ASX ANNOUNCEMENT

Actinogen presents XanaMIA trial screening efficiency and baseline population data at the Australian Dementia Research Forum

Sydney, 1 June 2026. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce the presentation of an academic poster highlighting screening efficiency and baseline population characteristics from the fully enrolled XanaMIA phase 2b/3 trial of Xanamem® (emestedastat) in patients with mild to moderate Alzheimer's disease (AD). The poster is being presented today at the Australian Dementia Network's Australian Dementia Research Forum (ADRF) in Sydney, Australia.

Highlights of the XanaMIA trial presentation are:

1. Xanamem® (emestedastat) is a promising, oral enzyme inhibitor designed to control elevated levels in the brain of the "stress hormone", cortisol, which are associated with the onset and progression of AD
2. The trial is fully enrolled with 247 participants
3. Participants have baseline clinical, genetic and laboratory characteristics comparable to those reported in other trials in patients with mild to moderate AD
4. The minimum requirement for elevated blood pTau181 level used to qualify patients, using the Lumipulse® assay, was 1.6 pg/mL and at baseline the mean level was 2.55 pg/mL (range 1.6 to 18.6 pg/mL)
5. Selecting patients 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 brain fluid biomarkers
6. Elevated pTau181 selects for patients with a more progressive disease course, increasing the trial's power to detect a treatment effect for Xanamem over 36 weeks and replicating the phase 2 patient population where a large treatment benefit for Xanamem was seen (Taylor et al. 2024)
7. The trial's relatively economical 2-stage screening approach improved screening efficiency and reduced costs by an estimated 43% by excluding a large number of people with low pTau levels at a brief "pre-screening" visit
8. The trial will report topline, final results in November.

A copy of the poster, titled "Optimised Screening Efficiency and Baseline Characteristics of a Phase 2b/3 Randomized, Placebo Controlled 36 Week Trial of Emestedastat in Mild to Moderate Alzheimer's Disease," is attached to this announcement.

View this announcement on our InvestorHub: https://investors.actinogen.com.au/link/P4zJze

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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.

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.

Optimised Screening Efficiency and Baseline Characteristics of a Ph2B/3 Randomized, Placebo-Controlled 36-Week Trial of Emestedastat in Mild to Moderate Alzheimer's Disease

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Actinogen

Background

Emestedastat is an oral, selective 11β-HSD1 inhibitor that decreases brain cortisol. Clinical trials of a 10mg daily dose have demonstrated adequate target engagement and/or clinical benefit by PET imaging, antidepressant activity, improvements in cognitive performance in healthy older adults, and attenuation of CDR-SB decline in pTau181-elevated clinically diagnosed Alzheimer's Disease (AD) patients.

As shown in Fig. 1, and by other groups ptau181 selects for progressive AD

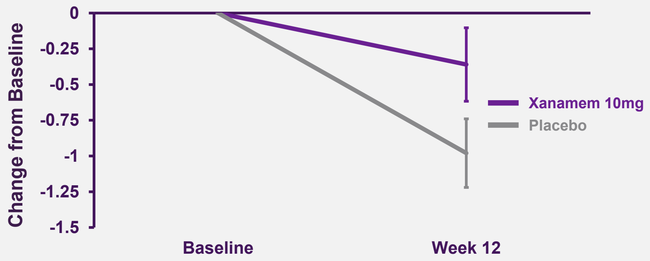

Fig 1: CDR-SB change from baseline scores over 12-week treatment period in previous Phase 2 randomised trial. In patients with a clinical diagnosis of AD and elevated plasma pTau181, 10mg daily emestedastat was associated with a slower mean rate of CDR-SB decline (0.36) vs placebo (0.98; Cohen's d=0.41, p=0.09).

Methods

XanaMIA is a multicentre, double-blind, randomised, placebo-controlled Phase 2B/3 trial in mild to moderate AD. Inclusion criteria include age ≥ 50, CDR global score 0.5-1.0, MMSE 18-26, and elevated plasma pTau181 (≥ 1.6 pg/ml; LumiPulse). Stable symptomatic AD medications were allowed. Participants were randomised 1:1 to daily emestedastat 10mg or placebo for 36 weeks, with 4 weeks blinded follow up.

The trial used a 2-staged screening process comprising a pre-screening visit followed by a screening visit. The primary purpose of the pre-screening was to exclude participants without elevated pTau181 early to improve efficiency and reduce participant screening burden.

The primary endpoint is change from baseline to Week 36 in CDR-SB. Key secondary endpoints include a digital cognitive test battery (CTB) assessing global cognition and the Amsterdam Instrumental Activities of Daily Living (A-iADL). Emestedastat's effect on plasma biomarkers of AD (pTau181, pTau217), neurodegeneration (NfL, GFAP), other markers of neuroinflammation will also be evaluated.

Demographics and baseline characteristics

Age (yrs) mean (SD), min to max	74.5 (8.0), 50 to 91
Sex n (%)	
Male	126 (51.0)
Female	121 (49.0)
Country enrolled (%)	
Australia	111 (44.9)
USA	136 (55.1)
Race n (%)	
White	233 (94.3)
Black / African American	6 (2.4)
Asian	4 (1.6)
Other	4 (1.6)
APOE* n (%)	
e2/e3	8 (3.3)
e2/e4	7 (2.9)
e3/e3	66 (27.3)
e3/e4	119 (49.2)
e4/e4	41 (16.9)
Concomitant AD medication n (%)	
Donepezil	107 (43.3)
Galantamine	8 (3.2)
Rivastigmine	9 (3.6)
Memantine	43 (17.4)
MMSE mean (SD)	21.8 (3.25)
CDR-Global mean (SD)	0.73 (0.33)
CDR-SB mean (SD)	4.3 (1.95)
pTau181 pg/mL mean (SD)	2.55 (1.33)
median (range)	2.31 (1.60 to 18.6)†

† 18.6 pg/mL is an outlier

Participant flow with staged screening approach

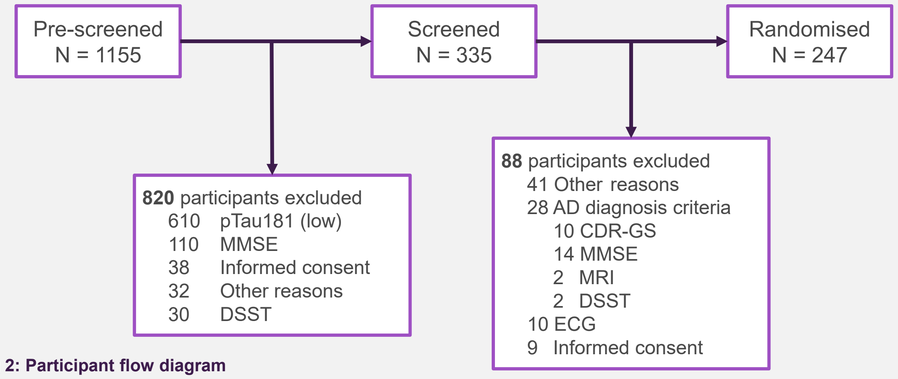

Fig 2: Participant flow diagram

Reducing cost and patient burden

The XanaMIA trial's 2-staged screening approach improved trial efficiency. By excluding participants with low pTau181 at the pre-screening visit, a total of 819 full patient screening visits were saved. This equates to a 42.9% reduction in screening costs compared to a single screening visit approach (Fig. 3).

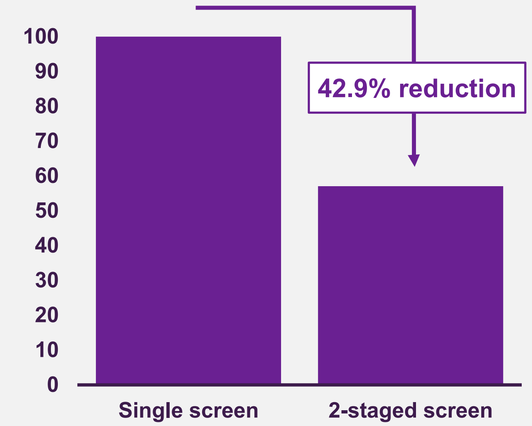

Fig 3: % cost reduction of a 2-staged screening approach compared to a single screening visit. Average site costs for the pre-screening and screening visits were used.

Conclusions

- **A 2-staged method improved screening efficiency in this contemporary AD trial**
- **Plasma pTau181 selects for a progressive AD population ideal for evaluating potential emestedastat benefits over 36-weeks**
- **The enrolled population is typical for a mild / moderate AD population**
- **Topline results are expected in November 2026**

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