ASX ANNOUNCEMENT

Actinogen March 2025 quarterly activity report and Appendix 4C

Sydney, 30 April 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 March 2025.

XanaMIA phase 2b/3 AD clinical trial accelerating patient screening and enrolment:

- 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
- More than 560 people have been pre-screened with a blood pTau test. Sixty have entered the 36-week treatment phase of the trial and another 35 have passed pTau, most of whom are expected to be enrolled in the coming weeks
- Patient recruitment and randomization activities are accelerating further with the opening of new US clinical sites. There are 15 active recruitment sites in each of Australia and the USA, with a further five more US sites commencing active screening, bringing the total number of clinical sites to 35
- An interim analysis of all available data, including patients who have completed 36 weeks of treatment, will be triggered when approximately 100 patients reach 24 weeks of treatment. Based on updated near-term enrolment projections, this is anticipated in Q4 2025
- Final results are expected in Q4 2026
- Patients or families and carers of those interested in participating in the XanaMIA phase 2b/3 AD trial in the USA or Australia can seek further information and check for eligibility to join the trial by visiting the company's website.

Successful regulatory meeting with FDA

- In late March, the Company announced the successful conduct of its scheduled Type C meeting on major depressive disorder (MDD) with the US Food & Drug Administration (FDA)
- In a successful and collaborative meeting, Actinogen and the FDA reached a common understanding of the additional clinical trials, ancillary clinical pharmacology trials and nonclinical studies required to apply for marketing approval of Xanamem for MDD
- The agreements reached at the meeting with the FDA's Psychiatry Division represent a major accomplishment for the Company and will be important in future discussions with potential partners and granting bodies as sources of non-dilutive funding are sought to support the program

® Xanamem is a registered trademark of Actinogen Medical Limited

- A similar Type C meeting for Alzheimer's disease will be held with the FDA's Neurology Division later in 2025 to define the optimal path to a marketing approval.

New and unique name 'emestedastat' granted to Xanamem by World Health Organization (WHO)

- In January, the WHO granted the nonproprietary name (INN) 'emestedastat' to Actinogen for Xanamem
- 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 and brain-penetrant 'tissue cortisol synthesis inhibitor' designed to control levels of toxic cortisol in the brain.

Clinical pharmacology academic manuscript published in peer-reviewed journal

- In February, the company announced the publication of its latest peer-reviewed journal article titled *Clinical Pharmacology and Approach to Dose Selection of Emestedastat, a Novel Tissue Cortisol Synthesis Inhibitor for the Treatment of Central Nervous System Disease* in the journal associated with the American College of Clinical Pharmacology, *Clinical Pharmacology in Drug Development*
- The review confirms the utility of the 10 mg daily dose of Xanamem being used in current clinical trial. The journal article can be accessed here.

Manufacturing

- During the period, the company progressed production of a 15kg scale-up batch of drug substance from its contract manufacturer, Asymchem, which will be manufactured into Xanamem tablets for use in current and future trials. Scaled-up manufacturing is a key step towards regulatory approval of a commercial production process and important for potential commercialization partners.

Other key activities

With further clinical validation of the Xanamem 10 mg dose provided by the improvements seen on depression symptoms last year, the Company is confidently engaging in an important range of initiatives appropriate to late-stage clinical development. These include:

- **Commercial planning** – Andy Udell, Chief Commercial Officer, has been actively expanding thought leader engagement with AD experts across the US and refining our communication materials to support a stronger presence at key AD scientific and business meetings, ensuring we are strategically positioned for upcoming market opportunities
- **Strategic team additions** – The company continues to fill strategic operational roles to ensure the success of its clinical development program, including those required for the XanaMIA phase 2b/3 Alzheimer's disease trial in Australia and the USA
- **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. The company is also investigating Australian and international grant opportunities that could be used to support expansion of the AD and MDD clinical trial programs
- **Intellectual property (IP) protection from future generic competition** – prosecution of national phase patent applications for multiple new patents continued in the quarter, designed to strengthen and extend the IP protection for Xanamem

- **Ancillary nonclinical and clinical studies** – clinical pharmacokinetic (measuring blood levels in the body) and nonclinical studies are being conducted in parallel with the XanaMIA trial to support the Xanamem development program.

Presented at international and Australian conferences and conducted investment and partnering meetings associated with events and conferences, including as set out below:

- CEO Dr Steven Gourlay presented at the ASX small & mid-caps conference in Sydney on 26 March 2025. His presentation was titled *Oral Xanamem®* (emestedastat) *Controlling brain cortisol to slow progression in Alzheimer's disease and treat depression: enrolling pivotal Phase 2b/3 trial in Alzheimer's.* It outlined the attractive therapeutic profile of ACW's novel small molecule drug Xanamem and provides an update as the company approaches critical milestones in its phase 2b/3 Alzheimer's trial
- In early April, CMO Dr Dana Hilt presented an academic poster at the *19th International Conference on Alzheimer's & Parkinson's Diseases and Related Neurological Disorders* (AD/PD™25). Dr Hilt's poster was titled *Plasma pTau181 predicts clinical progression in mild Alzheimer's Disease in a randomised controlled trial*. The poster detailed the promising benefits of Xanamem treatment over 12 weeks in patients with elevated blood pTau181. It also reported that higher levels of blood pTau181 can identify patients with AD who have more rapid clinical progression

  Taken together, these data inform the design of the current XanaMIA phase 2b/3 pivotal AD trial[1] using the pTau181 plasma biomarker for selection of patients and the choice of its key endpoints of CDR-SB,[2] cognition and activities of daily living
- On 15 May 2025 the Company will be conducting another 'plain English' **Clinical Trials Science Forum** webinar titled: *The critical importance of preparing for commercialization*. CMO Dr Dana Hilt and Chief Commercial Officer Andy Udell will be joined by guest geriatrician A/Prof Michael Woodward to discuss the latest developments in the quest for effective Alzheimer's treatments and how Actinogen is preparing for the future commercialization of its novel once-a-day oral medication, Xanamem. Click here for event registration.

Actinogen CEO, Dr Steven Gourlay said:

"The first quarter of 2025 was a busy period for the team as the XanaMIA trial accelerated and many essential initiatives commenced in parallel with the trial, designed to prepare the Company for partnering and eventual marketing approvals. I was particularly pleased with the positive and clear outcomes from our Type C meeting with the FDA on MDD that provided excellent guidance for the Xanamem program."

Financial position

Successful funding activities during 2024 via equity capital raisings and the R&D tax rebate put the Company in a strong cash position leading into 2025, with an opening cash balance of $22.9m and no debt.

During the March quarter, the focus of the Company's activities continued to be on the rapid advancement of recruitment for the XanaMIA Phase 2b Alzheimer's disease trial in Australia and the US, with approximately

[1] A "pivotal trial" refers to a late-stage trial that will produce a key dataset for a marketing approval application. It is customary to have two well-designed pivotal trials to achieve approval by regulators such as the FDA for common diseases such as AD and depression.
[2] CDR-SB is the *Clinical Dementia Rating – Sum of Boxes*, a measure of patient functional abilities and a composite of cognitive tests of mental abilities considered a measure of executive function. It is an FDA approved rating scale and almost universally used in modern AD trials

$2.9m in R&D expenditure incurred. The other major expenditure item during the quarter was employment costs ($929k), the bulk of which is directly attributable to clinical trial and other R&D related activities.

Total cash used in operating activities during the quarter was $4.2m, and as such the Company closed the quarter with $18.7m and a cash runway to mid-late 2026.

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.

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.

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. Initial results from an interim analysis triggered by the 100th participant reaching 24 weeks of treatment are anticipated in Q4 2025 and final results Q4 2026.

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 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 a first-in-class, once-a-day pill designed to deliver high levels of cortisol control in the brain.

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 March 2025

Consolidated statement of cash flows	**Current quarter $A'000**	**Year to date (9 months) $A'000**
1 Cash flows from operating activities		
1.1 Receipts from customers	-	-
1.2 Payments for		-
(a) research and development	(2,883)	(7,474)
(b) product manufacturing and operating costs	-	-
(c) advertising and marketing	-	-
(d) leased assets	-	-
(e) staff costs	(929)	(3,180)
(f) administration and corporate costs	(617)	(1,639)
1.3 Dividends received (see note 3)	-	-
1.4 Interest received	251	496
1.5 Interest and other costs of finance paid	(9)	(30)
1.6 Income taxes paid	-	-
1.7 Government grants and tax incentives	-	9,022
1.8 Other (working capital movements)	(29)	313
1.9 Net cash from / (used in) operating activities	**(4,216)**	**(2,492)**
2 Cash flows from investing activities		
2.1 Payments to acquire or for:		
(a) entities	-	-
(b) businesses	-	-
(c) property, plant and equipment	36	36
(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	**36**	**36**

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

4	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	22,866	9,451
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(4,216)	(2,492)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	36	36
4.4	Net cash from / (used in) financing activities (item 3.10 above)	-	11,693
4.5	Effect of movement/adjustment in exchange rates on cash held	(1)	(3)
4.6	**Cash and cash equivalents at end of period**	**18,685**	**18,685**

	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	3,885	4,066
5.2	Call deposits	14,800	18,800
5.3	Bank overdrafts	-	-
5.4	Other	-	-
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**18,685**	**22,866**

	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)	(4,216)
8.2 Cash and cash equivalents at quarter end (item 4.6)	18,685
8.3 Unused finance facilities available at quarter end (item 7.5)	-
8.4 Total available funding (item 8.2 + item 8.3)	18,685
8.5 **Estimated quarters of funding available (item 8.4 divided by item 8.1)**	4.43

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:

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: 30 April 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.