



ASX ANNOUNCEMENT

Strong recruitment enables early completion of pTau screening in Actinogen's XanaMIA Alzheimer's trial with final results projected mid Q4 2026

Sydney, 20 October 2025. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that due to the recent accelerated screening and enrolment in the XanaMIA phase 2b/3 Alzheimer's disease (AD) trial the Company will close pTau screening early on October 31.

Key points are:

- pTau biomarker screening closes to new participants October 31 (previously November 30)
- Projected total enrolment is now ~240 participants (previously 220)
- Currently 180 participants are enrolled
- Another ~60 participants expected to be enrolled by the end of the year
- Projected topline final results are confirmed for mid Q4 of next year (previously Q4)
- Data from the extra participants will boost the statistical power of the trial.

The robust enrolment in the XanaMIA trial validates the attractiveness of Xanamem® as an oral, easy-to-use therapy for AD with a novel mechanism designed to control elevated brain cortisol (aka the "stress hormone"). The trial was designed using data from the analysis of 34 AD patients from the previous XanADu phase 2 trial with a diagnosis confirmed by elevated pTau181 levels. This analysis showed a large Xanamem benefit on the CDR-SB endpoint after just 12 weeks of treatment. Xanamem has also shown benefits on depressive symptoms in a recent phase 2 trial.

The XanaMIA Phase 2b/3 Alzheimer's disease trial is a double-blind, 36-week treatment, placebo-controlled, parallel group design trial in participants with mild to moderate AD and progressive disease, determined by clinical criteria and confirmed by an elevated level of the pTau181 biomarker in blood. After a second screening visit to evaluate additional factors, participants then receive Xanamem 10 mg or placebo, once daily, and its ability to slow progression of AD 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.

A formal interim analysis of safety and efficacy futility will be conducted by an independent Data Monitoring Committee in late January 2026. Details of the interim analysis were announced on 30 June 2025 and can be viewed by [clicking here](#).

Actinogen CEO and MD, Dr Steven Gourlay commented:

"We are excited to be entering the last stages of the XanaMIA trial which, reflecting the recent agreement with the FDA, will be one of two pivotal trials forming the core of our marketing applications for regulatory approvals. Accelerated enrolment in the trial is consistent with our positive market research with physicians on the potential safety and efficacy advantages of oral Xanamem compared with approved Alzheimer's therapies such as anti-amyloid antibody infusions. We are grateful to the clinical teams, participants and their families for their dedication and keen interest in the Xanamem program."

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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 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.

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 will be fully enrolled by the end of 2025 with initial results from an interim analysis in late January 2026 and final topline results in mid Q4 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, 11 β -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 video, [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 11 β -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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