ASX ANNOUNCEMENT

Actinogen receives positive EMA scientific advice aligned with prior FDA guidance for its Alzheimer's disease program

Sydney, 28 May 2026. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce receipt of the successful outcomes of its scheduled scientific advice meeting (written response) on Alzheimer's disease (AD) with the European Medicines Agency (EMA).

Actinogen and the EMA reached a common understanding of the pathway to marketing approval in AD - meaning specification of regulatory starting materials in drug substance synthesis, design considerations for one additional pivotal clinical trial and the limited number of ancillary clinical pharmacology trials and nonclinical studies required. Key understandings include the:

1. Agreement on the suitability of the 'Regulatory starting materials' for the commercial manufacturing of Xanamem® (emestedastat) drug substance
2. Design of one additional, well-controlled, pivotal (phase 3) trial to follow a positive XanaMIA pivotal trial using a 10 mg dose vs. placebo
3. An EMA preference to broaden the inclusion criteria for the trial to encompass more AD patients with moderate disease severity
4. Total number of people to be treated with Xanamem to be described in the Marketing Authorization Application – that is, the proposed makeup of the planned safety database is consistent with EMA and FDA guidelines
5. Small number of ancillary clinical pharmacology trials to be conducted parallel with the next pivotal trial
6. Nonclinical studies required to further characterize the safety, metabolism and excretion pathways of Xanamem.

The outcome reached at this meeting aligns closely with the guidance received at an earlier meeting with the FDA's Neurology-I Division. With the new EMA advice, Actinogen now has a clear pathway and guidance towards marketing approvals in the two largest global pharmaceutical markets. Approvals in the US and EU also significantly contribute to approvals in many other countries and regions. The advice from both the FDA and EMA provides f regulatory clarity for ongoing discussions with potential development and marketing partners.

Dr Steven Gourlay, the Company's CEO and MD, said:

"We are pleased with the clear guidance from the EMA that closely conforms with our plans for streamlined development of Xanamem in Alzheimer's disease, as agreed previously with the FDA. Importantly, the EMA agreed with our approach for only one additional, pivotal trial using a single 10 mg Xanamem dose vs. placebo to support a marketing application for Alzheimer's in the EU."

® Xanamem is a registered trademark of Actinogen Medical Limited

Dr Dana Hilt, the Company's CMO said:

"With positive feedback from both the FDA and EMA on our Xanamem program, we look forward to potentially groundbreaking XanaMIA trial results in November. Such results would provide important evidence that control of brain cortisol can safely slow the progression of Alzheimer's disease. Our second pivotal trial in patients with mild to moderate Alzheimer's disease would then commence mid next year in multiple regions."

View this announcement on our InvestorHub: https://investors.actinogen.com.au/link/PQRK4y

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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. 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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