ASX ANNOUNCEMENT

Actinogen commences open-label phase of XanaMIA Alzheimer's trial

Sydney, 1 April 2026. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that it has commenced the open-label extension (OLE) phase of the XanaMIA trial with the first trial participant treated yesterday evening.

Highlights of the OLE:

- An open-label phase of up to 25 months of treatment, during which all participants will receive active Xanamem® 10 mg once daily, with no placebo control group
- Open to all former and current participants who have completed the randomized phase of the XanaMIA pivotal Alzheimer's disease trial in Australia and the US
- Generates longer term safety data and observational data on key efficacy endpoints such as the CDR- SB[1], cognition and activities of daily living
- Trial data will provide a valuable contribution to future regulatory marketing applications
- As an open-label trial, data can be analyzed and reported progressively and compared to relevant historical control cohorts of patients with mild to moderate Alzheimer's disease.

Meanwhile, the randomized phase of the XanaMIA trial continues in parallel, with final topline results due in November 2026.

Dr Dana Hilt, the Company's CMO said:

"The commencement of the open-label extension phase of the XanaMIA trial means that we can now offer current and past participants the opportunity to receive active Xanamem therapy for up to 25 months. This is an important opportunity for our trial participants, half of whom initially received placebo, as it enables all participants to contribute valuable data on the potential durability of Xanamem benefit and long-term safety."

"Xanamem has the potential to be a game-changer for Alzheimer's patients as a potentially safe and effective oral therapy to slow or halt disease progression. Unlike anti-amyloid antibody therapy, Xanamem does not require serial MRI scanning for safety evaluations as there is no suggestion it causes brain swelling also known as 'ARIA'."

View this announcement on our InvestorHub: https://investors.actinogen.com.au/link/yO1EXr

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[1] CDR-SB: Clinical Dementia Rating Scale – Sum of Boxes

Announcement authorised by the Disclosure Committee of Actinogen Medical Limited

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. It has also conducted a phase 2 trial in patients with cognitive impairment and depression and may 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.

Clinical Trials

The XanaMIA Phase 2b/3 Alzheimer's disease trial is a double-blind, 36-week treatment, placebo-controlled, parallel group design trial in 247 patients with mild to moderate AD and progressive disease, determined by clinical criteria and confirmed by an elevated level of the pTau181 protein biomarker in blood. Patients receive Xanamem 10 mg or placebo, once daily, and its ability to slow progression of Alzheimer's disease is assessed with a variety of endpoints. The primary endpoint of the trial is the internationally-recognized CDR-SB (Clinical Dementia Rating scale – Sum of Boxes). The trial is being conducted in Australia and the US and is now closed to participant recruitment. It has passed an independent Data Monitoring Committee safety and efficacy futility review and final topline results are expected in November 2026.

The XanaMIA-OLE Alzheimer's disease open-label extension is an open-label phase of up to 25 months treatment where all participants will receive active Xanamem 10 mg once daily. The trial evaluates safety and a limited number of efficacy endpoints such as the CDR-SB. The trial commenced in March 2026 and is open to all former and current participants in the XanaMIA Phase 2b/3 trial.

The XanaCIDD Phase 2a depression trial was a double-blind, six-week proof-of-concept, placebo-controlled, parallel group design trial in 167 patients with moderate, treatment-resistant depression and a degree of baseline cognitive impairment. Participants were evenly randomized to receive Xanamem 10 mg once daily or placebo, in most cases in addition to their existing antidepressant therapy, and effects on cognition and depression were assessed. Trial results were reported in August 2024 and showed clinically and statistically significant benefits on depression symptoms with positive effects on the MADRS scale (a validated scale of depression symptom measurement) and the PGI-S (a valid patient reported assessment of depression severity). Cognition improved markedly and to a similar extent in both Xanamem and placebo groups.

About Xanamem (emestedastat)

Xanamem's novel mechanism is to control elevated levels of cortisol (aka the "stress hormone") in the brain through the inhibition of the cortisol synthesis enzyme, 11β-HSD1, without affecting production of cortisol by the adrenal glands which is essential for the body's normal functioning. Xanamem is a first-in-class, once-a-day pill designed to deliver high levels of cortisol control in key areas of the brain related to Alzheimer's and other diseases such as the hippocampus and frontal cortex. To view Xanamem's two-minute Mechanism of Action animation, click here.

Chronically elevated cortisol is associated with progression in Alzheimer's Disease and excess cortisol is known to be toxic to brain cells. Cortisol itself is also associated with depressive symptoms and when targeted via other mechanisms has shown some promise in prior clinical trials. The recent XanaCIDD trial demonstrated clinically and sometimes statistically significant benefits on depressive symptoms, further validating the cortisol control mechanism for the Xanamem 10 mg oral daily dose.

The Company has studied 11β-HSD1 inhibition by Xanamem in more than 500 volunteers and patients in eight clinical trials. Xanamem has a promising safety profile and has demonstrated clinical activity in patients with depression, patients

with biomarker-positive Alzheimer's disease and cognitively normal volunteers. 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.

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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