ASX ANNOUNCEMENT

December 2021 Quarterly Activity Report and Appendix 4C

Sydney, 28 January 2022. Actinogen Medical ASX: ACW ("ACW" or "the Company") announces the release of its quarterly activity report and Appendix 4C for the three-month period ended 31 December 2021.

Key Highlights

- **Advancing the Xanamem® clinical development pipeline:**
  - Selected Major Depressive Disorder (MDD) as third indication for Xanamem based on strong scientific rationale. Planning underway for Phase 2 trial to commence in 2022, with headline results expected in 2023[1]
  - Received US FDA approval to proceed under Investigational New Drug (IND) for Phase 2 XanaFX trial in adolescent patients with Fragile X Syndrome (FXS), and signed Letter of Intent (LOI) with WorldWide Clinical Trials Limited (WWC) to operationalise the trial
  - Expanded XanaFX trial to include sites in North America, added 5mg dose group and increased target enrolment from 50 to 75. Headline results expected in 2023
  - Completed target enrolment of 105 patients for the XanaMIA Part A trial in Mild Cognitive Impairment (MCI) due to Alzheimer's Disease (AD). Results expected in Q2 2022
  - Added a retrospective analysis of the effects of Xanamem on biomarkers of possible disease modification using stored samples from prior Phase 2 XanADu study in mild AD with results expected in H2 2022
- **Successfully completed a $13.3[2] million capital raising to fund expansion of the clinical development pipeline**
- **Established two new Xanamem clinical advisory boards for FXS and Depression programs**
- **Finalised a clinical protocol for a strategic collaboration with Oxford University researchers to investigate the therapeutic potential for Xanamem to control the metabolic effects of excessive cortisol in a disease called Mild Autonomous Cortisol Secretion**
- **Updated potential pharmaceutical industry partners on expanded clinical development pipeline and multiple near and medium-term milestones at international industry conferences in January 2022**
- **Cash balance of A$22.2 million at 31 December 2021, including funds received from the capital raising and the $1.4 million tax incentive rebate received during the quarter.**

® Xanamem is a registered trademark of Actinogen Medical Limited

[1] Years refer to calendar years unless stated otherwise

[2] Including the proposed $107,625 subscription to the placement by CEO Dr Steven Gourlay that is subject to shareholder approval

Advancing the clinical development pipeline through multiple clinical trials

Actinogen continues to successfully execute its primary strategic priority of focusing on operational excellence in its clinical development program, which is designed to deliver timely and high-quality confirmation of clinical efficacy and safety in each of its disease programs. The Company is conducting its lead programs in AD and FXS under US IND oversight to ensure it adheres to a global standard of regulatory compliance for clinical development, non-clinical studies and manufacturing.

Dr Steven Gourlay, Actinogen CEO and MD, commented:

"The December quarter of 2021 marked significant advances in Actinogen's clinical development pipeline including selecting Major Depressive Disorder (MDD) as our third disease indication for Xanamem, expanding the scope and size of our Phase 2 XanaFX trial for Fragile X Syndrome, and completing target enrolment for the XanaMIA Part A trial in Mild Cognitive Impairment due to Alzheimer's Disease.

"We also successfully completed a $13 million capital raising to help support the expanded clinical pipeline, created two new specialist clinical advisory boards led by world class experts in Fragile X Syndrome, Depression, and Cognition, and struck a strategic collaboration with researchers at Oxford University.

"We look forward to continuing this outstanding momentum through 2022 as we pursue our revolutionary therapy to help make a material difference to the quality of life for people and their families living with serious neurological conditions such as Alzheimer's Disease, Depression, and Fragile X Syndrome."

MDD selected as third target indication for Xanamem

MDD was announced as the Company's third clinical development opportunity for Xanamem in November 2021. MDD is a significant medical condition associated with chronically dysregulated cortisol with a circa 5% prevalence globally and a one in seven lifetime risk.[3] [4]

Cognitive impairment is a feature in the majority of MDD patients and commonly persists even when depression symptoms subside. Elevated cortisol levels have been associated with depression, and modification of brain cell cortisol levels is proposed as a strategy to treat both depression itself and associated cognitive impairment.

Preparations are underway for the commencement of a Phase 2 MDD trial later in 2022, with headline results expected in 2023.

FXS XanaFX trial

In early November, Actinogen announced receipt of approval from the US FDA to proceed under an IND protocol for its Phase 2 XanaFX trial for cognition, anxiety, sleep and behavioural problems in male adolescents and young adults possessing the full genetic features associated with FXS.

XanaFX will be a randomised, placebo-controlled, double-blind, 12-week trial with 50 patients originally planned for enrolment at Australian sites. The trial scope was subsequently expanded to include sites in North America, Great Britain, and New Zealand, and a 5mg dosage arm added, which will increase the number of enrolments to 75, funded by the recent capital raising. Results are anticipated in 2023.

An LOI was signed in November with WWC to operationalise the trial and start-up activities have commenced while the full contract is negotiated, with key details of the contract to be announced when finalised.

[3] World Health Organization, Depression 2021.
[4] Kessler & Bromet 2013

AD XanaMIA trial and retrospective biomarker study

The Part A XanaMIA trial is designed to assess the efficacy of 5mg and 10mg Xanamem doses compared to placebo in 105 older healthy patients (aged 50 to 80 years old), over six weeks, to confirm the minimum effective dose needed to improve cognition (ability to think and remember things) and is being conducted at five outpatient clinical sites in Australia.

Target full enrolment in the trial was reached in late November 2021 and results are expected to be announced during the second quarter of 2022.

A retrospective analysis of Alzheimer's "disease-modifying" biomarker data from the earlier XanADu Phase 2 trial of 185 patients with mild AD was added to the clinical program during the quarter and results are expected in the second half of 2022.

The Part B study of the XanaMIA trial will be informed by the results of Part A and the retrospective biomarker study data and will investigate the efficacy of Xanamem in patients with the early stages of biomarker-confirmed AD.

Capital raising

In December, Actinogen announced the successful completion of a $13.3 million capital raising, comprising a $12 million institutional placement of 88,888,881 new, ordinary fully paid Actinogen shares at an offer price of $0.135 per new share,[5] and a $1.3 million Share Purchase Plan (SPP) of 9,796,389 new, ordinary fully paid shares to existing shareholders at the same $0.135 issue price.[6]

The funds raised are primarily being applied to the expanded clinical development pipeline including the addition of the MDD program, the expanded XanaFX trial and the retrospective AD biomarker study.

Shareholder approval is required for the proposed subscription by CEO Dr. Steven Gourlay of $107,625 worth of new shares under the $12 million placement.

Two new Xanamem clinical advisory boards for FXS and Depression

In December, the Company announced the establishment of two new Xanamem clinical advisory boards for its programs in FXS and Depression, and the inaugural expert appointments to those boards comprising four renowned global thought leaders in clinical trials for FXS, Depression and assessment of Cognition:

Fragile X Syndrome Clinical Advisory Board

Dr Elizabeth Berry-Kravis, MD, PhD and Dr Pam Ventola, PhD, both based in the USA

Depression and Cognition Clinical Advisory Board

Professor John Harrison, PhD, based in the UK, and Dr Dana C. Hilt, MD based in the USA

A third appointment has subsequently been made to the Depression and Cognition Advisory Board, Dr Christina Kurre Olsen, based in Denmark. Details of Dr Kurre Olsen's expertise and qualifications along with those of all other advisory board members can be found on the company's website. Several Australian investigators will become involved as the trial proceeds.

[5] Including the proposed $107,625 subscription to the placement by CEO Dr Steven Gourlay that is subject to shareholder approval

[6] Total dollar values may not equate to total shares issued at $0.135 offer price due to rounding up share allocations to the nearest whole share. $13,322,500 (before costs) was raised in aggregate through the issue of 98,685,270 new, ordinary shares at $0.135 per share.

Strategic collaboration with Oxford University

During the quarter, the Company announced the finalisation of a clinical protocol as part of its strategic collaboration with researchers at the Radcliffe Department of Medicine, University of Oxford, to investigate Xanamem and a condition called Mild Autonomous Cortisol Secretion (MACS). MACS is associated with over-production of the stress hormone cortisol by non-cancerous growths on the adrenal glands.

The placebo-controlled 12-week clinical trial will enrol approximately 40 participants and is designed to investigate the therapeutic potential for Xanamem in patients with MACS and will evaluate effects of Xanamem on metabolism, bone density, and cognitive function.

The trial is funded by a Medical Research Council (UK) grant, while Actinogen is supplying Xanamem to Oxford free-of-charge and providing trial design support. Results are anticipated in 2024.

Business development

In early January 2022, CEO Dr Steven Gourlay presented at the Biopartnering @JPM associated with the 40th annual JP Morgan HealthCare Conference in San Francisco and at the H.C. Wainwright BioConnect Virtual Conference that ran concurrently with the JP Morgan conference.

Dr Gourlay also used his time in San Francisco to conduct multiple business development and other stakeholder meetings during the conference week to update potential pharmaceutical industry partners on the Company's expanded clinical development pipeline and its near and medium-term milestones.

Cash position

Actinogen's cash balance as at 31 December 2021 was $22.23 million.[7] Net operating cash outflow for the quarter was $1.99 million, primarily related to R&D spend of $2.78 million, staff costs of $0.35 million and administration and corporate costs of $0.28 million. The increase in R&D expenditure from $0.76 million in the September quarter 2021 to $2.78 million in the December quarter was due to increased R&D activity and was consistent with expectations.

The net operating cash outflow includes the offset of A$1.43 million R&D tax incentive rebate received in October 2021. The Company remains well positioned to fund its current planned clinical trials and advance clinical development.

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 A$0.16 million, comprising the salary for the CEO/Managing Director, fees paid to Non-Executive Directors and superannuation.

ENDS

	Investors	**Media**
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Announcement authorised by the Board of Directors of Actinogen Medical

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

About Actinogen Medical

Actinogen Medical (ACW) is an ASX-listed, biotechnology company developing a novel therapy for neurological 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, reasoning, awareness and decision-making, and to a large extent, influence our personality.

We are currently developing our lead compound, Xanamem®, as a promising new therapy for Alzheimer's Disease, Fragile X Syndrome, Depression and other neurological diseases where reducing cortisol inside brain cells could have a positive impact. 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 works by blocking the production of intracellular cortisol 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.

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease, potentially linked to cognitive impairment and anxiety in Fragile X Syndrome, and cognitive impairment in Depression and other diseases.

The Company has studied 11β-HSD1 inhibition by Xanamem in more than 250 volunteers and patients, so far finding a statistically significant improvement in cognition over placebo in healthy, older volunteers. A series of Phase 2 studies in multiple diseases is being conducted to further confirm and characterise 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 based on subjective estimates and assumptions and relate to circumstances and events that have not taken place and may not take place. Such forward looking statements involve known and unknown risks, uncertainties, and other factors (such as significant business, economic and competitive uncertainties and contingencies, and regulatory and clinical development risks and uncertainties) which may cause the actual results or the performance of Actinogen Medical to be materially different from the results or performance expressed or implied by such forward looking statements. Past performance is not a reliable indicator of future performance. There can be no assurance that any forward-looking statements will be realised. Actinogen Medical does not make any representation or give any warranty as to the likelihood of achievement or reasonableness of any forward-looking statements.

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 2021

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	(2,777)	(3,539)
	(b) product manufacturing and operating costs		
	(c) advertising and marketing		
	(d) leased assets		
	(e) staff costs	(354)	(816)
	(f) administration and corporate costs	(284)	(685)
1.3	Dividends received (see note 3)		
1.4	Interest received	7	15
1.5	Interest and other costs of finance paid	(4)	(8)
1.6	Income taxes paid		
1.7	Government grants and tax incentives	1,435	1,435
1.8	Other (office lease)	(17)	(34)
1.9	**Net cash from / (used in) operating activities**	**(1,994)**	**(3,632)**

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		

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**		

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	13,215	13,215
3.2	Proceeds from issue of convertible debt securities		
3.3	Proceeds from exercise of options		
3.4	Transaction costs related to issues of equity securities or convertible debt securities	(811)	(811)
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**	**12,404**	**12,404**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	11,819	13,457
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(1,994)	(3,632)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	-

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)	12,404	12,404
4.5	Effect of movement in exchange rates on cash held	-	-
4.6	**Cash and cash equivalents at end of period**	**22,229**	**22,229**

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	15,194	4,784
5.2	Call deposits	7,000	7,000
5.3	Bank overdrafts		
5.4	Other – restricted cash re office lease	35	35
5.5	**Cash and cash equivalents at end of quarter (should equal item 4.6 above)**	22,229	11,819

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	158
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)	(1,994)
8.2	Cash and cash equivalents at quarter end (item 4.6)	22,229
8.3	Unused finance facilities available at quarter end (item 7.5)	
8.4	Total available funding (item 8.2 + item 8.3)	22,229
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	11.15

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: 28 January 2022

Authorised by: By the Board of Actinogen Medical Limited
(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.