ASX ANNOUNCEMENT

Actinogen Alzheimer's Disease Biomarker Study Timing and Design

Sydney, 13 July 2022. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to provide further information on the timing and design of the Company's upcoming Biomarker Study in patients with Mild Alzheimer's Disease (AD).

This study is analysing stored plasma 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 and results were first reported in 2019. At that time blood-based AD biomarker analysis was not available and the clinical diagnosis of AD was not confirmed by amyloid brain scans or biomarkers of the disease.

Results from the new study are now expected to be available by the end of October 2022. Previously the Company had guided shareholders to a H2 CY2022 timeframe.

Approximately 70 of the original patients had available and adequate samples for the analyses, representing a relatively large sample size for a biomarker study.

There are three key design elements of the biomarker analysis:

1. To eliminate "noise" in the data by removing patients without biomarker-confirmed AD. *It is estimated that up to 30-40% of the population studied may have had alternative causes of dementia.*
2. To analyse the difference between Xanamem 10mg daily and placebo in change in levels of biomarkers from Baseline to Week 12 using blinded assessment procedures. *This objective can be considered a surrogate endpoint for Xanamem's possible disease-modifying effects with longer treatment, to be confirmed in future trials.*
3. To analyse the therapeutic effects of Xanamem vs. placebo, using an a priori statistical analysis plan, on component cognitive scores more suitable to demonstrate efficacy of Xanamem in the mild AD population and for a short, 12-week study. *For example, the previously published XanADu ADASCog endpoint has typically been used in a more moderately severe population in trials of at least 24 weeks duration.*

Positive data on cognitive enhancement would further confirm the Company's strategy to focus on shorter term trials for *Cognitive Enhancement (a potentially useful treatment option for AD, with activity on working memory and attention demonstrated in two well-controlled trials in older volunteers)*.

Positive data from improvement in biomarkers would give the Company increased confidence to pursue *Disease-Modification (the Alzheimer's Disease "Holy Grail")* in addition to *Cognitive Enhancement.*

The biomarkers to be analysed in the blood are:

- Proteins that are considered pathological hallmarks of AD: Amyloid-beta and Tau
    - Amyloid-beta protein (Aβ)1-40, 1-42, and ratio of Aβ1-42/40
    - Total tau (T-tau) and Phospho-Tau181 (p-Tau181)

- Proteins that are considered markers of neuronal damage: NfL and GFAP
    - Neurofilament light chain protein (NfL)
    - Glial fibrillary acidic protein (GFAP)

The analysis of the samples will be conducted at the University of Gothenburg, Sweden, under the direction of world-leading AD researcher Professor Kaj Blennow, with statistical analysis to follow.

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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.

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