Actinogen Medical Ltd (ASX: ACW) – Desk Note

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Xanamem Approaches a Defining Readout

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Company Snapshot

Company	Actinogen Medical Ltd (ASX: ACW)
Lead asset	Xanamem (emestedastat), a once-daily tablet that blocks cortisol production inside brain cells
Lead indication	Mild to moderate Alzheimer's disease
Shares on issue (pro forma)	3,866.1m
Share Price (2 Sep 2026)	$0.043
Market cap. (pro forma)	$166.2m
Net cash (pro forma)	$17.2m

Source: Iress and company announcements. Net cash consists of $16.7m cash, minus total financing facilities of $4.3m plus underwritten option proceeds of $4.8m. Shares on issue and market cap calculation include the 127.2m shares that will be issued on 23 September 2026 on exercise of underwritten options.

Actinogen is built around one big idea. That high cortisol, the body's stress hormone contributes to Alzheimer's disease progression. Its drug, Xanamem, is a once-daily pill that blocks the enzyme brain cells use to make cortisol (an enzyme called 11beta-HSD1) while leaving the adrenal glands' normal cortisol production alone. It is a genuinely different approach in a field dominated by antibodies such as Eli Lilly's Kisunla (donanemab) and Eisai's Leqembi (lecanemab) which target amyloid plaques (protein clumps that build up in the brains of Alzheimer's patients).

In November, we find out whether the idea works with topline results expected from the pivotal XanaMIA trial, a 247-patient study in mild to moderate Alzheimer's.

The trial has passed three independent expert reviews, including a confidential January interim analysis in which outside specialists looked at unblinded efficacy data and told the company to keep going. And with a $16.8 million raise completed over February and March and this week's underwriting of the remaining options, near-term financing risk ahead of the November readout has been materially reduced.

XanaMIA Trial

XanaMIA is a phase 2b/3 trial that enrolled 247 people with mild to moderate Alzheimer's across 35 sites in the United States and Australia. All participants had elevated plasma pTau181, enriching the trial for patients with underlying Alzheimer's disease biology. Those pTau181 levels are important because in the earlier XanADu trial, some enrolled patients may not have had Alzheimer's, which muddies results. This time they've made sure the patients genuinely have the disease biology the drug is meant to act on.

Participants were randomly assigned to take either Xanamem 10 mg or a placebo, one tablet a day for 36 weeks, with neither patients nor doctors knowing who was on what. The main measure of success is the CDR-SB, short for Clinical Dementia Rating scale, Sum of Boxes. It is a clinician's combined score of memory, thinking and day-to-day function, and it is the same yardstick used in the trials of the recently approved antibody drugs (Leqembi in 2023 and Kisunla in 2024).

The final participant was enrolled in December 2025, the last patient visits wrap up around September to October, and then the statisticians lock the database, break the blind and produce the topline result in November.

Along the way there have been three formal check-ins by the independent Data Monitoring Committee, a panel of outside clinical and statistical experts chaired by Alzheimer's trials veteran Dr Hans Moebius. The January meeting was the big one. The committee reviewed unblinded safety and efficacy data covering roughly 37 per cent of the expected final dataset, including 52 patients who had finished the full 36 weeks, and confirmed the trial cleared its pre-set futility hurdle. The June meeting reviewed safety across all 247 participants and again recommended no changes. The open-label extension has also seen high uptake, with 89% of eligible completers transitioning immediately and 108 patients on treatment as of the latest update.

Purpose of the Trial

The first purpose is to confirm the Phase 2a signal that underpins the current pivotal program. In the earlier phase 2a study, the 34 patients who had elevated pTau181 and received Xanamem declined by about 0.6 CDR-SB points less than placebo over just 12 weeks, a large effect for such a short window, although at p = 0.09 it fell short of formal statistical significance in a group that small. XanaMIA was purpose-built to answer the question properly. The same biomarker-selected patients and the same endpoint, but with seven times the patient numbers and three times the treatment duration.

The second purpose is competitive positioning. The approved anti-amyloid antibodies slow decline only modestly, are given by infusion or injection, and carry risks of brain swelling and bleeding that require MRI monitoring; in Australia they are not currently PBS-subsidised. Xanamem's pitch is a simple daily pill with, so far, no drug-related serious adverse events across roughly 500 people in eight clinical trials. A clearly positive XanaMIA result would position Xanamem as the first oral therapy shown to convincingly slow Alzheimer's decline.

The third purpose is regulatory. Actinogen has reached alignment with the US FDA and EMA on key elements of the remaining development pathway, including one additional pivotal trial of Xanamem 10 mg versus placebo following a positive XanaMIA result. If XanaMIA is strongly positive, Actinogen intends to explore expedited approval pathways with regulators while commencing the second pivotal study.

Next Steps

After the readout, the plan is regulator discussions on the fastest route to market, a second and larger pivotal trial targeted to begin mid-2027 in multiple regions, and continued accumulation of long-term data from the open-label extension. Partnering conversations with potential global and regional licensees are already underway and have been set up so interested parties can move quickly once the data land.

The Potential Prize

An estimated 7.4 million Americans aged 65 and older are living with Alzheimer's dementia in 2026, equivalent to around one in nine people in that age group, with prevalence projected to reach 13.8 million by 2060. Globally, WHO estimates 57 million people live with dementia, with Alzheimer's accounting for around 60–70% of cases. This is one of the largest and fastest growing unmet needs in medicine, and populations are only ageing.

A real market exists: Eisai's Leqembi did JPY 29.3 billion in the June 2026 quarter alone, up from JPY 23.1 billion a year earlier, and is guided to roughly JPY 143.5 billion, about US$905 million, for fiscal 2026. Lilly's Kisunla generated US$167m of sales in Q2 2026. They are achieving sales at premium prices, US$26,500 a year for Leqembi and about US$32,000 for Kisunla.

The opportunity is matched by substantial clinical risk. A 2019 review found that 99% of Alzheimer's trials historically showed no drug-placebo difference. More recent failures include Novo Nordisk's oral semaglutide in two Phase 3 trials, Johnson & Johnson's anti-tau antibody posdinemab and Lilly's oral OGA inhibitor ceperognastat.

Future Catalysts

Catalyst	Expected timing	Significance
XanaMIA topline final results	November 2026	The defining binary event: first pivotal evidence on whether cortisol control slows Alzheimer's
Scientific presentation and peer-reviewed publication of results	From November 2026	Independent validation in front of clinicians and potential partners
Regulatory discussions, including possible accelerated approval	Late 2026 into 2027	Could shorten time to market if results are strong
Second pivotal Alzheimer's trial begins	Mid-2027	Additional pivotal study whose key design parameters are aligned with FDA and EMA guidance
Open-label extension data	Ongoing	Long-term safety and efficacy observations supporting future filings

Indicative timing only. Events may be delayed, modified or may not occur.

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Peer Comparisons

The table below sets out listed companies developing clinical-stage therapies for Alzheimer's disease and other neurological disorders.

1 USD = 1.40 AUD

Company (Ticker)	Lead Assets, Indication and Delivery	Clinical Stage	Market capitalisation (AUD, m)
Neuren Pharmaceuticals (ASX: NEU)	NNZ-2591; Phelan-McDermid syndrome; oral Trofinetide (DAYBUE); Rett syndrome; oral	Phase 3 Marketed in the US	2,530.4
Anavex Life Sciences (NASDAQ: AVXL)	Blarcamesine; Alzheimer's disease; oral	Phase 2b/3 completed; EU application withdrawn Mar 2026 following a negative EMA opinion	372.4
Actinogen Medical (ASX: ACW)	**Xanamem; Alzheimer's disease; once-daily oral tablet**	**Phase 2b/3; topline Nov 2026**	**166.2**
Cognition Therapeutics (NASDAQ: CGTX)	Zervimesine; Alzheimer's disease and dementia with Lewy bodies; oral	Phase 2 ongoing	134.5
Alterity Therapeutics (ASX: ATH)	ATH434; Multiple System Atrophy; oral	Phase 2 complete; Phase 3 to commence by year-end 2026	114.8
INmune Bio (NASDAQ: INMB)	XPro; Alzheimer's disease (neuroinflammation); subcutaneous injection	Phase 2 complete, 2b/3 registrational program planned	87.0

Market Cap. sourced from Iress on 2 Sep 2026

November's result will answer a question the field has circled for two decades. Does lowering cortisol inside the brain actually change the course of Alzheimer's? XanaMIA gives the mechanism a fair test, in the biomarker-defined patients where the drug looked best, on the endpoint regulators care about, at properly powered scale. Whichever way the number falls, it will be a clean read.

The bull case: a daily pill demonstrating a clinically meaningful benefit relative to currently approved anti-amyloid therapies would be significant both clinically and commercially, and the regulatory path beyond it is already mapped with both the FDA and EMA. The bear case: most Alzheimer's trials fail, and the phase 2a signal came from only 34 patients and did not reach statistical significance on its own.

On the day, we will be watching the size of the CDR-SB benefit, its statistical significance, consistency across the cognition and daily-function measures, and the safety tables. A strong result changes this company's trajectory overnight, and from there the conversation moves quickly to accelerated approval and partnering.

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