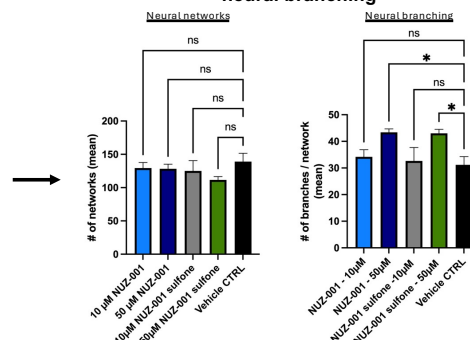
3D cell counting of DAPI+ nuclei



Confocal imaging and mapping of neural networks



NUZ-001 and NUZ-001 sulfone increase neural branching



5. Conclusions

These data demonstrate that Neurizon compound NUZ-001 and its major active metabolite, NUZ-001 sulfone, are safe and well tolerated in Tessara's ArtiBrain, a novel 3D neural model of the human brain that comprises a mixed population of frontal cortical neurons and mixed glial cells. Baseline cell viability was significantly elevated in the presence of NUZ-001 relative to vehicle control-treated ArtiBrain micro-tissues, with NUZ-001 also partially protecting against RSL3-mediated cytotoxicity. These data suggest that NUZ-001 has beneficial effects on cell health (both at baseline and in response to a neurotoxin). Further studies are required to define the mechanisms underlying these benefits and to assess their broader relevance to other forms of insult/toxicity. Confocal imaging and subsequent network analysis, using a Fiji-based Tessara algorithm, further revealed that NUZ-001 and NUZ-001 sulfone increased B3-tubulin+ neuronal branching. This suggests an effect on neural connectivity, with longer-term drug treatments potentially being required to elicit an overall effect on network density. Further work is underway to test NUZ-001 and NUZ-001 sulfone in Tessara's ADBrain™ model and to further elaborate on the neuroprotective and neuroplastic potential of this compound.