**ASX ANNOUNCEMENT**

# Xanamem Clinical Development and Investor Update

**Sydney, 26 June 2019. Actinogen Medical (ASX: ACW, 'ACW' or 'the Company')** is pleased to provide an update on the progress the Company is making with the ongoing clinical development program for Xanamem™. This update should be read in conjunction with the latest investor presentation (attached).

## XanADu Phase II Clinical Trial

- The Company has made good progress in performing deeper analyses of the XanADu data to better understand the study outcomes.
- These data analyses are continuing, and confirmation of any findings will become apparent once correlated with the outcomes from the other ongoing preclinical and clinical studies described below.
- When all study outcomes are known, they will be consolidated and form part of a detailed strategic review of the future development of Xanamem, expected in 3Q CY2019.

## XanaHES Phase I Higher Dose Safety Study

- This study, being conducted by Linear Clinical Research in Perth, is progressing well, with the final 20mg study subject expected to be enrolled this week.
- As previously announced, following a scheduled interim safety review, it was recommended that XanaHES continue – there do not appear to be any significant safety concerns with the 20mg daily dose.
- Results from this study will provide important data on using higher doses of Xanamem in future studies, if this is considered necessary.

## Target Occupancy: Phase I PET Study

- This study is being conducted by Professor Chris Rowe and Professor Victor Villemagne at the Austin Hospital in Melbourne.
- This is a technically complex competitive binding, radio-labelled tracer PET imaging study, and the Company is breaking new ground with it.
- The study is progressing to plan, and to date, the 10mg and 20mg subject cohorts of once daily Xanamem have completed the trial. Subject cohorts investigating 5mg and 30mg will follow to provide further insights over a dose gradient of Xanamem.
- The study has generated encouraging results that are being used to refine the protocol to ensure the Company receives the maximal value from this important study.
- In order to complete this study in humans, the Company performed multiple experiments leading up to the development of the Phase I protocol, and given the outcomes of these experiments, the study results as a whole will only be discerned once all cohorts have been completed.

- The Company is pleased to confirm that initial results observed demonstrate that Xanamem inhibits the 11β-HSD1 enzyme in the brain (refer to slide 11 of the attached Investor Presentation).

**Target Occupancy: Homogenate Binding Studies**

- This suite of complex in-vitro studies is being conducted in Birmingham, UK, and is designed to further confirm and enhance the data and conclusions from the Target Occupancy study.
- The suite of studies includes autoradiography involving competition, saturation and enzyme activity studies at varying concentrations of Xanamem

**Pre-Clinical Toxicology Studies**

- Long-term toxicology studies in two non-primate species are mandated by regulatory agencies for all drugs prior to the commencement of longer-term clinical studies.
- The long-term toxicology studies in rat and dog are progressing as planned and will read-out over the rest of 2019 and into 2020.
- Encouragingly and importantly, the feedback to date indicates no unexpected toxicological or safety concerns with longer term exposure to Xanamem.

**Expansion Opportunities into New Indications**

- The Company is progressing the planning for the new Xanamem indications of cognitive impairment in mood disorders and schizophrenia.
- Consolidation of a clinical development plan for these indications will occur over the next few months in consultation with an expert Advisory Board, and the Company looks forward to providing an update in due course.

**Manufacturing of Xanamem**

- In preparation for further clinical development of Xanamem, the Company has undertaken a rigorous process of selecting a Contract Development and Manufacturing Organisation (CDMO) with the expertise and capabilities to optimise the synthesis of Xanamem and scale up production required for clinical development and commercialisation.
- The Company is pleased to announce that it has recently selected Corden Pharma LLC (Liestal, Switzerland) as its new CDMO partner.
- Corden Pharma will provide various services to the Company including the manufacturing of the active pharmaceutical ingredient (API), manufacturing of drug product, and regulatory and packaging services. Corden has full commercial-scale capabilities.

**Partnering Update**

- In early June, the Company participated in the BIO 2019 International Convention, the world's largest biotech partnering meeting attracting pharmaceutical and biotech companies from around the world.
- Actinogen held more than 20 partnering meetings where the recent study results, progress to date, and the plans for the ongoing development of Xanamem were discussed.
- Actinogen received encouraging feedback from all the prospective partners, all of whom requested to be kept updated on ongoing study progress and the Company's plans.

**Updated Investor Presentation (attached)**

- The latest investor presentation highlights progress achieved to date.
- Particular emphasis is made to the impressive pharmacodynamic effects of Xanamem from the XanADu study (slide 9); the preliminary data from the Target Occupancy study (slides 10 and 11); and the interim review of the XanaHES higher dose safety study (slide 12).
- Also included is additional detail on the opportunity presented by the new indications of cognitive impairment in mood disorders and schizophrenia (slides 15-20 and 23-27).

Actinogen looks forward to updating investors on the progress of all of the ongoing studies, and the outcome of the Company's strategic review once more of the results become available.

**ENDS**


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**About Actinogen Medical**

Actinogen Medical (ASX: ACW) is an ASX-listed biotechnology company focused on innovative approaches to treating cognitive decline that occurs in chronic neurological and metabolic diseases. Actinogen Medical is developing its lead compound Xanamem, as a promising new therapy for Alzheimer's disease, a condition with multibillion-dollar market potential and material human impact. In the US alone, the cost of managing Alzheimer's disease is estimated to be US$250bn and is projected to increase to US$2tn by 2050, outstripping the treatment costs of all other diseases. Alzheimer's disease is now the leading cause of death in the UK and second only to ischaemic heart disease in Australia. In addition, Actinogen is currently planning an expanded clinical development program for Xanamem in cognitive impairment in mood disorders and schizophrenia. In the US alone, the collective economic costs of mood disorders and schizophrenia are estimated to exceed $550bn, with the burden increasing every year. The cognitive dysfunction associated with these conditions is significantly debilitating for affected patients, with a substantial unmet medical need for novel, improved treatments.

**About Xanamem™**

Xanamem's novel mechanism of action sets it apart from other Alzheimer's treatments. It works by blocking the excess production of cortisol - the stress hormone – through the inhibition of the 11β-HSD1 enzyme in the brain. There is a strong association between chronic stress and excess cortisol that leads to changes in the

brain affecting memory. The 11β-HSD1 enzyme is highly concentrated in the hippocampus and frontal cortex, the areas of the brain associated with cognitive impairment in neurological diseases, including Alzheimer's disease, mood disorders and schizophrenia.

**About XanADu**

XanADu is a Phase II double-blind, 12-week, randomised, placebo-controlled study to assess the safety, tolerability and efficacy of Xanamem in subjects with mild dementia due to Alzheimer's disease. XanADu has fully enrolled 186 patients from 25 research sites across Australia, the UK and the USA. The trial is registered on www.clinicaltrials.gov with the identifier: NCT02727699, where more details on the trial can be found, including the study design, patient eligibility criteria and the locations of the study sites.

**About XanaHES**

XanaHES is a Phase I, randomised, single blinded, central reader blinded, placebo-controlled, dose escalation study to assess the safety and tolerability of Xanamem™ 20mg & 30mg once daily in healthy elderly volunteers. Changes in cognitive performance from baseline to end-of-treatment will be measured as an exploratory efficacy outcome.

**Actinogen Medical encourages all current investors to go paperless by registering their details with the designated registry service provider, Link Market Services.**