ASX ANNOUNCEMENT

First investigational site activated in Actinogen XanaMIA Phase 2b AD trial

Sydney, 20 December 2023. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that that the first investigational site for the XanaMIA Phase 2b trial comprising 220 participants with mild to moderate Alzheimer's disease (AD) has now been activated. Initial results from the first 100 participants are expected in H1 CY2025.

Highlights of XanaMIA trial:

- Double-blind, placebo-controlled randomized trial design
- 10mg Xanamem® daily dose versus placebo for 36 weeks
- Participants have mild to moderate AD and elevated levels of the blood biomarker, pTau
- The primary endpoint for the trial is a cognitive test battery comprising seven different digital assessments
- Key secondary endpoints are the Clinical Dementia Rating – Sum of Boxes scale (CDR-SB), a combined cognitive and functional measure, and the Amsterdam Activity of Daily Living scale, which is purely a functional measure
- Recruitment will initially be conducted at investigational sites in Australia before expanding to other countries.

Previously, in an analysis of 34 patients with mild AD and elevated blood p-Tau treated with Xanamem or placebo, a clinically significant benefit of Xanamem was observed in a cognitive composite and the CDR-SB.

Dr Steven Gourlay, the Company's CEO and Managing Director said,

"We are excited to announce the start of the XanaMIA trial in patients with biomarker-positive Alzheimer's disease. Previously, positive data from three separate placebo-controlled trials suggests Xanamem may provide clinically significant benefits and reduce disease progression. The purpose of the new trial is to robustly confirm this benefit in a larger group of patients and thereby enable the expansion of the program toward regulatory approval and global access for patients."

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 and Upcoming 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 300 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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