ASX ANNOUNCEMENT

Actinogen enhances XanaMIA Phase 2b Alzheimer's disease trial design to reduce cost and time to initial results

Sydney, 26 September 2023. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce enhancement of the design of the XanaMIA Phase 2b trial in patients with mild-to-moderate Alzheimer's disease to reduce the cost and time to initial results.

The current FDA-approved three-arm trial was designed to confirm the safety, pro-cognitive and clinical benefits of Xanamem® and explore two dose levels, in what is called 'dose-ranging'. The new design keeps the same endpoints, 36-week treatment length and other features with the exception of dose-ranging.

Removal of the 5 mg dose group, while deferring the dose-ranging aspect of the Xanamem program to the next, likely Phase 3 trial, does not detract from the strong confirmatory value of the trial design. The trial retains its ability to robustly demonstrate the clinical benefit of Xanamem in patients with Alzheimer's disease.

Operationally, the trial has been streamlined with the following modifications:

- New: 10 mg or placebo daily vs. 10 mg, 5 mg or placebo previously
- New: 220 patients vs. 330 patients previously but still studying patients with the elevated blood pTau biomarker (the same group shown to have a large Xanamem clinical effect in the previous Phase 2a biomarker trial)
- New: Australian sites to enroll the first 100 patients vs. simultaneous global site activation previously
- New: Initial efficacy and safety results from an administrative interim analysis when approximately 100 patients reach 24 weeks of treatment vs. unspecified previously.

Collectively these changes reduce trial costs significantly and increase forecast receipts from Australian R&D tax incentive cash refunds by focusing on Australian R&D activities in the near term. Net forecast savings between now and June 2025 will be in the order of $30 million compared to the original plan.

The new implementation plan assumes that expansion of the XanaMIA trial will occur when potentially new, positive clinical data is received from the XanaCIDD trial by mid-2024 and/or the redesigned XanaMIA interim analysis, planned for H1 2025.

Xanamem's promising safety profile has been demonstrated in more than 300 people to date.

The XanaMIA Phase 2b trial will finalize Australian clinical site start up activities as soon as possible with patient recruitment expected before the end of the year.

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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 and Upcoming 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

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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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