



ASX / Media Release
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Exenatide Results in Improved Neuronal Cell Survival in a 3D Human Brain Model of Alzheimer's Disease

Key Points

- Initial significant scientific findings from the collaboration with the Tessara Therapeutics ADBrain™ platform, a 3D human brain model that replicates the neurodegeneration seen in Alzheimer's Disease (AD)
- Low dose Exenatide shown to increase cell viability by approx. 24% versus controls under similar oxidative stress conditions experienced in AD patients leading to cell death
- Moderate dose Exenatide resulted in a 45% increase in cell viability under conditions replicating ferroptosis, a distinct pathway of neuronal cell death and progression in AD
- Exenatide was well tolerated by ADBrain™ micro-tissues over the dose range tested
- Data consistent with emerging clinical evidence that GLP-1 receptor agonists (a class including Exenatide) may protect against AD dementia, a US\$17 billion market in 2023¹

Invex Therapeutics Ltd (Invex, ASX:IXC, or the Company) a biopharmaceutical company focused on the development and commercialisation of Exenatide for neurological conditions relating to raised intracranial pressure (ICP), is pleased to announce the results of an analysis of the therapeutic efficacy and safety of Exenatide on Tessara Therapeutics Pty Ltd (Tessara) Alzheimer's Disease (AD) model, ADBrain™ neural micro-tissues. ADBrain™ models the A β 42-mediated neurodegeneration seen in AD.

Two validated quantitative biochemical assays – LDH release and Resazurin – determined that there were no adverse effects from Exenatide on neural cell health in ADBrain™ micro-tissues from 1 μ M up to 100 μ M over a 3-day incubation period, demonstrating that Exenatide was well tolerated. The capacity of Exenatide to prevent cell death was tested through two disease-relevant pathways for ferroptosis via the known inducer RSL3 and oxidative stress via administration of hydrogen peroxide, in ADBrain™ micro-tissues. These compounds have multiple mechanisms of action and are also relevant to modelling cellular processes involved in multiple neurodegenerative diseases (such as Alzheimer's Disease, traumatic brain injury, Parkinson's Disease and others).

Ferroptosis is a type of cell death that is triggered by a buildup of reactive oxygen species (ROS) and iron-dependent lipid peroxides in cells. Several hallmarks of AD, such as excess iron, elevated lipid peroxides, and reduced glutathione (GSH) levels, are consistent with ferroptosis.

¹ Source; Grandview Research

The main efficacy findings were:

- (1) Low dose Exenatide (0.1 μ M) increased cell viability by approximately 24% in the presence of a sub-lethal concentration of hydrogen peroxide (H_2O_2), a potent inducer of oxidative stress in cell culture systems.
- (2) Exenatide protected cell membrane integrity in ADBrain™ micro-tissues when H_2O_2 was increased to a normally lethal concentration.
- (3) In the RSL3/ferroptosis assay 10 μ M Exenatide was associated with a 45% increase in cell viability relative to vehicle only control in the presence of 1 μ M RSL3.
- (4) A 25% increase in cell viability associated with 0.1 and 1 μ M Exenatide respectively in the absence of RSL3 similar to the positive effect observed for the hydrogen peroxide assay.

The data generated by the collaboration has yielded important new information for Invex as it relates to the applicability of Exenatide in alternative neurological diseases, including AD. This is the first time a GLP-1 receptor agonist (GLP-1RA), namely Exenatide has shown evidence of benefit in a three-dimensional human brain model in AD.

There is now emerging evidence that GLP-1RAs may protect against AD dementia shrinking in the parts of the brain that control memory, learning, language and decision-making by up to 50%.² In addition, based on Medicare data in the United States, the use of Exenatide by type 2 diabetics is associated with reduced incidence of AD³.

Tessara is an Australian company commercialising its RealBrain® technology, scalable 3D human brain tissue models, for application to drug discovery and regenerative medicine treatments.

The Company plans to explore additional activities with Tessara that may provide additional new insights into the mechanism of action of Exenatide in AD and potential effects in other neurodegenerative diseases, including traumatic brain injury.

- ENDS -

This release dated 16 December 2024 has been authorised for lodgement to ASX by the Board of Directors of Invex Therapeutics.

² <https://aaic.alz.org/releases-2024/glp-drug-liraglutide-may-protect-against-dementia.asp>

³ <https://alz-journals.onlinelibrary.wiley.com/doi/full/10.1002/trc2.12139>

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About Invex Therapeutics Ltd

Invex is a biopharmaceutical company focused on the repurposing of an already approved drug, Exenatide, for efficacious treatment of neurological conditions derived from or involving raised intracranial pressure. Invex has trademarked its repurposed Exenatide as Presendin™. www.invextherapeutics.com.