ASX ANNOUNCEMENT

Actinogen prioritizes phase 2 trials in Alzheimer's Disease and Depression

Sydney, 4 May 2022. Actinogen Medical ASX: ACW ("ACW" or "the Company") announces that following strongly positive results for attention and working memory (cognition) in its recent double-blind XanaMIA Part A trial, it has conducted a reassessment of its priorities and planned expenditures, resulting in the following strategic adjustments to:

- Prioritize the Alzheimer's Disease (AD) and Major Depressive Disorder (MDD) clinical programs for Xanamem®, where cognition is the primary focus, ahead of the Fragile X Syndrome (FXS) program where cognition is one of several factors
- Expedite the XanaMIA Part B Phase 2 AD trial, which will measure safety and cognitive performance in patients with the early stages of AD
- Expedite the MDD Phase 2 trial, which will measure safety, levels of depression and cognitive performance in patients who are inadequately treated by their anti-depressant medication
- Suspend clinical trial operations for its more complex, global XanaFX Fragile X Syndrome trial and reallocate those resources (forecast to be approximately $12 million[1]) to AD and MDD
- Investigate alternative funding, partnership and implementation models to study the utility of Xanamem in people with FXS. The strong scientific rationale for the 11β-HSD1 enzyme as a therapeutic target has not changed.

Actinogen had a cash balance of $19.0 million at the end of the March 2022 quarter which will be supplemented by annual rebates from the Australian government under the R&D tax rebate scheme. The Company is now focused on capital-efficient, Australian clinical trial operations for its clinical trials wherever feasible. Subject to trial design and operational considerations, Actinogen is well-placed to achieve several important milestones in the coming 24 months, including:

- Completing the AD biomarker and efficacy reanalysis of the prior XanADu AD Phase 2 trial (2022)
- Commencing the AD and MDD Phase 2 trials (2022)
- Completing the AD and MDD trials (2023-24).

Dr Steven Gourlay, Actinogen CEO and MD, commented:

"The recently announced, strongly positive results for the XanaMIA Part A trial triggered our review of Actinogen's strategic priorities for the next 24 months. It makes business and scientific sense to devote resources and capability to our clinical programs focused on cognition, given the XanaMIA data, and expedite

® Xanamem is a registered trademark of Actinogen Medical Limited.

[1] All financial data is expressed in Australian dollars unless otherwise stated.

the phase 2 trials in Alzheimer's Disease and Depression. This is clearly now the optimal path to commercialisation of our revolutionary small molecule drug, Xanamem.

"The strong scientific rationale for our Fragile X program has not changed and we hope to be able to study Xanamem in this disease with the help of strategic partners in industry or academia."

Positive XanaMIA Part A trial and topline results announced on 27 April 2022

- The dose-ranging, Phase 1b trial comprised 107 healthy, cognitively normal, older adults aged 50-80 years who received 10 mg or 5 mg doses of Xanamem or matching placebo for 6 weeks
- Assessed cognitive abilities using the internationally recognized Cogstate computerized Cognitive Test Battery (CTB) supplemented by the International Digit Symbol Substitution Test-Symbols (IDSSTS)
- Met primary safety, pharmacodynamic and efficacy endpoints
- Confirmed Xanamem's ability to rapidly enhance attention and working memory, with a similar pattern of cognitive test findings as the prior 20 mg dose trial. No effect was observed for the IDSSTS.
- Results were consistent with a prior Positron Emission Tomography (PET) dose-ranging study that indicated dose levels of 10 mg daily or lower are likely to be effective.

The trial met its objectives. The efficacy endpoint was defined as clinically significant Effect Size (ES) of Xanamem treatment on cognitive ability versus placebo, measured with well validated tests of attention and working memory from the Cogstate CTB. Daily Xanamem doses of 10 mg and 5 mg demonstrated a good safety profile and full pharmacodynamic activity supportive of continued development.

The XanaMIA results confirm Xanamem's ability to enhance cognition even in a cognitively normal population and are consistent with:

1) the prior PET dose-ranging study which found high levels of Xanamem target occupancy at 5 mg and 10 mg daily doses; and,

2) significantly improved attention and working memory tests also seen in the prior XanaHES trial.

ENDS

	Investors	**Media**
Dr. Steven Gourlay CEO & Managing Director P: +61 2 8964 7401 E. steven.gourlay@actinogen.com.au	**Michael Roberts** Investor Relations M: +61 423 866 231 E. michael.roberts@actinogen.com.au	**Randal Killip** Profile for Media M: +61 425 714 159 E. randal@profileformedia.com.au

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.

We are currently developing our lead compound, Xanamem, as a promising new therapy for Alzheimer's Disease and Depression and hope 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 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, and Xanamem has shown the ability to improve working memory and attention 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 cognition over placebo in healthy, older volunteers in two consecutive trials. 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 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.