ASX ANNOUNCEMENT

Actinogen trial using intended commercial Xanamem tablet formulation confirms target exposures in fed and fasted states

Sydney, 26 August 2025. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that a recent trial designed to confirm therapeutic blood levels of the intended commercial tablet formulation of Xanamem®, given both with and without food, demonstrated the expected blood levels or "exposure", comparable with prior studies of a capsule formulation. This indicates that 10 mg once daily remains the target therapeutic dose for the clinical program.

The trial was conducted at the CMAX clinical research centre in Adelaide, where 16 individuals were studied on two occasions, one week apart. Each received a 10 mg tablet of Xanamem once while fasting and once after a high fat meal. Blood levels of Xanamem were then measured frequently over the ensuing 48 hours.

Key results include the median time to maximum blood concentration of 4 to 6 hours (4 hours fasted, 6 hours after a high fat meal), and very similar Xanamem exposures (area under the concentration-time curve) and elimination half-life of 15 hours in both fed and fasted situations.

Professor Paul Rolan, Actinogen's Clinical Pharmacologist commented:

"This trial confirmed that the intended commercial formulation of Xanamem produces consistent and therapeutic levels in the blood that are similar when given with or without food, giving full flexibility for dosing. These data support the use of the 10 mg daily dose irrespective of food intake in the on-going XanaMIA phase 2b/3 trial in people with mild to moderate Alzheimer's disease. Xanamem is a remarkable oral therapeutic with low drug interaction potential, and a 15-hour half-life suitable for once daily dosing in an elderly population."

ENDS

Dr. Steven Gourlay
CEO & Managing Director
P: +61 2 8964 7401
E. steven.gourlay@actinogen.com.au

Investors

Michael Roberts
Investor Relations
M: +61 423 866 231
E. michael.roberts@actinogen.com.au

Media

George Hazim
Media & Public Affairs Australia
M: +61 417 516 262
E: georgehazim@mediaaffairs.com.au

Announcement authorised by the Board of Directors of Actinogen Medical

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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 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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