ASX ANNOUNCEMENT

Actinogen June 2022 Quarterly Activity Report and Appendix 4C

Sydney, 28 July 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 30 June 2022.

Key Highlights

- **Accelerating Xanamem® clinical development:**
    - Reported strongly positive results for attention and working memory (cognition) in the XanaMIA Part A trial
    - Initiated strategic adjustments to prioritize Alzheimer's Disease (AD) and Cognitive Impairment in Depressive Disorder (CIDD) clinical trial programs where cognition is the primary focus, and re-allocated circa $12 million of resources from suspended Fragile X Syndrome (FXS) program
    - Announced high level trial design and commencement of activities for:
        - XanaMIA Part B Phase 2 AD trial, which will be a placebo-controlled, 6-month, parallel group design, measuring the effects of Xanamem on safety and cognitive performance in patients with early stages of AD
        - XanaCIDD Phase 2 depression trial, which will be a placebo-controlled, 6-week, parallel group design, measuring 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
    - Provided information on the timing and design of the Phase 2 biomarker study in patients with Mild AD in post-quarter announcement on 13 July 2022. This study is a prospective analysis of the effects of Xanamem on AD biomarkers using stored blood samples from the prior placebo-controlled XanADu Phase 2 trial.
    - Signed Letter of Intent on 6 July with Axiom Real-Time Metrics to provide clinical research services for the XanaCIDD Phase 2 trial.
- **CEO and the Head of Business Development attended the BIO International Convention in San Diego USA in June, which is the world's largest gathering of the biotechnology industry. The Senior Vice President of Product Development presented to the Bioshares Biotech Summit 2022 in May.**
- **Launched new and enhanced corporate website in early April**

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- **Continued scale-up manufacturing with Corden Pharma and initiated tablet formulation with Metrics Contract Services**
- **General Meeting held on 5 April 2022 to approve resolutions in relation to share placements as part of capital-raising activities in November 2021**
- **CEO and MD Dr Steven Gourlay purchased 797,222 shares @13.5 cents per share (cps) related to the 2021 share placement upon shareholder approval at the April General Meeting. Dr Gourlay purchased a further 2 million shares on market in May 2022 @6.4cps and Chairman Dr Geoff Brooke purchased 340,000 shares on market in May 2022 @7.5cps**
- **Cash balance of $16.4 million at 30 June 2022.**[1]

Accelerating Xanamem's clinical development with a focus on cognition

Actinogen is now actively commencing a robust Phase 2 program in AD and MDD and continues to evaluate alternate funding solutions to progress the FXS Phase 2 trial. The key to success is operational excellence in the design, implementation, and analysis of these clinical trials, including the upcoming Phase 2 Biomarker Study using stored blood samples from the prior Phase 2 study in patients with mild AD.

Dr Steven Gourlay, Actinogen CEO and MD, commented:

"We continue to build momentum in our clinical development program after receiving positive results for improvement in attention and working memory in our XanaMIA Part A trial. We initiated a strategic adjustment to 'follow the science' by prioritizing our Alzheimer's Disease and Depression programs where the primary endpoints are cognition. We believe a focus on cognitive enhancement in these diseases will accelerate and optimize the path to commercialisation for our small molecule drug, Xanamem.®"

Alzheimer's Disease XanaMIA Part A trial

On 27 April 2022, the Company announced positive XanaMIA Part A trial results which confirmed Xanamem's ability to rapidly enhance attention and working memory (referred to as cognition – the ability to think and remember things). These findings replicated the pattern of improvement seen in the prior XanaHES trial.

The XanaMIA Part A trial was established to assess the efficacy of 5 mg and 10 mg Xanamem doses compared to placebo in older healthy patients (aged 50 to 80 years old), over six weeks, to confirm the minimum effective dose needed to improve cognition. The target dose range was determined by the results of a dose-ranging positron emission tomography (PET) clinical trial of Xanamem's inhibition of its target in the brain.

The XanaMIA-Part A trial achieved its primary endpoints of safety, efficacy and pharmacodynamics. In particular, it achieved the prespecified endpoint of a clinically significant effect on cognition with a Cohen's d effect size of 0.32 ($p < 0.05$).

For further information, please refer to the detailed XanaMIA trial results announcement along with the associated webcast slide presentation released to the ASX on 27 April 2022. Alternatively, please refer to the *ASX announcements* section in the *Investor Centre* on the Actinogen website www.actinogen.com.au.

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

Designs for Phase 2 trials in Alzheimer's Disease and Major Depressive Disorder

On 14 June 2022, the Company announced that it had finalised designs for its planned Phase 2 trials in AD and MDD:

- The **XanaMIA Part B AD trial** is a six-month dose-ranging, placebo-controlled trial in approximately 300 patients with early stages of AD, including patients with Mild Cognitive Impairment (MCI) as well as patients with mild AD, where some functional impairment (difficulty completing activities of daily living) is present over and above the purely cognitive difficulties experienced by MCI patients.

  Effects of 5mg and 10mg Xanamem dose levels on cognition will be measured by the same Cogstate Cognitive Test Battery (CTB) used in the XanaMIA Part A trial, supplemented by a variety of other tests of memory, attention, and executive function. Results are expected in 2024.

- The **XanaCIDD trial** is a six-week proof-of-concept, placebo-controlled trial in approximately 160 patients with persistent 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 both cognition and depression will be assessed. Results are expected in late 2023 or 2024.

AD biomarker study

On 13 July 2022, the Company released additional information on the timing and design of its upcoming Biomarker Study in patients with Mild AD.

This study is analysing stored blood samples from the previously completed XanADu Phase 2 trial that was conducted in 185 patients with mild dementia and a clinical diagnosis consistent with AD in Australia, the USA, and the UK. This study used a 10mg dose vs. placebo over 12 weeks and results were first reported in 2019. At that time blood-based AD biomarker analyses were not available, and the clinical diagnosis of AD was not confirmed by amyloid brain scans or biomarkers of the disease. In this AD biomarker study, analyses will be 'double-blind' and guided by an *a priori* Statistical Analysis Plan. The main objectives of the study are to examine 1) the effects on cognition of Xanamem in patients with biomarker-positive AD, and 2) the effects of Xanamem on a variety of AD biomarkers.

The Company has access to adequate samples from approximately 70 of the original XanADu Phase 2 trial patients, representing a relatively large sample size for a biomarker study.

Results are expected to be available before the end of October 2022.

For further information on the key design elements of the study and the details of biomarkers to be analysed, please refer to the *ASX announcements* section in the *Investor Centre* on the Actinogen website www.actinogen.com.au.

Signed Letter of Intent (LOI) with Axiom Real-Time Metrics for XanaCIDD trial

The Company signed an LOI with Axiom Real-Time Metrics, Inc (Axiom) on 6 July 2022 to provide clinical research services to help operationalise the XanaCIDD Phase 2 trial. Axiom is the premier provider of eClinical (trial automation) services to small and medium life sciences organisations. Axiom's platform technology will support the internal Actinogen team by providing cost-effective operational solutions to manage the XanaCIDD trial.

The LOI value of US$605,195 is to initiate work on the trial while a full work order is negotiated. The LOI duration is 60 days (extendable), and cancellable with 30 days' notice and subsequent refund of unused funds up to 50% of the LOI value.

Fragile X Syndrome XanaFX trial

As a result of the positive XanaMIA Part A trial data and the consequent strategic adjustment to devote resources and capability to clinical programs focused on cognition, the Company suspended clinical trial operations for its more complex global XanaFX trial and reallocated those resources (approximately $12 million) to its expedited AD and MDD trial programs.

The strong scientific rationale for the FXS program has not changed and the Company will investigate alternative funding, partnership and implementation models to study the utility of Xanamem in people with FXS.

Business development

In June 2022, ACW's CEO Dr Steven Gourlay, accompanied by the Company's Head of Business Development, Dr Christian Toouli attended the BIO International Convention in San Diego, USA. The convention is the world's largest gathering of the biotechnology industry and the ACW team used the opportunity to conduct approximately 30 business development and stakeholder meetings to update potential pharmaceutical and biotech industry partners on the Company's clinical development pipeline and its near and medium-term milestones.

On 11 May 2022, the Senior Vice President Product Development, Tamara Miller presented to the Bioshares Biotech Summit in Albury, NSW, a key annual conference event for the Australasian biotechnology industry.

New corporate website

On 6 April 2022 the Company launched its new corporate website with new and improved sections in all key areas including streamlined and enhanced scientific/medical focused sections on Xanamem and Clinical Development.[2] The *landing page*, *Our Company*, *Investor Centre* and *News* sections have also been improved and expanded. The website can be accessed at www.actinogen.com.au.

General Meeting

The Company held a General Meeting on 5 April 2022 to seek shareholder approval of two resolutions:

1. The issue of 797,222 shares to CEO Dr Steven Gourlay who subscribed for the shares at an issue price of $0.135 per share in conjunction with, and at the same price as, the placement of 88,091,659 shares to sophisticated investors
2. Ratification of the 88,091,659 shares issued to sophisticated investors on 30 November 2021 under the capital raising placement.

Both resolutions were approved as set out in an announcement dated 5 April 2022. Dr Gourlay subsequently completed the $107,625 share subscription payment following shareholder approval of Resolution 1.

Cash position

Actinogen's cash balance at 30 June 2022 was $16.37 million. Net operating cash outflow for the quarter was $2.79 million, primarily related to R&D spend of $1.84 million, staff costs of $0.48 million and administration and corporate costs of $0.46 million.

The circa 30% decline in R&D spend for the June quarter ($1.84 million) compared to the March quarter ($2.62 million) was primarily due to a change in trial activity[3] and payment timing differences.

[2] The Clinical Development section now includes an online patient portal to enable website visitors to check on the status of trials and register for participation in open trials.

[3] The XanaMIA Part A trial result was announced in April 2022, after which activity switched to future trial preparations.

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 $0.16 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.

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. 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 2022

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	(1,843)	(8,002)
	(b) product manufacturing and operating costs		
	(c) advertising and marketing		
	(d) leased assets		
	(e) staff costs	(479)	(1,681)
	(f) administration and corporate costs	(457)	(1,296)
1.3	Dividends received (see note 3)		
1.4	Interest received	16	41
1.5	Interest and other costs of finance paid	(5)	(16)
	Income taxes paid		
1.7	Government grants and tax incentives	-	1,435
1.8	Other (office lease)	(17)	(69)
1.9	**Net cash from / (used in) operating activities**	**(2,785)**	**(9,588)**

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

Consolidated statement of cash flows		Current quarter $A'000	Year to date (12 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**	**(2)**	**(2)**

3.	**Cash flows from financing activities**		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	108	13,323
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		(833)
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**	**108**	**12,490**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	19,036	13,457
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(2,785)	(9,588)
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(2)	(2)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (12 months) $A'000
4.4	Net cash from / (used in) financing activities (item 3.10 above)	108	12,490
4.5	Effect of movement in exchange rates on cash held	13	13
4.6	**Cash and cash equivalents at end of period**	**16,370**	**16,370**

5.	Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	Current quarter $A'000	Previous quarter $A'000
5.1	Bank balances	4,335	7,001
5.2	Call deposits	12,000	12,000
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)**	16,370	19,036

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	164
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)	(2,785)
8.2	Cash and cash equivalents at quarter end (item 4.6)	16,370
8.3	Unused finance facilities available at quarter end (item 7.5)	
8.4	Total available funding (item 8.2 + item 8.3)	16,370
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	5.87

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 July 2022

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.