ASX ANNOUNCEMENT

Actinogen December 2022 Quarterly Activity Report and Appendix 4C

Sydney, 30 January 2023. 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 2022.

Key Highlights

- **Advancing rapidly into Phase 2 programs:**
    - Validated the design and outcome measures of the upcoming Phase 2b trial in patients with early Alzheimer's disease (AD) in the Phase 2a Clinical Biomarker Study by showing clinically significant effects on key endpoints (CDR-SB and cognition) [1] in patients with elevated blood levels of the protein pTau
    - Following review of updated clinical and nonclinical information, received approval from the US Food and Drug Administration (FDA) to proceed with a six-month Phase 2b clinical trial of Xanamem® in patients with early AD
    - Treated the first patient in the XanaCIDD Phase 2a trial in patients who are inadequately treated by their anti-depressant medication and have on-going depression associated with cognitive impairment.
- **Completed initial development of the to-be-marketed tablet formulation that will be used in the XanaMIA Phase 2b AD trial and future Phase 3 clinical trials**
- **Presented an academic poster at the Clinical Trials on Alzheimer's Disease (CTAD) conference in San Francisco of the XanaMIA Phase 1b trial results[2]**
- **Cash balance of $14.48 million at 31 December 2022.**[3]

[1] Clinical Dementia Rating Scale – Sum of Boxes (CDR-SB) is a measure of patient functional abilities and a composite of cognitive tests of mental abilities considered a measure of "executive function"

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[2] XanaMIA Phase 1b (Part A) trial results announced 27 April 2022

[3] Unless stated otherwise, all financial data is in Australian dollars

Dr Steven Gourlay, Actinogen CEO and MD, commented:

"We were very pleased to announce just prior to year-end the FDA approval of our upcoming XanaMIA Phase 2b Alzheimer's Disease (AD) trial, which is a significant milestone for Actinogen as it marks our progression to longer term trials that can be used for regulatory approvals.

"Commencement of the XanaCIDD Phase 2 trial in patients with major depressive disorder (MDD) and cognitive impairment is another major milestone for our clinical program and promises to deliver results as early as late 2023. There is a strong scientific rationale for reducing brain cortisol levels to improve symptoms in depression.

"Xanamem® has the potential to be an effective low-dose daily oral therapy for the treatment Alzheimer's disease, depression and many other neurological conditions where it may be used alone or in combination with other treatments. Xanamem has already been proven to enhance cognition in three independent clinical trials with safety demonstrated in more than 300 patients and volunteers to date."

FDA approval received to proceed with XanaMIA Phase 2b AD clinical trial

On 22 December 2022, the Company announced receipt of US FDA approval to proceed with its six-month, Phase 2b, placebo-controlled clinical trial of Xanamem in patients with early stages of Alzheimer's disease.

The approval was granted in the context of the Company updating its FDA Investigational New Drug (IND) dossier with new nonclinical and clinical information to support the trial protocol.

The planned Phase 2b trial will enrol 330 patients with mild AD and progressive disease, determined by clinical criteria and confirmed by an elevated level of pTau181 protein in the blood. Use of pTau181 replaces the need to use expensive amyloid brain scans to confirm the diagnosis of AD and the likelihood of progressive disease. Patients will be randomized to treatment over six months with 5 mg, 10 mg or placebo once a day. A follow-on trial will allow participants to continue on Xanamem and provide valuable long-term safety and efficacy data.

Key efficacy endpoints will be those that have shown Xanamem effect in prior trials: CDR-SB and a test battery measuring attention and working memory.

The trial will use to-be-marketed tablets and is expected to have results in late 2024 or early 2025.

First patient randomized and treated in XanaCIDD clinical trial

On 8 December 2022, the first patient was randomized and treated in the XanaCIDD Phase 2 Depression clinical trial that will measure the effects of Xanamem on safety, cognitive performance and depression in patients who are inadequately treated by their anti-depressant medication and have both depressive symptoms and cognitive impairment.

The XanaCIDD trial is a six-week proof-of-concept, placebo-controlled, parallel group design trial in approximately 160 patients with persistent major depressive disorder (MDD) and cognitive impairment despite a standard course of anti-depressant therapy. Xanamem 10 mg daily or placebo will be added to the existing anti-depressant therapy and effects on cognition, using the Cogstate Cognitive Test Battery, and depression, using the Montgomery Asberg Depression Rating Scale, will be assessed.

Results are expected in late 2023 or early 2024.

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Large clinical benefit shown in AD biomarker study - validates Xanamem program

On 10 October 2022, the Company announced positive Phase 2a clinical data from its Alzheimer's disease biomarker study.

The prospectively conducted, double-blind analysis using new biomarker data was effectively a simulation of the upcoming Phase 2b trial and validated and de-risked Actinogen's AD program by showing:

- Clinical activity in a third clinical trial
- Large clinical effect size in patients with mild AD and elevated blood pTau on the CDR-SB endpoint used to approve anti-amyloid antibodies by the FDA
- Utility of blood pTau levels to select suitable patients with early-stage AD for the Phase 2b trial.

The biomarker study was conducted in 72 patients with available blood biomarker samples from the prior Phase 2a placebo controlled XanADu study of 185 patients. Patients in the original trial had a clinical diagnosis of mild AD,[4] and were treated with Xanamem 10 mg or placebo once daily for 12 weeks.

The biomarker analysis was 'double-blind' and 'pre-specified' meaning the results were generated according to an analysis plan where the biomarker laboratory and company personnel were unaware of which treatment patients had used. This method is standard in the biopharmaceutical industry to avoid bias in the results. Key blood biomarkers studied were phosphorylated tau (pTau) and amyloid levels.

For further information, please refer to the detailed biomarker study results announcement along with the associated webcast slide presentation released to the ASX on 10 October 2022. Alternatively, please refer to the *ASX announcements* section in the *Investor Centre* on the Actinogen website www.actinogen.com.au.

Academic poster presentation at CTAD and ongoing business development activities

The Company presented an academic poster of the XanaMIA Phase 1b (Part A) trial results at the Clinical Trials on Alzheimer's Disease (CTAD) conference in San Francisco on 2 December 2022.[5]

The poster presentation reported encouraging safety data and concluded that the trial observed positive effects on attention and working memory in cognitively normal, older volunteers at 5 and 10 mg daily doses of Xanamem.

The results were consistent with similar, positive data in a prior trial of a cognitively normal population with a 20 mg daily dose,[6] and with the recent Phase 2a clinical biomarker study showing a large clinical effect on the CDR-SB endpoint in the group of patients with mild AD most likely to progress.[7]

Xanamem's safety profile continues to be excellent and demonstrates a favourable profile for chronic therapy.

New year activity commenced quickly with CEO Dr Steven Gourlay presenting at the Sachs Associates 6th Annual Neuroscience Innovation Forum in San Francisco on 8 January 2023. While in San Francisco, Dr Gourlay also participated in meetings at BIO Partnering @JPM associated with the 41st Annual J.P. Morgan Healthcare Conference from 9 to 12 January as well as at the annual H.C. Wainwright Bioconnect Virtual Conference that ran concurrently with the J.P. Morgan conference.

Dr Gourlay also conducted multiple business development and other stakeholder meetings during the conference week.

[4] Measured by a Mini Mental State Examination (MMSE) score of 20 to 26. MMSE is a 30-point scale of simple questions to assess mental abilities

[5] XanaMIA Phase 1b (Part A) trial results announced 27 April 2022

[6] XanaHES Phase 1 trial results announced 1 October 2019

[7] Phase 2a AD biomarker study results announced 10 October 2022

Cash position

Actinogen's cash balance at 31 December 2022 was $14.48 million.

Net operating cash inflow for the quarter was $0.57 million, primarily related the receipt of a $4.17 million R&D tax incentive cash rebate relating to the 2022 financial year, offset by R&D spend of $2.58 million, staff costs of $0.69 million and administration and corporate costs of $0.34 million.

The decrease in staff costs spend for the quarter ($0.69 million) compared to the September quarter ($0.84 million) was primarily due to the payment of annual bonuses to staff in the September quarter ($0.26 million).

Cash from financing activities of $0.90 million was due to the exercise of options by Non-Executive Director Dr George Morstyn ($0.15 million) and the former CEO and Managing Director Dr Bill Ketelbey ($0.75 million).

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 approximately $0.17 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.

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 its capsule.

® Xanamem is a registered trademark of Actinogen Medical Limited

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease, and Xanamem has shown the ability to enhance cognition in healthy, older volunteers. 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 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	31 December 2022

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	(2,581)	(4,868)
	(b) product manufacturing and operating costs		
	(c) advertising and marketing		
	(d) leased assets		
	(e) staff costs	(686)	(1,522)
	(f) administration and corporate costs	(338)	(695)
1.3	Dividends received (see note 3)		
1.4	Interest received	95	141
1.5	Interest and other costs of finance paid	(5)	(10)
	Income taxes paid		
1.7	Government grants and tax incentives	4,165	4,165
1.8	Other (working capital movements)	(85)	(28)
1.9	**Net cash from / (used in) operating activities**	**565**	**(2,817)**

2.	**Cash flows from investing activities**		
2.1	Payments to acquire or for:		
	(a) entities		
	(b) businesses		
	(c) property, plant and equipment	(5)	(13)
	(d) investments		
	(e) intellectual property		
	(f) other non-current assets		

Consolidated statement of cash flows		Current quarter $A'000	Year to date (6 months) $A'000
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**	**(5)**	**(13)**

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	903	903
3.4	Transaction costs related to issues of equity securities or convertible debt securities		
3.5	Proceeds from borrowings		
3.6	Repayment of loan shares by Managing Director		
3.7	Transaction costs related to loans and borrowings		
3.8	Dividends paid		
3.9	Other		
3.10	**Net cash from / (used in) financing activities**	**903**	**903**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	12,983	16,370
4.2	Net cash from / (used in) operating activities (item 1.9 above)	565	(2,817)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(5)	(13)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (6 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	903	903
4.5	Effect of movement in exchange rates on cash held	37	40
4.6	**Cash and cash equivalents at end of period**	**14,483**	**14,483**

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	2,483	983
5.2	Call deposits	12,000	12,000
5.3	Bank overdrafts		
5.4	Other – restricted cash re office lease		
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	14,483	12,983

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	166
6.2	Aggregate amount of payments to related parties and their associates included in item 2	

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.

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)	565
8.2	Cash and cash equivalents at quarter end (item 4.6)	14,483
8.3	Unused finance facilities available at quarter end (item 7.5)	
8.4	Total available funding (item 8.2 + item 8.3)	14,483
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	N/A

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: N/A

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: N/A

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: N/A

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 January 2023

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.