ASX ANNOUNCEMENT

Positive Xanamem® human PET study published in the *Journal of Alzheimer's Disease* demonstrating robust CNS[1] target enzyme occupancy

The study confirms that Xanamem is a brain-penetrant inhibitor of the tissue cortisol synthesis enzyme, 11β-HSD1, with high levels of target occupancy at doses as low as 5 mg

Sydney, 24 January 2024. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that its human Positron Emission Tomography (PET) study, confirming high levels of Xanamem target occupancy in the brain at safe, well tolerated, and biologically active doses, has been published in the *Journal of Alzheimer's Disease*.

Highlights of the PET study publication include:

- Participants were 23 cognitively normal, elderly volunteers and 17 people with Alzheimer's disease
- Xanamem doses of 5 mg, 10 mg, 20 mg and 30 mg were given daily for 7 days to 10 participants at each dose level
- The PET study assessed the degree of Xanamem occupancy using a tracer called ^{11}C-TARACT
- The primary conclusion from the study was that Xanamem achieved high target occupancy of 66-85%, which exceeded the 30-60% inhibition required for effectiveness in animal models
- The authors further concluded that a dose level of 10 mg daily achieved near saturation of the enzyme target, meaning that higher doses achieved little additional occupancy
- The study results support exploring doses of ≤10 mg in clinical trials, consistent with the on-going XanaCIDD (Phase 2a, depression) and XanaMIA trials (Phase 2b, Alzheimer's disease).

The original article can be accessed here: https://pubmed.ncbi.nlm.nih.gov/38250767/

Dr Dana Hilt, the Company's Chief Medical Officer said:

"To our knowledge Xanamem is the first drug of this class to have such compelling data. The PET study highlights just how effective Xanamem is at reaching its target enzyme in the brain. No other inhibitor of 11β-HSD1 has ever demonstrated robust central nervous system (CNS) target engagement in this way.

"The results are consistent with our phase 1b and phase 2a clinical trial data, which showed evidence of activity on cognition in the brain with doses of 5 & 10 mg daily. These same dose levels have also shown excellent safety and tolerability, and to date more than 350 people have been treated with Xanamem.

"Oral Xanamem as a 10 mg daily dose is now in Phase 2 trials in Major Depressive disorder (MDD) and Alzheimer's disease, with the initial Phase 2 results in the MDD trial due to report in Q2 2024."

® Xanamem is a registered trademark of Actinogen Medical Limited
[1] Central nervous system

ENDS

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Announcement authorised by the Board of Directors of Actinogen Medical

About Actinogen Medical

Actinogen Medical (ACW) is an ASX-listed, biotechnology company developing a novel therapy for neurological and neuropsychiatric diseases associated with dysregulated brain cortisol. There is a strong association between cortisol and detrimental changes in the brain, affecting cognitive function, harm to brain cells and long-term cognitive health.

Cognitive function means how a person understands, remembers and thinks clearly. Cognitive functions include memory, attention, reasoning, awareness and decision-making.

Actinogen is currently developing its lead compound, Xanamem,® as a promising new therapy for Alzheimer's Disease and Depression and hopes to study Fragile X Syndrome and other neurological and psychiatric diseases in the future. Reducing cortisol inside brain cells could have a positive impact in these and many other diseases. The cognitive dysfunction, behavioural abnormalities, and neuropsychological burden associated with these conditions is debilitating for patients, and there is a substantial unmet medical need for new and improved treatments.

Current Clinical Trials

The **XanaCIDD Phase 2a depression trial** is a double-blind, six-week proof-of-concept, placebo-controlled, parallel group design trial in 160 patients. Patients are evenly randomized to receive Xanamem 10 mg once daily or placebo, in some cases in addition to their existing antidepressant therapy, and effects on cognition and depression are assessed.

The **XanaMIA Phase 2b Alzheimer's disease trial** is a double-blind, 36-week treatment, placebo-controlled, parallel group design trial in 220 patients with mild to moderate AD and progressive disease, determined by clinical criteria and confirmed by an elevated level of a pTau protein biomarker in blood. Patients receive Xanamem 10 mg or placebo, once daily, and effects on cognition, function and progression of Alzheimer's disease are assessed. Thus, Xanamem is being assessed in this trial for its potential effects as both a cognitive enhancer and a disease course modifier.

About Xanamem

Xanamem's novel mechanism of action is to block the production of cortisol inside cells through the inhibition of the 11β-HSD1 enzyme in the brain. Xanamem is designed to get into the brain after it is absorbed in the intestines upon swallowing.

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease and excess cortisol is known to be toxic to brain cells. Cognitive impairment is also a feature in Depression and many other diseases. Cortisol itself is also associated with depressive symptoms and when targeted via other mechanisms has shown some promise in prior clinical trials.

The Company has studied 11β-HSD1 inhibition by Xanamem in more than 350 volunteers and patients, so far finding a statistically significant improvement in working memory and attention, compared with placebo, in healthy, older volunteers in two consecutive trials and clinically significant improvements in functional and cognitive ability in patients with biomarker-

positive mild AD. Previously, high levels of target engagement in the brain with doses as low as 5 mg daily have been demonstrated in a human PET imaging study. A series of Phase 2 studies in multiple diseases is being conducted to further confirm and characterize Xanamem's therapeutic potential.

Xanamem is an investigational product and is not approved for use outside of a clinical trial by the FDA or by any global regulatory authority. Xanamem® is a trademark of Actinogen Medical.

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