ASX ANNOUNCEMENT

Actinogen XanaCIDD trial enrolment exceeds 50 percent and on track for results in Q2 CY2024

Sydney, 28 November 2023. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that enrolment in the XanaCIDD Phase 2a trial comprising 160 participants with cognitive impairment associated with persistent major depressive disorder (MDD) now exceeds 50 percent (that is, more than 80 participants enrolled to date). Results remain on track for Q2 CY2024.

Highlights of XanaCIDD trial:

- Double-blind, placebo-controlled randomized trial design
- 10mg Xanamem® daily dose versus placebo for six weeks (a common duration for Phase 2a trials in MDD)
- Participants have a history of persistent MDD despite previous treatment and objective cognitive impairment
- The primary endpoint for the trial is the computerized Cogstate "attention composite" test battery, measuring attention and working memory and shown previously to be a sensitive measure of Xanamem benefit in the XanaMIA Part A and XanaHES trials
- The key secondary endpoint for the trial is the MADRS structured interview evaluating MDD symptoms and is a fundamental endpoint used for regulatory approvals of anti-depressant medication
- Recruitment in the UK is now accelerating (previously site activation was impacted by industry-wide delays at the UK regulator)
- Recruitment in Australia is further accelerating due to enhanced screening and recruitment procedures
- Due to rapid recruitment in Australia and now also in the UK, expansion to US sites is no longer necessary for this trial. US sites will be included in future clinical trials.

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

"We are looking forward to sharing the results of the XanaCIDD trial in Q2 CY2024 in approximately 6 months' time. This trial represents the first large scale test of whether lowering tissue cortisol in the brain can improve cognition and depression in patients with MDD. We are optimistic that Xanamem treatment will benefit patients, in part because the primary endpoint of the trial is the attention composite previously shown to be a sensitive measure of Xanamem effect."

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.

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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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