ASX ANNOUNCEMENT

Actinogen confirms 100th participant in XanaMIA phase 2b/3 Alzheimer's disease trial and interim analysis timeline

Sydney, 30 June 2025. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that the 100th participant in its pivotal XanaMIA phase 2b/3 randomized trial of Xanamem® for Alzheimer's disease (AD) has now passed all screening tests and is scheduled for randomization and treatment in July. This establishes the timeline for the planned safety and efficacy futility interim analysis by an independent Data Monitoring Committee (DMC).

Highlights:

- More than 100 eligible participants are now enrolled in the XanaMIA AD trial, with the 24-week visit "trigger" for interim data analysis based on those participants occurring in late December 2025
- The DMC review of all available interim data will occur in January 2026 after which the results of the interim analysis will be announced
- Final trial results for 220 participants are anticipated in Q4 2026.

The DMC comprises independent clinical and statistical experts who are not connected to the day-to-day conduct or analysis of the trial. The committee will review, in a highly confidential process, unblinded data for safety and efficacy futility from all available participant visits including many who will have completed the 36-week treatment period.

"Unblinded data" refers to data tables, figures and listings where the assignment of participants to Xanamem or the placebo control treatment will be known only to the DMC members. It will then make a recommendation to the Company about the continuation and conduct of the trial without disclosing details of the data review.

While Xanamem's safety is carefully monitored throughout the trial in an ongoing process, DMC review of unblinded safety data will add a significant amount of additional information to ensure the conduct of the trial is optimal.

An "efficacy futility" analysis will review key efficacy endpoints to ensure that the eventual outcome of the trial is not futile according to customary analytic methods for DMC reviews of this type. The DMC may not stop the trial early for 'success' and would recommend stopping the trial only if the futility criteria are met or there are major safety concerns. Actinogen believes that fully enrolling the 220 planned participants will ensure that the safety and efficacy of oral Xanamem 10 mg daily will be robustly demonstrated and as a result support the earliest possible regulatory approval of the drug.

During the second half of 2025, the Actinogen clinical, nonclinical, manufacturing and regulatory teams will meet with the US FDA[1] to discuss the detailed potential pathways to FDA approval of Xanamem for Alzheimer's disease, including expedited pathways should the XanaMIA trial show much stronger efficacy and

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[1] US FDA is the United States Food & Drug Administration

safety than currently available treatments. As a base case, Actinogen is planning its regulatory approval pathways according to "conventional" oral therapy guidelines for important and common diseases such as AD. The next, phase 3 stage of development may involve one or more commercial partnerships to assist in trial conduct, regulatory submissions and commercial launch preparation.

Oral Xanamem is a unique treatment approach that targets control of cortisol levels in brain regions relevant to memory and cognitive function where the 11-β HSD1 enzyme is highly expressed. It has the potential to be used alone or in combination with other approved treatments because of its low drug interaction potential and the ease and convenience of a once-daily pill.

Summary of Xanamem's Alzheimer's disease program timeline:

- H2 2025 – FDA meeting to review planned program for US regulatory approval
- Q4 2025 or January 2026 – Full enrolment of 220 XanaMIA phase 2b/3 trial participants
- January 2026 – Independent DMC review of safety and efficacy data for XanaMIA
- Q1 2026 – Open-label extension trial enrols the first patient following on from XanaMIA
- Q4 2026 – Final XanaMIA results announced
- Q1 2027 – Commencement of second pivotal, phase 3 trial.

Actinogen Chief Executive Officer, Dr Steven Gourlay, said:

"We are delighted to confirm the timeline for our independent Data Monitoring Committee review of safety and efficacy data based on the enrolment of the 100th patient in the XanaMIA phase 2b/3 Alzheimer's trial. This confidential review of unblinded data will ensure the XanaMIA trial is on-track and that Xanamem continues to perform as a promising and well-tolerated, once-a-day oral therapy."

"Furthermore, with our 35 Australian and US clinical sites now enrolling at full pace, we are able to reconfirm our guidance for final results in late 2026. The availability of a follow-on, open-label trial where all will receive active Xanamem therapy should give participants and their families more incentive to participate in the current XanaMIA trial as well as provide valuable long-term safety and efficacy data."

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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.

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. Initial results from an interim analysis triggered by the 100th participant reaching 24 weeks of treatment are anticipated in January 2026 and final results Q4 2026.

The XanaMIA-DUR Alzheimer's disease open-label extension trial is an open-label trial of up to 24 months 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 of action is to control the level of cortisol in the brain through the inhibition of the cortisol synthesis enzyme, 11β-HSD1, without affecting production of cortisol by the adrenal glands. Xanamem is a first-in-class, once-a-day pill designed to deliver high levels of cortisol control in the brain. 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.

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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