ASX ANNOUNCEMENT

Actinogen June 2024 quarterly activity report and Appendix 4C

Sydney, 22 July 2024. 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 June 2024.

- **Positive Xanamem® phase 2a biomarker trial published in 100th edition of peer-reviewed journal, *The Journal of Alzheimer's Disease*[1]:**
    - Participants comprised 72 patients from the previous XanADu phase 2a trial of mild Alzheimer's disease (AD) who had available stored plasma (blood) samples and gave informed consent for the new trial
    - Patients with elevated pTau181 above the median level had much more rapid progression than patients with lower levels in four key clinical endpoints: ADCOMS ($p<0.001$), CDR-SB ($p<0.001$), MMSE ($p=0.12$) and ADAS-Cog14 ($p=0.19$)[2]
    - In the 34 patients with elevated pTau181 a potentially clinically meaningful Xanamem treatment effect compared to placebo was seen in the CDR-SB (LS[3] mean difference 0.6 units, $p=0.09$) and positive trends were observed in a Neuropsychological Test Battery of cognition (LS mean difference 1.8 units, p=NS).
- **XanaCIDD phase 2a clinical trial activities concluding:**
    - Achieved full enrolment of 167 participants - final patient visit was completed on 1 July 2024
    - The XanaCIDD trial is a phase 2a, proof-of-concept, placebo-controlled, parallel group trial in patients with cognitive impairment in major depressive disorder (MDD). Xanamem (10 mg) or placebo is added to the existing anti-depressant therapy or, in patients with a previous history of anti-depressant treatment, as a stand-alone treatment
    - The primary endpoint is the "Attention Composite" measuring attention and working memory, comprising three computerized cognition tests. This composite measure was observed to be a sensitive measure of Xanamem benefit in two prior trials in cognitively normal volunteers. Secondary endpoints include the Montgomery-Asberg Depression Rating Scale (MADRS) and other measures of cognition
    - Trial results are expected in the first half of August 2024.
- **XanaMIA phase 2b clinical trial start up progress:**
    - The Australian trial site start up process nears completion with twelve Australian clinical sites active, and three additional sites in the process of activation

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[1] Access the Journal of Alzheimer's Disease publication here

[2] ADCOMS: Alzheimer's Disease Composite Score; CDR-SB: Clinical Disease Rating Scale – Sum of Boxes; MMSE: Mini Mental State Examination; ADAS-Cog14: Alzheimer's Disease Assessment Scale – Cognition version 14

[3] Least squares

- The US site activation process has commenced with successful submission of the protocol to the FDA and processing of multiple trial contracts – it is anticipated that between five and ten US clinical sites will be added to the trial to maintain target enrolment
- The XanaMIA phase 2b Alzheimer's disease (AD) trial will enrol 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 thus augment the ability to detect a Xanamem treatment benefit
- Use of the tau protein as an imaging biomarker was successfully used by Eli Lilly Inc. in their program for donanemab, the newly approved anti-amyloid antibody for AD
- Sixty-eight participants from the first nine active sites have undergone pre-screening for elevated pTau181 levels with the planned "fail rate" of approximately half observed. Ten participants have been randomized and treated with additional participants at various stages in the screening phase
- An interim analysis will occur when approximately 100 patients reach 24 weeks of treatment (expected mid CY2025)
- Final results are anticipated in mid CY2026.

- **Presented successful Clinical Trials Science Forum focused on cognition**
  - In another informative Clinical Trials Science Forum in May, ACW CMO Dr Dana Hilt and guest experts explored the unique properties of Xanamem for the potential treatment of cognitive impairment in multiple diseases. Click here to view the video recording.
- **Presentations at key conferences and industry meetings:**
  - Clinical Scientist Dr Jack Taylor presented an academic poster at the Australian Dementia Research Forum (ADRF2024) in June. The poster, entitled *Clinical pharmacology and development of Xanamem®, a tissue specific inhibitor of 11β- HSD1*, describes Xanamem's clinical pharmacology, including Actinogen's innovative approach to dose selection. It summarized the multiple streams of data supporting the selection of Xanamem doses of ≤ 10 mg daily for the treatment of cognitive impairment in a number of diseases.
  - CMO Dr Dana Hilt will present a poster at the upcoming Alzheimer's Association International Conference (AAIC) in Philadelphia USA from 28 July to 1 August 2024. The AAIC is a leading global forum to advance dementia science
  - The Clinical Trials on Alzheimer's Disease (CTAD) conference scientific program has accepted an Actinogen poster submission which Dr Hilt will present during the conference in Madrid, Spain from 29 October to 1 November 2024.

Actinogen CEO, Dr Steven Gourlay said:

"We look forward to reporting on the results of our XanaCIDD phase 2a trial in patients with cognitive impairment and major depressive disorder. This robust, placebo-controlled trial of 167 people will inform us if Xanamem can improve cognition in these patients and assess any related effects on symptoms of depression itself.

"We sincerely thank the many investigators, patients and trial personnel in the XanaCIDD trial for their contributions to the investigation of this novel tissue cortisol synthesis inhibitor."

Financial position

During the quarter, the company continued to progress both the XanaCIDD Phase 2a cognition and depression trial, and the XanaMIA Phase 2b Alzheimer's disease trial, with $3.78 million incurred in relation to these programs. Staff costs of $0.95 million, and other cash outflows remained consistent with prior quarters,

resulting in overall net operating cash outflows for the quarter of $5.09 million. As the XanaCIDD Phase 2a trial concludes, cash outflows related to R&D will moderate in the second quarter of FY2025.

During the period, the company successfully closed an $8.9 million capital raising, comprising a $5 million placement and a $3.9 million entitlement offer. The capital raising was strongly supported with oversubscriptions of approximately 1.8x received in the entitlement offer.

During the quarter, approximately $15,000 was received from the conversion of options. Following the close of the quarter, the rate and volume of option conversion applications has accelerated, with a further $612,000 in funding received post quarter-end. If the share price and the volume of shares being traded remains strong, it is anticipated that there will be further funds received from option conversions, with total potential funding of $16.1 million available from the options not yet exercised.

The total amount of R&D spend in the FY2024 year is approximately twice that which was spent in FY2023 and as such, depending on several factors, the R&D rebate for FY2024 is anticipated to be proportionately higher (FY2023 rebate $4.8 million). This funding is expected to be received in Q4 2024.

With a cash balance at 30 June 2024 of $9.45 million and the additional significant funding sources described above, the company is funded to late CY2025.

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 $0.20 million, comprising the salary for the CEO/Managing Director, fees paid to Non-Executive Directors, and superannuation.

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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 cognition & depression trial** is a double-blind, six-week proof-of-concept, placebo-controlled, parallel group design trial in 167 patients. Participants are evenly randomized to receive Xanamem 10 mg once daily or placebo, in some cases in addition to their existing antidepressant therapy, and effects on cognition and depression are assessed. Results are anticipated in the first half of August CY2024.

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 effects on cognition, function and progression of Alzheimer's disease are assessed. Thus, Xanamem is being assessed in this trial for its potential effects as a both a cognitive enhancer and a disease course modifier. Initial results from an interim analysis of the first 100 participants are anticipated in mid 2025.

About Xanamem

Xanamem's novel mechanism of action is to block the production of cortisol inside cells through the inhibition of the 11β-HSD1 enzyme in the brain. Xanamem is designed to get into the brain after it is absorbed in the intestines upon swallowing.

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease and excess cortisol is known to be toxic to brain cells. Cognitive impairment is also a feature in Depression and many other diseases. Cortisol itself is also associated with depressive symptoms and when targeted via other mechanisms has shown some promise in prior clinical trials.

The Company has studied 11β-HSD1 inhibition by Xanamem in more than 300 volunteers and patients, so far finding a statistically significant improvement in working memory and attention, compared with placebo, in healthy, older volunteers in two consecutive trials and clinically significant improvements in functional and cognitive ability in patients with biomarker-positive mild AD. Previously, 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. A series of Phase 2 studies in multiple diseases is being conducted to further confirm and characterize Xanamem's therapeutic potential.

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 June 2024

Consolidated statement of cash flows	**Current quarter $A'000**	**Year to date (12 months) $A'000**
1 Cash flows from operating activities		
1.1 Receipts from customers	-	-
1.2 Payments for		
(a) research and development	(3,779)	(16,304)
(b) product manufacturing and operating costs	-	-
(c) advertising and marketing	-	-
(d) leased assets	-	-
(e) staff costs	(954)	(4,127)
(f) administration and corporate costs	(376)	(1,880)
1.3 Dividends received (see note 3)	-	-
1.4 Interest received	81	291
1.5 Interest and other costs of finance paid	(6)	(19)
1.6 Income taxes paid	-	-
1.7 Government grants and tax incentives	-	4,793
1.8 Other (working capital movements)	(55)	189
1.9 Net cash from / (used in) operating activities	**(5,089)**	**(17,057)**
2 Cash flows from investing activities		
2.1 Payments to acquire or for:		
(a) entities	-	-
(b) businesses	-	-
(c) property, plant and equipment	-	-
(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	-	(8)
(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	**-**	**(8)**

3	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	8,878	18,879
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	-	226
3.4	Transaction costs related to issues of equity securities or convertible debt securities	(610)	(1,064)
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)	15	15
3.10	**Net cash from / (used in) financing activities**	**8,283**	**18,056**

4	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	6,258	8,460
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(5,089)	(17,057)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	(8)
4.4	Net cash from / (used in) financing activities (item 3.10 above)	8,283	18,056
4.5	Effect of movement/adjustment in exchange rates on cash held	(1)	-
4.6	**Cash and cash equivalents at end of period**	**9,451**	**9,451**

	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	2,451	1,258
5.2	Call deposits	7,000	5,000
5.3	Bank overdrafts	-	-
5.4	Other	-	-
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	**9,451**	**6,258**

	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	195
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)	(5,089)
8.2	Cash and cash equivalents at quarter end (item 4.6)	9,451
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	9,451
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	1.86

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: No, As the XanaCIDD Phase 2a trial concludes, cash outflows related to R&D will begin to moderate in the second quarter of FY2025, as the company completes spending related to the trial.

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: The company has a successful track record of raising funds, has received significant additional funding post quarter-end from options conversions ($612k), and has the potential to receive up to a further $16.1m in funding from options not yet converted. Further, the company has a significant accrued R&D rebate due in Q4 CY 2024.

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 funding sources available and has cash runway to late CY2025.

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: 22 July 2024

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.