Alzheimer’s Pill Trial Results: Xanamem Misses Main Goal; Over-75 Gain Rests on No-Progression Rate

Actinogen shares plunge 82% after only no-progression rate in patients over 75 reached significance

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Blood specimen collection tubes are seen in the laboratory of Bellville Medical Center, in Bellville, Texas, September 1, 2021. - Hospitals in Texas are overwhelmed due to record numbers of Covid-19 hospitalizations. In rural areas, the most seriously ill patients are stuck in facilities that are not equipped to handle them. Every day, one of them dies because they cannot find a place in a facility better suited to their needs. (Photo by Francois PICARD / AFP) (PHOTO: FRANCOIS PICARD/AFP VIA GETTY IMAGES)

Actinogen Medical's once-daily Alzheimer's pill Xanamem (emestedastat) missed the primary goal of its pivotal XanaMIA trial, with a **0.10-point gap versus placebo** on the 18-point Clinical Dementia Rating Sum of Boxes (CDR-SB) that was not statistically significant, the Sydney company said Thursday. The only significant result came from patients older than 75, and it was an analysis of **how many people did not worsen**, not the company's headline 30% slowing of decline, which missed significance.

Shares in the ASX-listed company (ACW) **fell 82% to A$0.008**, about half a U.S. cent. For patients, caregivers and investors, the question is what a result that misses overall and succeeds on one measure in one subgroup can actually support. All efficacy figures come from **Actinogen's own topline release** and have not been peer reviewed.

Primary Endpoint Missed: Dementia Scale Gap of 0.10 Points, p=0.65

XanaMIA **randomized 247 people** in Australia and the US who had mild to moderate Alzheimer's disease and elevated blood levels of the biomarker pTau181. Participants received 10 mg of Xanamem daily or placebo for 36 weeks. The primary endpoint was change on CDR-SB, an 18-point scale on which higher scores mean worse dementia. Xanamem **led placebo numerically** at weeks 12, 24 and 36, but **the gap at week 36** was 0.10 points (p=0.65).

Only Zero-Progression Rate in Patients Over 75 Reached Significance

	Overall population	Over 75 (prespecified subgroup)
CDR-SB benefit at week 36	0.10 points (p=0.65)	0.39 points (p=0.22)
Slowing of progression	Not reported	About 30% (company's figure)
Share with no CDR-SB progression	Not reported	40% Xanamem vs. 22% placebo (p=0.02)

Actinogen's **own release headline** reports clinical benefit in older patients, yet the 0.39-point gap in that group carried a p-value of 0.22. The release **does not state the subgroup size**. The subgroup is defined as patients older than the trial's median age of 75, so it likely holds around half the participants, though that is our inference. By our arithmetic, a 0.39-point gap equal to 30% slowing implies placebo patients over 75 declined about 1.3 points over 36 weeks.

Why Does Responder Analysis After Primary Miss Carry Less Weight?

A responder analysis counts how many people cross a threshold, here "no CDR-SB progression," instead of averaging scores. Actinogen calls the over-75 analysis prespecified, but the 0.02 result is still one of several looks at the data after the main test missed. When many tests run on the same data, the chance of **at least one false positive** rises with each added test; with 100 independent tests at the 5% level, it is roughly 99.4%. The sources we reviewed do not describe any adjustment for multiple testing.

Statistical significance is also separate from clinical importance. The **minimal clinically important difference** is the smallest change a patient would consider important, and no single method for calculating it is preferred. A **commentator quoted by Alzforum** said many would not count a 0.45-point CDR-SB gap as clinically important, putting that threshold closer to 0.9 points; others quoted in the same article argued that 0.45 points over 18 months is meaningful. That debate applies to Xanamem's 0.39-point over-75 gap even if it holds up.

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Interim Look Showed 0.58-Point Benefit in 88 Patients Before It Faded

In January 2026, an independent monitoring committee **reviewed an interim futility analysis** and recommended the trial continue without changes. That review covered 136 participants with at least one efficacy data point, and the committee **did not comment on efficacy** signals. Biotech Dispatch now reports that the unblinded interim data showed **a 0.58-point benefit at week 24** (p=0.03) among 88 participants, which Actinogen said was not fully sustained across all 247. The two participant counts differ, and the sources we reviewed do not explain why.

Lecanemab Slowed Decline 27% With Robust Statistics; Xanamem's 30% Did Not Reach Significance

In the 1,795-person Clarity AD trial, Eisai and Biogen's lecanemab slowed CDR-SB decline by 0.45 points at 18 months (p<0.001), about 27%. The trials differ in duration, population and size, and lecanemab's result was statistically robust while Xanamem's was not. Even lecanemab's gap drew debate over clinical meaningfulness among researchers.

Cortisol-Blocking Mechanism Has Now Missed Primary Goals in Trials by Two Companies

Xanamem inhibits 11β-HSD1, an enzyme that converts inactive cortisone into active cortisol and is highly expressed in the central nervous system. The hypothesis is that excess brain cortisol contributes to cognitive impairment, so lowering it might slow decline. This route pursues non-amyloid approaches to Alzheimer's, unlike the amyloid-clearing antibodies now on the market.

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The record for the class is mixed at best. AbbVie's 11β-HSD1 inhibitor ABT-384 was stopped for futility after 267 participants in a 12-week Alzheimer's trial and did not improve ADAS-Cog scores or any secondary endpoint. Actinogen's 2019 Phase 2 XanADu trial missed its primary and secondary endpoints, and shares fell 67% in morning trading. XanaMIA's overall result adds a third miss for the approach. The company chose to enrich XanaMIA for elevated pTau181 after a re-analysis of earlier XanADu data in biomarker-positive patients that did not meet conventional significance (p=0.09).

Gourlay said the company remains confident in Xanamem's risk-benefit profile in mild to moderate Alzheimer's disease. Market Index lists his direct holdings at about 181 million shares as of a June 24 notice.

Safety Record Held, but Adverse-Event Tables Are Not Public

The company says Xanamem's safety profile seen in earlier studies held over 36 weeks, with no serious adverse events attributed to the drug. It cites an established safety profile across more than 500 participants. We found no detailed adverse-event tables in the coverage reviewed.

is a small sample. Enrollment closed at 168 participants, and the next update is due in the first quarter of 2027.

Phase 3 Spending Suspended as Company Searches for Partner

Actinogen has suspended future Phase 3 spending. It said it will discuss the results with potential co-development partners, with a focus on older patients, and a new patent filing covers treating older patients with more advanced disease. The company also plans to **explore the data with the FDA** over the coming months. We found no confirmation that an FDA meeting is scheduled and no named partner in talks. The company had said earlier this year that a **second, larger pivotal trial** would start in 2027.

Actinogen held **A$18.9 million in cash** (approximately $12.3 million U.S.) with no debt, and the company expects its runway to extend into 2028.

Xanamem Remains Investigational and Unavailable Outside Trials

Xanamem is not approved by the FDA or any other regulator and is available only in clinical trials. Investors should note that the company is seeking a partner and has a commercial interest in how the results are read.

The full picture: XanaMIA missed its primary endpoint, the 0.39-point over-75 gap was not significant, only a no-progression rate reached significance in one subgroup, the early interim signal faded, and the same mechanism has failed two earlier primary tests. Further analyses are ongoing and will be **presented at a future scientific meeting**.

Decisions about Alzheimer's care belong with a patient's physician; this article is for information only and is not medical advice. This article is for informational purposes only and does not constitute investment advice. Readers should conduct their own due diligence before making investment decisions.

Currency conversions in this article use a rate of about 0.65 U.S. dollars per Australian dollar as of Nov. 19, 2026, and are approximate.

Frequently Asked Questions

Did the Xanamem trial succeed?

No on the primary goal. The overall gap on CDR-SB at week 36 was **0.10 points (p=0.65)**, which was not statistically significant.

No. It is investigational and available only in clinical trials.

Would a 0.39-point CDR-SB gain matter to patients even if it were real?

That is disputed. A commentator quoted by Alzforum put the threshold many consider clinically important **closer to 0.9 points**, while others in the same article argued that even 0.45 points is meaningful.

What does "no progression" mean for patients over 75?

It is a yes-or-no count of people whose CDR-SB score did not rise over 36 weeks: **40% on Xanamem versus 22%** on placebo (p=0.02). Actinogen calls it a prespecified analysis, but it was reported after the main test missed, so it is a lead for further testing, not proof of benefit.

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