



ASX ANNOUNCEMENT

Actinogen XanaMIA pivotal Alzheimer's disease trial completes final patient visit, confirming topline results remain on track for November

Sydney, 23 September 2026. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that following the final trial participant visit yesterday in the USA, the Company can now confirm that topline results for the XanaMIA phase 2b/3 Alzheimer's disease (AD) clinical trial remain on track for November this year.

Highlights of the XanaMIA trial of oral Xanamem® are:

1. Xanamem (emestedastat) is a promising, oral enzyme inhibitor designed to control elevated levels of the "stress hormone" cortisol in the brain, which are associated with the onset and progression of AD
2. XanaMIA is designed as a randomized (1:1), double-blind, placebo-controlled pivotal trial comparing Xanamem 10 mg to placebo treatment over 36 weeks
3. Following the randomized phase of the trial all participants may enrol in an open-label extension phase where they receive Xanamem 10 mg
4. The trial has now completed all patient visits with 247 participants enrolled in both Australia (45%) and the US (55%)
5. Selecting participants with elevated pTau181 is a key feature of the trial, using a clinically validated blood test instead of more complex methods such as amyloid brain scans or cerebrospinal fluid biomarkers to diagnose AD
6. Elevated pTau181 selects for participants with a more progressive disease course, increasing the trial's power to detect a treatment effect for Xanamem over 36 weeks and replicating the diagnostic profile of the phase 2a patient population where a large treatment benefit for Xanamem was seen ([Taylor et al. 2024](#))
7. As reported earlier in the year, enrolled participants have baseline clinical, genetic and laboratory characteristics similar to those reported in other trials of patients with mild to moderate AD:
 - a. Average age of 75 years
 - b. 49% female
 - c. 66% ApoE4 carriers (main AD genetic risk factor)
 - d. Mean (SD) pTau181 2.6 (1.3) pg/mL
 - e. Mean (SD) CDR-SB 4.3 (2.0) points.
8. The trial will report topline, final results in November.

Dr Dana Hilt, Actinogen CMO, commented:

"Xanamem is a unique oral therapy with the potential to become a transformational treatment option for patients and their families living with Alzheimer's disease. Our key focus is to finalise high-quality data from the XanaMIA pivotal trial for release in November while planning streamlined pathways to the fastest possible regulatory approvals for Xanamem."

View this announcement on our InvestorHub: <https://investors.actinogen.com.au/link/e9BXBr>

© Xanamem is a registered trademark of Actinogen Medical Limited

Actinogen Medical Limited ACN 086 778 476
Suite 901, Level 9, 109 Pitt Street, Sydney NSW 2000

+61 2 8964 7401 | actinogen.com.au

ENDS

Investors

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

Michael Roberts
Communications
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 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. The peer-reviewed publication relating to this trial can be accessed for free via this link: <https://tinyurl.com/ckm63z63>.

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 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 11 β -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.

Disclaimer

This announcement and attachments may contain certain "forward-looking statements" that are not historical facts; are based on subjective estimates, assumptions and qualifications; and relate to circumstances and events that have not taken place and may not take place. Such forward looking statements should be considered "at-risk statements" - not to be relied upon as they are subject to known and unknown risks, uncertainties and other factors (such as significant business, economic and competitive uncertainties / contingencies and regulatory and clinical development risks, future outcomes and uncertainties) that may lead to actual results being materially different from any forward looking statement or the performance expressed or implied by such forward looking statements. You are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof. Actinogen Medical does not undertake any obligation to revise such statements to reflect events or any change in circumstances arising after the date hereof, or to reflect the occurrence of or non-occurrence of any future events. Past performance is not a reliable indicator of future performance. Actinogen Medical does not make any guarantee, representation or warranty as to the likelihood of achievement or reasonableness of any forward-looking statements and there can be no assurance or guarantee that any forward-looking statements will be realised.

ACTINOGEN MEDICAL ENCOURAGES ALL CURRENT INVESTORS TO GO PAPERLESS BY REGISTERING THEIR DETAILS WITH THE DESIGNATED REGISTRY SERVICE PROVIDER, AUTOMIC GROUP.