ASX ANNOUNCEMENT

Actinogen announces Depression as its third disease program, expands Fragile X Syndrome program and launches capital raising

Sydney, 25 November 2021. Actinogen Medical ASX:ACW ("ACW" or "the Company") is pleased to announce several strategic initiatives:

Key Highlights

- **Major Depressive Disorder (MDD) selected as third indication for Xanamem®, based on a strong scientific rationale, with a fully funded phase 2 clinical trial scheduled to commence in 2022. Headline results expected in 2023**
- **Phase 2 XanaFX clinical trial for patients with Fragile X Syndrome (FXS) expanded to include sites in North America and a new 5mg dose group with planned enrolment increased from 50 to 75. US FDA IND approval received in November 2021, trial commencing in 2021, with results expected in 2023**
- **Retrospective analysis of the effects of Xanamem on "disease modifying" biomarkers using stored samples from the prior Phase 2 study in mild Alzheimer's Disease expected in H2 CY2022**
- **Alzheimer's Disease (AD) XanaMIA Part A trial in older volunteers approaching full enrolment. Top line cognition data expected Q2 CY2022**
- **Received commitments for $12 million via an oversubscribed institutional placement at an issue price of $0.135 per share**
- **Initiating a share purchase plan (SPP) with a target raise of circa $3 million through the issue of approximately 22 million shares at A$0.135 per share**
- **Actinogen will host a webcast and teleconference call at 11.30am AEDT today to provide a strategic update on its clinical development plans and the capital raising as set out in an investor presentation released in a separate announcement to the ASX this morning. The webcast and teleconference call can be accessed via a link on the home page of the Actinogen website: www.actinogen.com.au**

Clinical Development Pipeline Update

Following today's announcement, Actinogen will now have three fully funded Phase 2 trials in three Central Nervous System (CNS) indications reading out in 2022 and 2023.

® Xanamem is a registered trademark of Actinogen Medical Limited

MDD selected as a new, third indication for Xanamem

MDD has been selected as the Company's third clinical development opportunity for Xanamem, following significant clinical and scientific interest in evaluating Xanamem across a range of medical conditions associated with chronically dysregulated cortisol.

MDD is a common disorder, with a circa 5% prevalence globally and a one in seven lifetime risk.[1] [2] Cognitive impairment is a feature in the majority of 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.

FXS XanaFX trial

The Company is well advanced with the planning for the Phase 2 XanaFX trial for cognition, anxiety, sleep and behavioural problems in male adolescents and young adults possessing the full genetic features associated with Fragile X Syndrome. There are currently no approved treatment options that specifically target these symptoms associated with FXS, which have a substantial impact on the day-to-day functioning of patients and their caregivers

Earlier this month, Actinogen announced receipt of approval from the US FDA to proceed under the Investigational New Drug (IND) application for the Phase 2 protocol entitled "XanaFX: A Phase II Double-Blind, Randomized, Placebo-Controlled trial, to Assess the Safety, Tolerability, and Efficacy of the 11β-HSD1 Inhibitor Xanamem in Treating Male Adolescents and Young Adults with Fragile X Syndrome".

XanaFX will be a randomised, placebo-controlled, double-blind, 12-week trial. It was originally intended to enrol 50 patients, but today's announcement of expansion of the trial into North America and the addition of a 5mg dosing level will result in an increase in the number of enrolments to 75. Results of the study are anticipated in 2023.

Alzheimer's Disease (AD) XanaMIA trial and biomarkers

The Part A XanaMIA trial is assessing the efficacy of 5mg and 10mg Xanamem doses compared to placebo in approximately 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). The target dose range was determined by the results of a dose-ranging positron emission tomography (PET) study of Xanamem's inhibition of its target in the brain. It is being conducted at five outpatient sites in Australia.

This study will use the Cogstate Neuropsychological Test Battery, which previously showed improvements in cognition at a higher dose, supplemented by the Digit Symbol Substitution Test (iDSST) which has been recognised in the past by the FDA as an appropriate endpoint for a cognitive marketing claim. Full enrolment in the Part A study is imminent and top-line data is expected to read out in Q2 CY2022.

In addition, retrospective analysis of new "disease-modifying" biomarker data from the earlier XanADu Phase 2 trial of 185 people with mild AD is expected in H2 CY2022.

The Part B study of the XanaMIA trial will be informed by the results of Part A and the retrospective biomarker data and will investigate the efficacy of Xanamem in patients with the early stages of biomarker-confirmed AD. The Part B trial results are anticipated in CY2023.

[1] World Health Organization, Depression. 2021.
[2] Kessler & Bromet 2013

Dr Steven Gourlay, Actinogen CEO and MD, commented:

"We are delighted to announce Major Depressive Disorder (MDD) as our third disease indication for Xanamem, which is a key piece of our clinical development strategy. In the Phase 2 trial we will test the ability of a once-daily capsule of Xanamem to control dysregulated cortisol, which is associated with depression, that may not only help reduce depression itself, but also assist in improving impaired cognition.

"The expansion of our Fragile X Syndrome (FXS) Phase 2 trial to North American clinical centres along with a broadened dose range and higher enrolments is an exciting development for Actinogen. By increasing the scope of the trial, we will have a higher quality dataset from which we can judge the effectiveness of Xanamem, which in turn will help us to design a pivotal trial aimed at achieving marketing approvals. We hope that Xanamem will make a material difference to the quality of life for people with this serious clinical syndrome.

"We are very pleased to offer eligible shareholders the opportunity to participate in a Share Purchase Plan on the same terms as an institutional placement to help fund the expansion of our vital clinical development pipeline, as we pursue a revolutionary therapy to improve the quality of life of neurology patients."

Capital Raising

The $12 million capital raising consists of an institutional placement (**Placement**), while the share purchase plan (**SPP**) targets raising $3 million (together, the **Capital Raising**). The offer price for the Capital Raising is $0.135 per new share (Offer Price), representing a 15.6% discount to the last closing price (22 November 2021).

Actinogen's largest institutional shareholder, BVF Partners (BVF), is participating in the Placement as are several new institutional shareholders. Bell Potter Securities Limited acted as Lead Manager.

Placement

The oversubscribed placement to institutions, and sophisticated and professional investors will raise $12 million, before transaction-related costs. The Placement comprises the issue of 88.89 million new, ordinary fully paid Actinogen shares (**New Shares**), at the Offer Price of $0.135 per New Share, and has attracted strong demand from existing shareholders and new investors.

The Placement is to be undertaken using the Company's existing capacity under ASX Listing Rule 7.1. No shareholder approval is required other than for the proposed subscription by Dr. Steven Gourlay of $107,625. New Shares subscribed for under the Placement are expected to settle on Tuesday 30 November 2021 and commence trading on the ASX on or before Wednesday 1 December 2021.

Share Purchase Plan

In addition to the Placement, the Company plans to offer a Share Purchase Plan **(SPP)** to eligible shareholders with a target raise of approximately $3 million. The company reserves the right to accept oversubscriptions of up to a further $2 million. Eligible shareholders at the Record Date of 7:00pm (AEDT) on Wednesday, 24 November 2021 with a registered address in Australia and New Zealand will be invited to participate in the SPP, at the Offer Price (the same issue price as the Placement). The Company also reserves the right to place any shortfall under the SPP (at the same issue price) utilising its remaining capacity under ASX Listing Rules 7.1 and 7.1A. No shareholder approval is required for the SPP or a subsequent placement by the Company of any shortfall under the SPP.

The SPP will open on Monday, 29 November 2021 and close at 5:00pm (AEDT) on Monday, 13 December 2021. The SPP Offer is not underwritten.

Based on the capital structure of the Company as at the Record Date, where the Company raises the targeted $3 million (before costs of the offer), approximately 22 million Shares will be issued under the SPP

(**SPP Shares**). An application for quotation on ASX of the SPP Shares will be made immediately following the issue of those Shares.

An offer booklet containing the terms and conditions of the SPP (**Offer Booklet**) will be lodged with ASX and sent to eligible shareholders on 29 November 2021. The Offer Booklet will include a link to a personalised application form. Shareholders should read the Offer Booklet in full prior to making an application under the SPP.

The Non-executive Directors have elected to take up their full allotment of $30,000 each in the SPP; Dr Gourlay has committed, subject to shareholder approval, to subscribe $107,625 in the Placement.

Key dates for the SPP Offer

Record Date	7pm (AEDT), Wednesday 24 November 2021
Announcement Date	Thursday 25 November 2021
Despatch of SPP Offer Booklet **Opening Date**	Monday 29 November 2021
Expected Placement Issue Date	Tuesday 30 November 2021
Closing Date	5pm (AEDT), Monday 13 December 2021
Announcement of Results of SPP	Monday, 20 December 2021
SPP Shares Issue Date	Monday, 20 December 2021
New Shares quoted on ASX	Tuesday, 21 December 2021

This timetable is indicative only and subject to change. The Company reserves the right to amend the dates at its discretion and without notice, subject to ASX Listing Rules and the *Corporations Act 2001* (Cth).

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 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, 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 other diseases such as Depression.

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.