Actinogen

ASX ANNOUNCEMENT

Actinogen September 2025 quarterly activity report and Appendix 4C

Sydney, 23 October 2025. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce the release of its quarterly activity report and Appendix 4C for the three-month period ended 30 September 2025.

Highlights and key events:

XanaMIA phase 2b/3 AD trial – accelerated enrolment achieves early closing of pTau screening and updated timeline for topline final results of mid Q4 2026 (previously Q4 2026). Interim analysis in January 2026

- The pivotal XanaMIA phase 2b/3 Alzheimer's disease (AD) trial is projected to enrol up to ~240 participants (original target 220) with elevated levels of the blood biomarker pTau181, designed to identify participants with biomarker-positive AD whose disease is likely to progress during the 36-week treatment period of the trial, and therefore augment the ability to detect a Xanamem® (emestedastat) treatment benefit
- As at 22 October 2025, 182 participants are enrolled in the trial at 35 sites across the US and Australia, with another ~60 expected to enrol before year's end
- A planned safety and efficacy futility interim analysis (IA) of all available data by an independent Data Monitoring Committee (DMC) will occur in late January 2026 after which the decision to continue or stop the trial will be announced
- Topline final results for ~240 participants are now expected in mid Q4 2026 (previously Q4).

Successful meeting with FDA on Alzheimer's program

- On 15 September 2025, the Company announced the successful conduct of its scheduled Type C meeting (written response) on AD with the US Food & Drug Administration's (FDA) Neurology-I Division
- Actinogen and the FDA reached a common understanding of the pathway to marketing approval in AD - meaning agreement on regulatory starting materials in drug substance synthesis, the streamlined design of one additional pivotal clinical trial and the limited number of ancillary clinical pharmacology trials and nonclinical studies required
- The outcome reached with the FDA represents a major milestone for Actinogen as the Company prepares for the earliest possible NDA[1] submission in the US and submissions to other global regulators. It also provides important clarity for ongoing discussions with potential development and marketing partners.

Clinical pharmacokinetic trial success

- In late August 2025, the Company announced the successful completion of a trial confirming 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
- The results were comparable with prior studies of a capsule formulation and indicate that 10 mg once daily remains the target therapeutic dose for the clinical program including the ongoing XanaMIA phase 2b/3 trial in people with mild to moderate Alzheimer's disease
- For further information, click here.

® Xanamem is a registered trademark of Actinogen Medical Limited

[1] NDA: New Drug Application

InvestorHub launch

- On 11 September 2025, the Company launched its new Investor Hub site for dedicated investor engagement
- The new site provides shareholders with the opportunity to view recent ASX announcements, shareholder news and key company updates all in one place
- Actinogen encourages investors to post questions and share feedback through the Q&A function accompanying each piece of content to engage with the leadership team and gain a better understanding of the company's announcements.
- To see and join the new Actinogen Investor Hub, visit: https://investors.actinogen.com.au/link/yMNWle

Manufacturing

- During the quarter, the newly manufactured batch of drug substance was successfully imported into the US without tariff imposition. This is being used for tablet manufacturing at a larger scale by Catalent in the US to supply the Xanamem clinical trial program. Scaled-up manufacturing is a key step towards regulatory approval of a commercial production process and an important component of preparedness for potential commercialization partnerships.

Other key activities

The Company continues to progress an important range of initiatives appropriate to late-stage clinical development. These include:

- **Commercial planning** – CCO, Mr Andy Udell, continues to refine the Company's communication materials to support a stronger presence at key AD scientific and business meetings and has updated information in the commercial readiness sections of corporate presentations
- **Partnering** – dialogue continues with multiple parties spanning potential regional and/or global partnership arrangements, with an emphasis on those organizations that are interested in AD or both AD and MDD. A number of parties are active in the Company's dataroom performing due diligence on Xanamem and the Company. The Company continues to engage with potential partners directly and at international partnering conferences such as the upcoming European BIO[2] biopartnering convention in early November
- **Intellectual property (IP) protection from future generic competition** – ACW continues prosecution of national phase patent applications for multiple new patents, designed to strengthen and extend IP protection for Xanamem beyond that afforded by earlier patents and the data exclusivity laws that apply to novel medicines
- **Other ancillary studies** – preparations continue for an open-label extension (OLE) trial to allow all participants in the XanaMIA trial access to longer-term active Xanamem therapy. This trial is due to commence in Q1 2026.

Presented at international and Australian conferences and conducted investment and partnering meetings:

- In late July 2025, CMO Dr Dana Hilt, and Senior Clinical Scientist, Dr Jack Taylor, presented an academic poster at the Alzheimer's Association International Conference (AAIC 2025) in Toronto, Canada. The poster was titled *Validating the cortisol hypothesis: Xanamem demonstrates positive clinical effects by lowering CNS cortisol in MDD* and describes the clinically and statistically significant benefits of Xanamem in patients with moderately severe major depressive disorder (MDD)

[2] Biotechnology Innovation Organization (BIO) is the world's largest advocacy association representing biotechnology companies, academic and research institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations.

- In early August 2025, CEO Dr Steven Gourlay presented to investors at the 2025 Bioshares Biotech Summit in Hobart in the *Drug Development Journey* session of the conference. Dr Gourlay's Q&A style presentation was titled *Oral Xanamem® (emestedastat) Controlling brain cortisol to slow progression in Alzheimer's disease and treat depression* and was designed to address important investor questions in ACW's drug development story to date. Dr Gourlay was joined at the conference by ACW's CFO Mr Will Souter
- On 21 October 2025, Dr Gourlay presented a short review to analysts and investors at the Canaccord Drug & Device Conference and conducted a number of small group meetings. The presence at this conference was designed to increase awareness of the advancing Xanamem program and the strong investment proposition Actinogen shares represent at the current market capitalization of ~$100m.

Actinogen CEO and MD, Dr Steven Gourlay said:

"The September quarter was significant for the achievement of further milestones for Actinogen. We are excited to be entering the last stages of the XanaMIA trial which, reflecting the recent agreement with the FDA, will be one of two pivotal trials forming the core of our marketing applications for regulatory approval in Alzheimer's disease. Rapid progress on XanaMIA trial enrolment has been amply demonstrated by achieving early closing of pTau screening and likely greater trial enrolment than originally anticipated. Guidance for the timing of expected topline results has been updated from Q4 2026 to mid Q4 2026."

Financial position

The Company incurred operating expenditure of $6.1m during the September quarter as XanaMIA clinical trial activity continued to ramp up, with all 35 sites actively recruiting.

On 15 October 2025, the Company received $5.5m in funding from the first tranche of its FY25 R&D tax incentive (RDTI) rebate.

After repaying the $3.0m Endpoints Capital loan (as announced on 30 June 2025), the Company received net proceeds of $2.4m. This additional funding supplemented the quarter end cash balance of $10.4m, such that after the recent rapid acceleration in enrolment during September and October the Company's net cash position as at the date of this report is $10.5m with an additional RDTI receivable of $1.9m pending, giving a proforma cash position of $12.4m.

The Company continues to have a cash runway to mid 2026.

It is anticipated that the additional RDTI funding of $1.9m will be received during the current quarter following the recent receipt of a positive Advance Overseas Finding in relation to eligible overseas R&D activities in FY25, primarily in relation to the XanaMIA trial. Following receipt of this further tranche, FY25 RDTI funding will total $7.4m.

Consistent with ASX Listing Rule 4.7c.3, item 6 of the attached Appendix 4C of the cashflow report for the quarter included payments to Related Parties of $0.28 million, comprising the salary and FY25 bonus for the CEO/Managing Director, fees paid to Non-Executive Directors, and superannuation.

View this announcement on our InvestorHub: https://investors.actinogen.com.au/link/rD1glP

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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 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. The trial will be fully enrolled by the end of 2025 with initial results from an interim analysis in late January 2026 and final topline results in mid Q4 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 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 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 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, further validating the cortisol control mechanism for the Xanamem 10 mg oral daily dose.

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.

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.

Appendix 4C

Quarterly cash flow report for entities subject to Listing Rule 4.7B

Name of entity

ACTINOGEN MEDICAL LIMITED

ABN	**Quarter ended ("current quarter")**
14 086 778 476	30 September 2025

Consolidated statement of cash flows	**Current quarter $A'000**	**Year to date (3 months) $A'000**
1 Cash flows from operating activities		
1.1 Receipts from customers	-	-
1.2 Payments for		-
(a) research and development	(4,309)	(4,309)
(b) product manufacturing and operating costs		-
(c) advertising and marketing		-
(d) leased assets		-
(e) staff costs	(1,611)	(1,611)
(f) administration and corporate costs	(608)	(608)
1.3 Dividends received (see note 3)		-
1.4 Interest received	127	127
1.5 Interest and other costs of finance paid	(7)	(7)
1.6 Income taxes paid		-
1.7 Government grants and tax incentives		-
1.8 Other (working capital movements)	308	308
1.9 Net cash from / (used in) operating activities	**(6,100)**	**(6,100)**
2 Cash flows from investing activities		
2.1 Payments to acquire or for:		
(a) entities	-	-
(b) businesses	-	-
(c) property, plant and equipment	(3)	(3)
(d) investments	-	-
(e) intellectual property	-	-
(f) other non-current assets	-	-
2.2 Proceeds from disposal of:		-
(a) entities	-	-
(b) businesses	-	-
(c) property, plant and equipment	-	-
(d) investments	-	-
(e) intellectual property	-	-
(f) other non-current assets	-	-
2.3 Cash flows from loans to other entities	-	-
2.4 Dividends received (see note 3)	-	-
2.5 Other (provide details if material)	-	-
2.6 Net cash from / (used in) investing activities	**(3)**	**(3)**

3	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	-	-
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	12	12
3.4	Transaction costs related to issues of equity securities or convertible debt securities	-	-
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings	-	-
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (application for exercise of options not yet allotted)		-
3.10	**Net cash from / (used in) financing activities**	**12**	**12**

4	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	16,504	16,504
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(6,100)	(6,100)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(3)	(3)
4.4	Net cash from / (used in) financing activities (item 3.10 above)	12	12
4.5	Effect of movement/adjustment in exchange rates on cash held	-	-
4.6	**Cash and cash equivalents at end of period**	**10,413**	**10,413**

	5 Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	**Current quarter $A'000**	**Previous quarter $A'000**
5.1	Bank balances	3,113	6,204
5.2	Call deposits	7,300	10,300
5.3	Bank overdrafts	-	-
5.4	Other	-	-
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**10,413**	**16,504**

	6 Payments to related parties of the entity and their associates	**Current quarter $A'000**
6.1	Aggregate amount of payments to related parties and their associates included in item 1	275
6.2	Aggregate amount of payments to related parties and their associates included in item 2	0

Note: if any amounts are shown in items 6.1 or 6.2, your quarterly activity report must include a description of, and an explanation for, such payments.

Payments relate to salaries & fees paid to Directors of the Company during the quarter.

	7 Financing facilities *Note: the term "facility' includes all forms of financing arrangements available to the entity.* *Add notes as necessary for an understanding of the sources of finance available to the entity.*	Total facility amount at quarter end $A'000	Amount drawn at quarter end $A'000
7.1	Loan facilities	-	-
7.2	Credit standby arrangements	-	-
7.3	Other (please specify)	-	-
7.4	**Total financing facilities**	-	-
7.5	**Unused financing facilities available at quarter end**		-

7.6 Include in the box below a description of each facility above, including the lender, interest rate, maturity date and whether it is secured or unsecured. If any additional financing facilities have been entered into or are proposed to be entered into after quarter end, include a note providing details of those facilities as well.

8 Estimated cash available for future operating activities	$A'000
8.1 Net cash from / (used in) operating activities (item 1.9)	(6,100)
8.2 Cash and cash equivalents at quarter end (item 4.6)	10,413
8.3 Unused finance facilities available at quarter end (item 7.5)	-
8.4 Total available funding (item 8.2 + item 8.3)	10,413
8.5 **Estimated quarters of funding available (item 8.4 divided by item 8.1)**	1.71

Note: if the entity has reported positive net operating cash flows in item 1.9, answer item 8.5 as "N/A". Otherwise, a figure for the estimated quarters of funding available must be included in item 8.5.

8.6 If item 8.5 is less than 2 quarters, please provide answers to the following questions:

8.6.1 Does the entity expect that it will continue to have the current level of net operating cash flows for the time being and, if not, why not?

Answer: Yes, the Company will have the current level of cash flows similar to the September 2025 quarter and anticipates being able to fund these as described below.

8.6.2 Has the entity taken any steps, or does it propose to take any steps, to raise further cash to fund its operations and, if so, what are those steps and how likely does it believe that they will be successful?

Answer: Post-quarter end, the Company received the Research & Development Tax Incentive (RDTI) proceeds of $5.5M (net $2.4M to the Company after repaying $3.1M loan) and an Advanced Overseas Finding confirming eligibility for a further $1.9M of RDTI rebate. The Company has access to other sources of capital through potential partnership transactions, R&D loan funding or further equity raising.

8.6.3 Does the entity expect to be able to continue its operations and to meet its business objectives and, if so, on what basis?

Answer: Yes, the Company has access to funding as described above.

Note: where item 8.5 is less than 2 quarters, all of questions 8.6.1, 8.6.2 and 8.6.3 above must be answered.

Compliance statement

1 This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.

2 This statement gives a true and fair view of the matters disclosed.

Date: 23 October 2025

Authorised by: By the Board
(Name of body or officer authorising release – see note 4)

Notes

1. This quarterly cash flow report and the accompanying activity report provide a basis for informing the market about the entity's activities for the past quarter, how they have been financed and the effect this has had on its cash position. An entity that wishes to disclose additional information over and above the minimum required under the Listing Rules is encouraged to do so.

2. If this quarterly cash flow report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, *AASB 107: Statement of Cash Flows* apply to this report. If this quarterly cash flow report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.

3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.

4. If this report has been authorised for release to the market by your board of directors, you can insert here: "By the board". If it has been authorised for release to the market by a committee of your board of directors, you can insert here: "By the [*name of board committee – eg Audit and Risk Committee*]". If it has been authorised for release to the market by a disclosure committee, you can insert here: "By the Disclosure Committee".

5. If this report has been authorised for release to the market by your board of directors and you wish to hold yourself out as complying with recommendation 4.2 of the ASX Corporate Governance Council's *Corporate Governance Principles and Recommendations*, the board should have received a declaration from its CEO and CFO that, in their opinion, the financial records of the entity have been properly maintained, that this report complies with the appropriate accounting standards and gives a true and fair view of the cash flows of the entity, and that their opinion has been formed on the basis of a sound system of risk management and internal control which is operating effectively.