ASX ANNOUNCEMENT

Actinogen receives positive Interim Analysis recommendation from its independent Data Monitoring Committee to continue the XanaMIA pivotal Alzheimer's disease trial

Sydney, 30 January 2026. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that the XanaMIA pivotal Alzheimer's disease (AD) trial's independent Data Monitoring Committee (DMC) has recommended that the trial continue without amendment after its interim analysis. In doing so, the DMC determined that the unblinded safety and efficacy data it reviewed support continuing the trial to its completion later in the year.

Highlights:

- In a confidential process designed to preserve the statistical power of the trial, the external DMC considered unblinded safety and efficacy data (decoded for Xanamem or placebo treatment) from approximately 37% of the expected final dataset, including data from 136 participants with one or more efficacy datapoints and 52 participants who had finished the full 36 weeks of treatment. All ACW staff and XanaMIA trial personnel remain blinded to participant treatment assignment.
- Following the positive DMC recommendation, the XanaMIA trial will continue to treat ongoing participants with either Xanamem 10 mg or placebo for a total of 36 weeks – enrolment of the final 247th participant occurred in December last year and the last participant's final evaluation visit is expected in September this year
- Topline final results are due in November of this year, with subsequent presentation at a key Alzheimer's disease scientific meeting and publication in a peer-reviewed journal
- All XanaMIA participants are potentially eligible to participate in the open-label extension phase of the trial, due to open for enrolment in March, and will receive active Xanamem 10 mg
- A second pivotal trial, similar to XanaMIA but larger, will commence in 2027 in multiple countries including Australia, along with open-label and clinical pharmacology trials. This relatively streamlined path to approval in the US, including the design of the new trials, was agreed with the FDA in a Type C meeting last year.

Actinogen CEO and MD, Dr Steven Gourlay said:

"The positive recommendation from our independent Data Monitoring Committee is an important milestone in the successful conduct of our XanaMIA pivotal trial in patients with Alzheimer's disease. We look forward to November when we can report final topline results for the full dataset of 247 participants. In the meanwhile, we hope that as many XanaMIA participants as possible take up the opportunity for a longer period of active Xanamem therapy in the new open-label extension phase of the trial which will run for approximately two years."

Dr Dana Hilt, CMO, commented:

"*We are highly confident in the expert review conducted by the Data Monitoring Committee which was chaired by Dr Hans Moebius, who is a highly experienced Alzheimer's leader and trials expert. 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.*"

View this announcement on our InvestorHub: https://investors.actinogen.com.au/link/ya3Npr

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Announcement authorised by the Board 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 220 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. The trial is now closed to recruitment, with final topline results 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 will evaluate safety and a limited number of efficacy endpoints such as the CDR-SB. The trial will commence in Q1 2026 and be 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 approximately 400 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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