ASX ANNOUNCEMENT

Actinogen December 2024 quarterly activity report and Appendix 4C

Sydney, 29 January 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 31 December 2024.

XanaMIA phase 2b/3 AD clinical trial progressing patient recruitment and randomization:

- The XanaMIA phase 2b/3 Alzheimer's disease (AD) trial is enrolling 220 participants 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
- The first US patient was randomized on 9 December 2024. Patient recruitment and randomization activities are stepping up following the expected slowdown over the holiday period, with the tenth US site recently reaching the active recruitment stage in addition to the 15 established sites in Australia
- The Company has an active recruitment 'funnel' consisting of more than 300 patients pre-screened for elevated blood pTau levels, with approximately 40 randomized and treated and more than 20 in the intermediate stages of the screening process
- An interim analysis is planned when approximately 100 patients reach 24 weeks of treatment – based on updated near-term enrolment projections this is anticipated in Q4 2025. The timeline for final results is unchanged and these are anticipated in H2 2026.

Commercial readiness initiatives:

The Company has provided clinical 'proof of concept' in two separate clinical indications to date – AD and major depressive disorder (MDD). These phase 2 trial data add to the validation of the Xanamem program from prior clinical trials in healthy volunteers and the high levels of target engagement in the brain seen with PET imaging. At this stage the Company believes Xanamem's action to control tissue production of cortisol in the brain, 'The Cortisol Hypothesis', is now well-established as a bona fide therapeutic mechanism.

With the Xanamem program in late-stage clinical development, the Company is actively engaging in an important range of initiatives to prepare for the approaching commercialisation phase. These initiatives include:

- **Regulatory meetings** – the Company continues to plan its path forward in both AD and MDD, with the focus for 2025 being implementation of the XanaMIA phase 2b/3 trial and meetings with regulators for both AD and MDD in order to understand registrational requirements for marketing approvals
- **Partnering** – with an emphasis on companies who are interested in both AD and MDD, dialogue continues with multiple parties spanning potential regional and global partnership arrangements, as well as

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investigation of Australian and overseas grant opportunities that could be used to support expansion of the AD and MDD clinical trial programs. Most recently, a team consisting of the CEO, CMO, CCO and CFO attended the Sachs Neuroscience Innovation Forum and other partnering meetings associated with the JPM Healthcare conference week in San Francisco. Numerous other conferences and meetings are scheduled in the 2025 calendar to facilitate discussions and highlight the quality of ACW's clinical data

- **Manufacturing** – during the quarter, the Company commenced production of a scale-up batch of drug substance from its contract manufacturer which will progressively be manufactured into Xanamem tablets for use in current and future trials. This step will also confirm readiness for eventual commercial quantity production to potential pharma partners and regulators
- **Publication of peer-reviewed academic papers** – two academic manuscripts were published in 2024 in the peer-reviewed *Journal of Alzheimer's Disease.* In 2025, we expect a clinical pharmacology peer-reviewed manuscript to be published during the March quarter and are in the process of submitting the XanaCIDD MDD trial manuscript for peer-reviewed journal publication later in the year
- **Unique International Nonproprietary Name (INN) granted by the World Health Organization (WHO)** earlier in January the WHO granted the nonproprietary name 'emestedastat' to Actinogen for Xanamem. An INN is a unique, globally recognized name for a pharmaceutical drug or active ingredient. Each active substance that is to be marketed as a pharmaceutical must be granted a unique name of worldwide acceptability to ensure the clear identification, safe prescription and dispensing of medicines to patients. Nonproprietary names are intended for wide use ranging from labelling and product information to drug regulation and scientific literature

  By granting the INN, the WHO recognized Xanamem (emestedastat) as the first drug to be named for the class of enzyme inhibitors of 11β-HSD1 by assigning it the unique suffix of '-stedastat' pertaining to its mechanism of action on 11β-HSD1. Emestedastat is a unique orally administered molecule in its own class as a 'brain tissue cortisol synthesis inhibitor'
- **Intellectual property protection from future generic competition** – as a new chemical entity and unique class of drug, Xanamem has additional commercial protection from data exclusivity laws independent of protection from approved patents. Data exclusivity means that generic manufacturers cannot use Actinogen's clinical or nonclinical data for a substantial period from the date of marketing approval and are thus effectively blocked from the market during that time. Data exclusivity periods vary by country, for example, five years in Australia and the US and ten years in the EU

  In contrast, patents typically have a period of 20 years from the date of grant. Actinogen has key patents granted for the Xanamem molecule's chemistry and during the quarter continued to prosecute newer patents in multiple countries covering the treatment of cognitively normal people, manufacturing process and the treatment of patients with depression
- **Ancillary nonclinical and clinical studies** – small clinical pharmacokinetic (measuring blood levels in the body) and nonclinical studies are being conducted in parallel with the XanaMIA trial appropriate to Xanamem's late-stage clinical development.

Presentations at key conferences and industry meetings:

- CEO Dr Steven Gourlay presented at the Dementia Trials Australia Annual Scientific Meeting in Sydney on 11 October 2024. His presentation, titled *Oral Xanamem:® How Xanamem's benefit on depressive symptoms translates to possible efficacy in Alzheimer's disease* included analysis of the important validation of Xanamem's mechanism of action to control brain cortisol provided by the anti-depressant activity identified in the XanaCIDD phase 2a depression trial

- CMO Dr Dana Hilt and Senior Clinical Scientist Dr Jack Taylor presented an academic poster at the Clinical Trials on Alzheimer's Disease (CTAD) conference in Madrid, Spain on 31 October 2024. The poster was titled: *Plasma pTau181 predicts clinical progression in mild Alzheimer's Disease in a randomized controlled trial* and presented data to show that elevated plasma pTau181 is useful in predicting clinical decline in patients with mild, clinically diagnosed AD
- Chief Medical Officer, Dr Dana Hilt, and CEO, Dr Steven Gourlay, presented at the Sachs Associates 8th Annual Neuroscience Innovation Forum in San Francisco earlier this month on 12 January. Their presentation was titled *Oral emestedastat (Xanamem®/UE2343): Controlling brain cortisol to slow progression in Alzheimer's disease*. While in San Francisco, members of the ACW leadership team participated in a significant number of partnering, analyst and investor meetings associated with the 43rd Annual J.P. Morgan Healthcare Conference from January 13 to 16, 2025 (JPM Week).

Actinogen CEO, Dr Steven Gourlay said:

"The new year has started strongly with a robust program of activities. We continue to step up recruitment in the XanaMIA Alzheimer's trial with growing confidence in a positive outcome, while putting the necessary ancillary activities in place to assess and meet regulatory requirements for future marketing approvals for AD and potentially MDD."

Financial position

During the quarter, the company's R&D expenditure ($2.3m) was consistent with the September quarter and primarily focused on accelerating recruitment for the XanaMIA Phase 2b Alzheimer's disease trial in Australia and the US. The significant influx of cash from the R&D tax incentive ($9.0m) which is classified as operating cash flow in the Appendix 4C, resulted in a positive operating cash position for the quarter of $5.3m.

A further $4.1m in cash inflows (before costs) was received from the final tranche of the company's $11.1m capital raising announced in the September quarter.

After accounting for these items above, the company's total cash position improved by $9.3m, resulting in a closing cash balance of $22.9m at 31 December 2024. Based on the current enrolment profile for the Alzheimer's clinical trial and other committed expenditure, the company is funded to mid-late CY2026.

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 $0.2 million, comprising the salary for the CEO/Managing Director, fees paid to Non-Executive Directors, and superannuation.

During December 2024, the Company issued 59.5m loan shares at an exercise price of $0.04 (4 cents) per share to 14 non-Director employees and key contractors pursuant to its employee incentive share plan.

ENDS

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Announcement authorised by the Board of Directors of Actinogen Medical

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.

Current Clinical Trials

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).

The **XanaMIA Phase 2b 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. Initial results from an interim analysis of the first 100 participants are anticipated in Q3 2025 and final results H2 2026.

About Xanamem (emestedastat)

Xanamem's novel mechanism of action is to control the level of cortisol in the brain through the inhibition of the cortisol synthesis enzyme, 11β-HSD1, without affecting production of cortisol by the adrenal glands. Xanamem is designed to get into the brain after it is absorbed in the intestines upon swallowing.

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.

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	31 December 2024

Consolidated statement of cash flows	**Current quarter $A'000**	**Year to date (6 months) $A'000**
1 Cash flows from operating activities		
1.1 Receipts from customers	-	-
1.2 Payments for		-
(a) research and development	(2,298)	(4,587)
(b) product manufacturing and operating costs	-	-
(c) advertising and marketing	-	-
(d) leased assets	-	-
(e) staff costs	(970)	(2,237)
(f) administration and corporate costs	(518)	(1,026)
1.3 Dividends received (see note 3)	-	-
1.4 Interest received	154	245
1.5 Interest and other costs of finance paid	(18)	(35)
1.6 Income taxes paid	-	-
1.7 Government grants and tax incentives	9,022	9,022
1.8 Other (working capital movements)	(70)	342
1.9 Net cash from / (used in) operating activities	**5,302**	**1,724**
2 Cash flows from investing activities		
2.1 Payments to acquire or for:		
(a) entities	-	-
(b) businesses	-	-
(c) property, plant and equipment	-	(2)
(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	**-**	**(2)**

3	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	4,130	11,105
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	3	1,118
3.4	Transaction costs related to issues of equity securities or convertible debt securities	(146)	(530)
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**	**3,987**	**11,693**

4	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	13,577	9,451
4.2	Net cash from / (used in) operating activities (item 1.9 above)	5,302	1,724
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	(2)
4.4	Net cash from / (used in) financing activities (item 3.10 above)	3,987	11,693
4.5	Effect of movement/adjustment in exchange rates on cash held	-	-
4.6	**Cash and cash equivalents at end of period**	**22,866**	**22,866**

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	4,066	3,077
5.2	Call deposits	18,800	10,500
5.3	Bank overdrafts	-	-
5.4	Other	-	-
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**22,866**	**13,577**

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	199
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)	(5,302)
8.2	Cash and cash equivalents at quarter end (item 4.6)	22,866
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	22,866
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	N/A
8.6	*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.* 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: 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: 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: *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: 29 JANUARY 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.