

ASX ANNOUNCEMENT

First patient treated in Actinogen's XanaMIA phase 2b Alzheimer's disease trial

Sydney, 15 April 2024. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce the first patient randomized and treated on Friday 12 April in the XanaMIA phase 2b clinical trial in patients with biomarker-positive mild to moderate Alzheimer's disease (AD).

The trial of 220 participants, with elevated levels of the blood biomarker pTau, measures the effects of a Xanamem[®] 10 mg daily dose versus placebo over a 36-week treatment period. The trial has commenced at thirteen Australian sites and will subsequently expand to the USA.

Dr Steven Gourlay, Actinogen's CEO and MD, said:

"We are very pleased to announce the first patient treated in our phase 2b trial in patients with Alzheimer's disease. Based on encouraging safety and clinical activity seen in multiple prior trials of Xanamem, and a strong scientific rationale for reducing brain cortisol levels, we are confident that the trial will confirm clinically and statistically meaningful results."

"This phase 2b trial is designed to confirm that Xanamem is a safe and effective new treatment for Alzheimer's disease and represents a major opportunity for patients and the Company."

"The clear priority for the next 18 months is to deliver high quality results from our on-going phase 2 clinical trials in depression and Alzheimer's disease, the first of which will report results in Q3 this year."

The primary endpoint for the AD trial is a cognitive test battery comprising seven different digital assessments (Xanamem benefits on cognition were observed in three earlier placebo-controlled trials including an initial study in AD).

A key secondary endpoint is the Clinical Dementia Rating – Sum of Boxes scale (CDR-SB), a validated combined cognitive and functional measure, used by the FDA and many companies as a primary or secondary endpoint for regulatory approval. Previously, in an analysis of biomarker-positive patients with mild AD treated with Xanamem, clinically significant benefits were seen on cognition and the CDR-SB endpoint. A variety of other secondary endpoints include the Amsterdam Activity of Daily Living scale, which measures the ability to perform everyday tasks.

An interim analysis is planned for mid-2025 when approximately 100 patients reach 24 weeks of treatment, with final results anticipated in H1 CY26.

ENDS

[®] Xanamem is a registered trademark of Actinogen Medical Limited

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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.

Current Clinical Trials

The XanaCIDD Phase 2a depression trial is a double-blind, six-week proof-of-concept, placebo-controlled, parallel group design trial in 160 patients. Patients are evenly randomized to receive Xanamem 10 mg once daily or placebo, in some cases in addition to their existing antidepressant therapy, and effects on cognition and depression are assessed.

The XanaMIA Phase 2b Alzheimer's disease trial is a double-blind, 36-week treatment, placebo-controlled, parallel group design trial in 220 patients with mild to moderate AD and progressive disease, determined by clinical criteria and confirmed by an elevated level of the pTau181 protein biomarker in blood. Patients receive Xanamem 10 mg or placebo, once daily, and effects on cognition, function and progression of Alzheimer's disease are assessed. Thus, Xanamem is being assessed in this trial for its potential effects as a both a cognitive enhancer and a disease course modifier.

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.

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease and excess cortisol is known to be toxic to brain cells. 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

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 and clinically significant improvements in functional and cognitive ability in patients with biomarkerpositive mild AD. 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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