ASX ANNOUNCEMENT

Enrolment completed in Actinogen's XanaCIDD phase 2a depression trial

Sydney, 22 April 2024. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce achievement of full enrolment of 167 participants in the Company's XanaCIDD phase 2a clinical trial in patients with cognitive impairment in major depressive disorder (MDD). The XanaCIDD trial is a proof-of-concept, placebo-controlled, parallel group trial with a six-week treatment period.

Results are anticipated in early Q3 this year after all participants complete treatment plus four weeks of follow-up, data are cleaned, and the pre-specified analysis is performed.

This is an important and unique trial in the neuropsychiatric field because of its focus on the ability of Xanamem® to improve cognitive function in patients with MDD by reducing levels of the "stress hormone", cortisol, in the brain, while leaving normal cortisol stress response intact in the body. Xanamem does this by inhibiting tissue cortisol synthesis in the brain by an enzyme called 11β-HSD1, without affecting cortisol synthesis by different enzymes in the adrenal gland.

Cognitive impairment, or "foggy thinking" is reported by the majority of patients with MDD and may not respond to traditional anti-depressant therapy. Xanamem is being developed as an easy-to-use, oral therapy to improve cognitive impairment associated with MDD and Alzheimer's disease. It has potential uses in other diseases where cognitive impairment is a significant problem such as schizophrenia and other types of dementia.

Dr Dana Hilt Actinogen's Chief Medical Officer, said:

"*We are pleased to announce the final patient has enrolled in our XanaCIDD phase 2a clinical trial in patients with cognitive impairment in major depressive disorder. This robust, placebo-controlled trial of 167 people will inform us if Xanamem can improve cognition in these patients and assess any related effects on symptoms of depression itself.*

Any positive effects on cognition in this trial would confirm prior trial findings of cognitive enhancement and support the likelihood of future success in the on-going 36-week phase 2b XanaMIA trial in patients with Alzheimer's disease.

We continue to observe the excellent safety profile for Xanamem and believe its low drug-drug interaction potential makes it an ideal candidate for use in multiple diseases and populations."

The XanaCIDD trial is a phase 2a, proof-of-concept, placebo-controlled, parallel group trial in patients with persistent MDD and measurable cognitive impairment. Xanamem (10 mg) or placebo is added to the existing anti-depressant therapy or, in patients with a previous history of anti-depressant treatment, as a stand-alone treatment.

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The primary endpoint for the trial is the computerized Cogstate "attention composite" test battery, measuring attention and working memory and shown previously to be a sensitive measure of Xanamem benefit in the prior XanaMIA Part A and XanaHES trials. Attention and working memory, sometimes characterized as the ability to focus, is a critical and essential component of cognitive ability.

The key secondary endpoint is the Montgomery-Asberg Depression Rating Scale (MADRS) which is a structured interview evaluating MDD symptoms and is a fundamental endpoint used for regulatory approvals of anti-depressant medication. Other secondary endpoints include an executive function cognitive composite, a memory function cognitive composite, proportions of responders and global clinical assessment scores.

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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 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 and clinically significant improvements in functional and cognitive ability in patients with biomarker-positive 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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