ASX ANNOUNCEMENT

Actinogen CMO presents academic poster to Alzheimer's Association International Conference in Amsterdam

Sydney, 17 July 2023. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that its Chief Medical Officer, Dr Dana Hilt MD is presenting an academic poster to the ***Alzheimer's Association International Conference*** (AAIC) later today in Amsterdam, The Netherlands. AAIC is a global forum to advance dementia science.

The Actinogen academic poster is titled *Xanamem shows pro-cognitive activity with clinically meaningful effect sizes across 3 independent, placebo-controlled clinical trials*. An image of the poster is attached to this announcement.

The poster and the associated abstract summarize data from three earlier Phase 1 and Phase 2a Xanamem® trials and concludes that Xanamem displays activity in multiple domains of cognition including attention, working memory, and executive function with clinically meaningful effects in normal subjects and in patients with pTau-elevated mild Alzheimer's disease. These data suggest Xanamem may be both a pro-cognitive drug and disease-modifying agent and guide design of future trials, including the upcoming XanaMIA Phase 2b trial in patients with early Alzheimer's disease, due to treat its first patient prior to the end of 2023.

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

"Actinogen is excited to present its novel Phase 2a dataset that is one of the first to show that the blood pTau biomarker is a highly effective method for selection of patients with a progressive form of mild Alzheimer's disease. In these patients, Xanamem showed multiple indications of both clinical benefit (slowed progression of CDR-SB which assesses clinical function) and tests of cognition. Xanamem has now shown precognitive effects in a number of studies. As a simulation of the upcoming 330-patient XanaMIA Phase 2b trial the data give us confidence in our study design, endpoints and patient selection criteria."

ENDS

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Announcement authorised by the Board of Directors of Actinogen Medical

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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.

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.

Disclaimer

This announcement and attachments may contain certain "forward-looking statements" that are not historical facts; are based on subjective estimates, assumptions and qualifications; and relate to circumstances and events that have not taken place and may not take place. Such forward looking statements should be considered "at-risk statements" - not to be relied upon as they are subject to known and unknown risks, uncertainties and other factors (such as significant business, economic and competitive uncertainties / contingencies and regulatory and clinical development risks, future outcomes and uncertainties) that may lead to actual results being materially different from any forward looking statement or the performance expressed or implied by such forward looking statements. You are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof. Actinogen Medical does not undertake any obligation to revise such statements to reflect events or any change in circumstances arising after the date hereof, or to reflect the occurrence of or non-occurrence of any future events. Past performance is not a reliable indicator of future performance. Actinogen Medical does not make any guarantee, representation or warranty as to the likelihood of achievement or reasonableness of any forward-looking statements and there can be no assurance or guarantee that any forward-looking statements will be realised.

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Xanamem shows pro-cognitive activity with clinically meaningful effect sizes across 3 independent, placebo-controlled clinical trials

Dana Hilt[1], Jack Taylor[1], Paul Rolan[1] , Tamara Miller[1], Mark Jaros[2], John Harrison[3,4], Craig Ritchie[3]

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Background

- Xanamem® is a potent and selective inhibitor of 11β hydroxysteroid dehydrogenase type 1 (11β-HSD1).
- 11β-HSD1 is highly expressed in regions such as the hippocampus, frontal cortex, and cerebellum.
- Elevated cortisol is associated with cognitive dysfunction and neurotoxicity in animals and in human studies.
- Reducing cortisol levels in the brain is considered an important therapeutic goal in the treatment of Alzheimer's Disease (AD) and other conditions where cognitive impairment and cortisol excess is a major component of the disease.
- Nonclinical and clinical studies to date indicate that Xanamem offers potential to be rapidly cognitive enhancing.

Phase 1 studies (older NHV)

XanaHES (n=42) and XanaMIA-DR (n=107):

- Phase 1 double-blind, placebo-controlled, dose-ranging trials
- Healthy older health normal volunteers (NHV) 50-80 years
- XanaHES: 20mg Xanamem or placebo orally for 12 weeks
- XanaMIA-DR: 5mg Xanamem, 10mg Xanamem, or placebo orally for 6 weeks
- Primary objectives were safety, and effects on cognition measured by the Brief Cogstate Cognitive Test Battery (CTB)
- Assessment of treatment effect sizes using Cohen's d and Standardized Mean Response (SMR)

Phase 2a XanADu Biomarker Ext.

- Phase 2 double-blind, placebo-controlled trial
- Probable mild AD (MMSE 20-26)
- 10mg Xanamem or placebo orally for 12 weeks (n=185)
- Biomarker extension prospectively analysed stored plasma samples (n=72) on the Quanterix SIMOA platform
- Plasma biomarkers included p-tau181, Amyloid 42/40, and GFAP
- A prespecified analysis explored clinical and cognitive outcomes in subgroups of above and below median p-tau181 conc.:
  - Higher (H; > 6.74pg/mL) or
  - Lower (L; ≤ 6.74pg/mL)

Xanamem improves cognition across multiple clinical trials

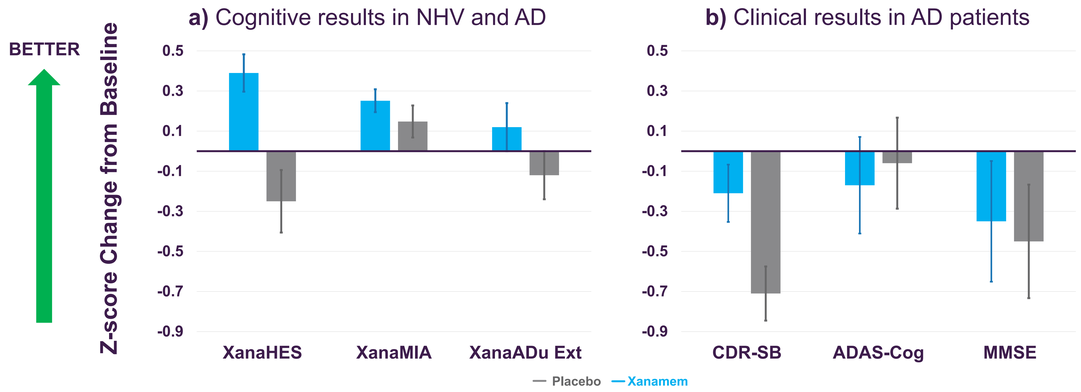

Fig 1: a) Z-score change from baseline in cognitive tests of attention, working memory in the XanaHES, XanaMIA-DR trial, and of executive function in XanADu Biomarker Ext trial. **b)** Z-score change from baseline on selected clinical outcomes measures in the prespecified high p-tau181 group from the XanADu biomarker Ext. trial. Error bars represent ± SE.

Administrations and clinical safety

- Easy, oral once-a-day administration
- Can be given with or without food
- Safe and well tolerated in >300 patients dosed
- No drug-related SAEs across all trials

Phase 1 trial results

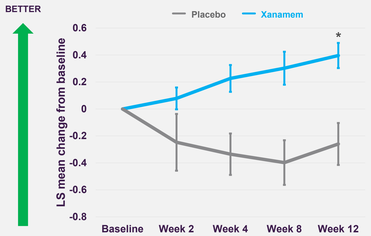

Fig 2: XanaHES: Least Squares (LS) mean change from baseline in scores in the Attention Composite of the CTB. Error bars represent ± SE.
*** Cohen's d = 1.27.**

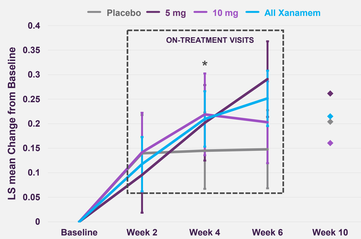

Fig 3: XanaMIA-DR: Least Squares (LS) mean change from baseline in scores in the Attention Composite of the CTB. Error bars represent ± SE.
*** p = 0.05, SMR = 0.32**

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Phase 2 trial results

Activity consistent with Xanamem action as a cognitive enhancer & disease-modifier

Fig 4: XanADu phase 2 exploratory analysis. Least Squares (LS) mean change from baseline in cognitive composite scores. Trends in change of composite of word recall & recognition (ADAS-Cog), CFT & COWAT. Error bars represent ± SE.

Xanamem largely prevented clinical progression over 12 weeks

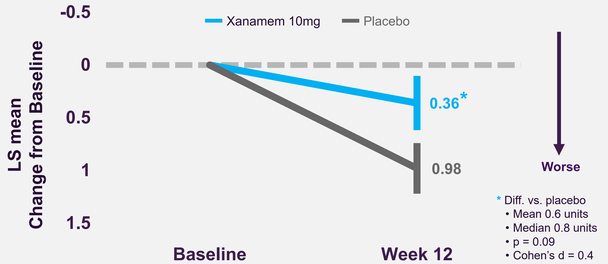

Fig 5: XanADu phase 2: Least Squares (LS) mean change from baseline in CDR-SB in high p-tau181 subgroup demonstrating large clinical effect size vs placebo. Error bars represent ± SE.

Conclusions

- **Xanamem displays positive activity in multiple domains of cognition including attention, working memory, and executive function, with clinically meaningful effect sizes**
- **Data from multiple clinical trials suggest Xanamem to be both a procognitive and disease-course modifying agent.**
- **A larger Phase 2b trial in patients with early AD is will begin in H2 2023 to confirm Xanamem's cognitive and clinical benefits.**