ASX ANNOUNCEMENT

ACW academic presentation at Clinical Trials on Alzheimer's Disease conference

Sydney, 03 December 2022. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce the academic presentation of the XanaMIA Phase 1b (Part A) trial results at the Clinical Trials on Alzheimer's Disease (CTAD) conference in San Francisco on 2 December 2022.[1]

The poster presentation reports encouraging safety data and concludes that the trial observed positive effects on attention and working memory in cognitively normal, older volunteers at 5 and 10 mg daily doses of the Company's novel small molecule lead compound, Xanamem.®

The results were consistent with similar, positive data in a prior trial of a cognitively normal population with a 20 mg daily dose,[2] and with the recent Phase 2a clinical biomarker study showing a large clinical effect on the Clinical Dementia Rating Scale – Sum of Boxes in the group of patients with mild Alzheimer's Disease (AD) most likely to progress.[3]

The safety profile of Xanamem continues to be excellent and demonstrate a favourable profile for chronic therapy.

The next XanaMIA Phase 2b (Part B) trial of 330 patients with early AD will commence in H1CY2023.

A copy of the academic poster presented at the conference is attached.

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Announcement authorised by the Board of Directors of Actinogen Medical

[1] XanaMIA Phase 1b (Part A) trial results announced 27 April 2022
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[2] XanaHES Phase 1 trial results announced 1 October 2019
[3] Phase 2a AD biomarker study results announced 10 October 2022

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 and clinically significant improvements 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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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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XanaMIA-DR: A Double-Blind, Placebo-Controlled, Dose Ranging Study to Assess the Efficacy, Pharmacodynamics and Safety of Xanamem® in Healthy Elderly Volunteers

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Background

Xanamem® is a potent and selective inhibitor of 11β hydroxysteroid dehydrogenase type 1 (11β-HSD1), which catalyzes the conversion of cortisone to cortisol. In the brain, 11β-HSD1 is highly expressed in regions such as the hippocampus, frontal cortex, and cerebellum. There is evidence from studies in animals and in humans linking elevated cortisol with cognitive dysfunction and neurotoxicity. Thus, 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.

Methods

The main features of the XanaMIA Phase 1b trial were:

- Double-blind, placebo-controlled, dose-ranging
- Healthy older volunteers 50-80 years
- 5 mg Xanamem (n=36), 10 mg Xanamem (n=34), or matching placebo (n=37) orally for 6 weeks
- Primary objectives were safety, pharmacodynamics of ACTH and effects on cognition measured by the 6-domain Brief Cogstate Cognitive Test Battery (CTB)
- Main objective was estimation of the magnitude and consistency of clinical effect sizes in attention and memory composites
- Effect sizes were estimated from modeled data as Z scores and raw data as Standardized Mean Response (SMR) - a version of the Cohen's d statistic
- The a priori criterion for effect detection was SMR (d) ≥ 0.3 in one or more tests.

Adverse Events

Xanamem was safe and well-tolerated over the 6-week treatment period in this cognitively normal population aged 50-80 years (mean age 64 years, 65% female). There were no treatment-related serious adverse events, and other predominantly mild adverse events were generally equally distributed across the 3 groups (Table 1).

Table 1: Number (%) of Subjects with common TEAEs

	Placebo (N = 37)	5 mg Xanamem (N = 36)	10 mg Xanamem (N = 34)	All Subjects (N = 107)
All TEAEs	32 (86.5)	26 (72.2)	23 (67.6)	81 (75.7)
IP-related TEAEs	13 (35.1)	16 (44.4)	15 (44.1)	44 (41.1)
Headache	11 (29.7)	10 (27.7)	10 (29.4)	31 (28.9)
Nausea	1 (2.7)	4 (11.1)	3 (9)	8 (7.4)
Arthralgia	5 (13.5)	3 (8.3)	-	8 (7.4)

Cogstate "attention composite" benefit in working memory & attention replicate prior trial findings

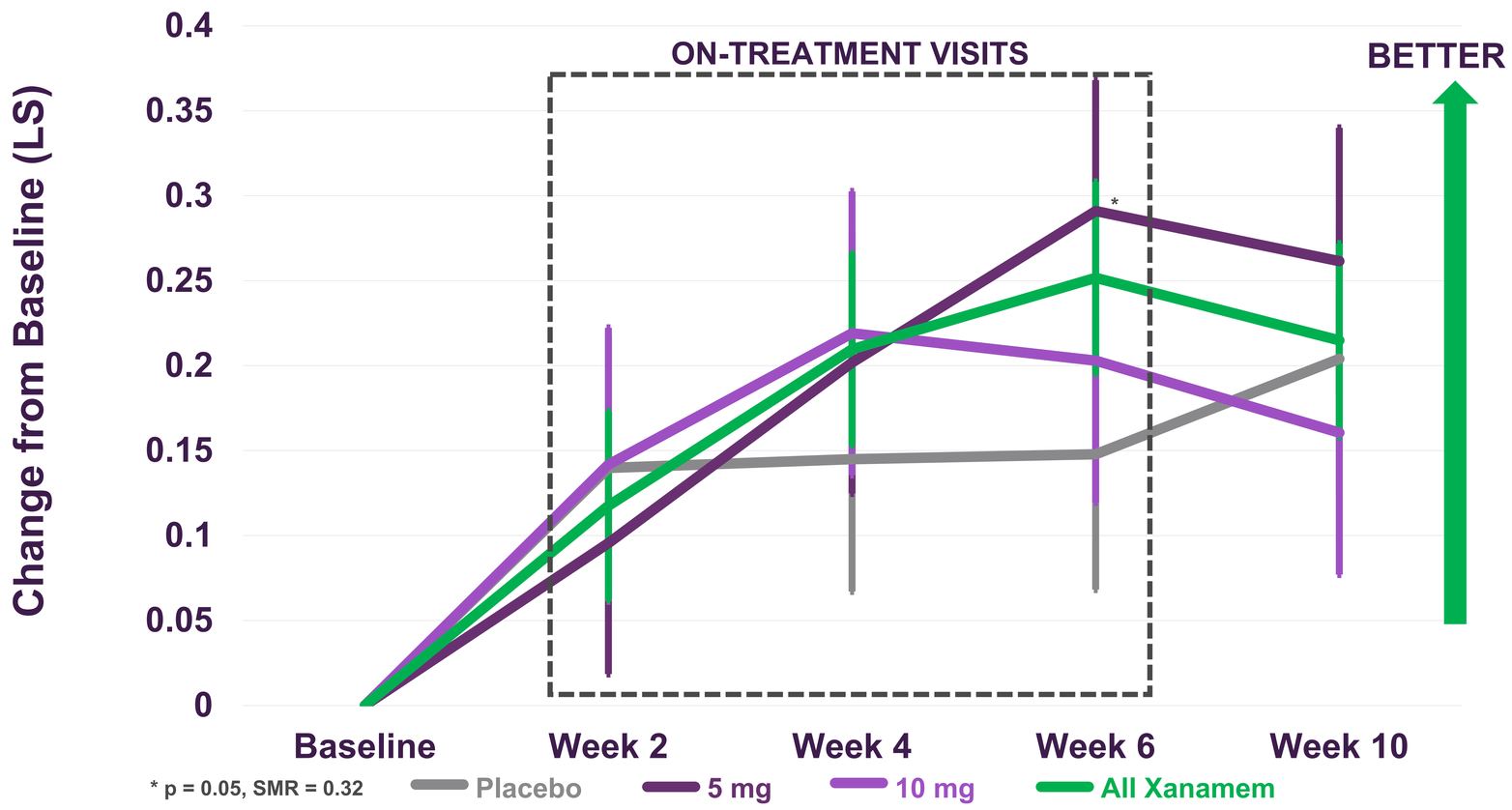

Fig 1: Mean (LS) change from baseline in scores in the Attention Composite of the CTB. Error bars represent ± SE.

Pharmacodynamics

Increases in plasma ACTH were similar to those observed previously and confirmed biologic activity of both doses (Fig 2).

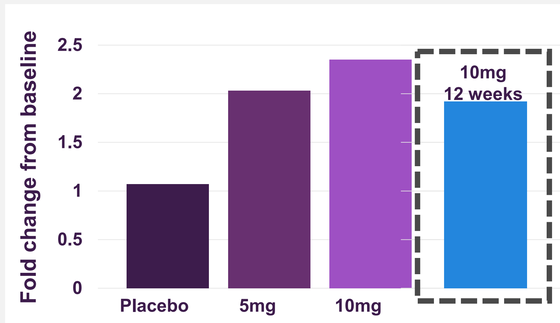

Fig 2: Mean fold increase in plasma ACTH concentration at end of treatment. Box represents fold change in previous 12 week trial XanaHES

Cognitive Results

Practice or placebo effects

Not unexpectedly for a cognitively normal population, practice or placebo effects were seen to Week 2 in the attention composite and to Week 10 in the memory composite.

Attention domain

Clinically significant improvements greater than placebo were seen beyond Week 2 for both dose levels in the attention composite, and for its three tests, including working memory. Performance declined after treatment cessation, consistent with removal of drug effect.

Memory domain and IDSST

Improvements in performance were seen during treatment in all groups including placebo in those test making up a memory domain composite (Fig 3). Performance did not decline after treatment cessation. For the IDSST active and placebo groups both had a mean improvement to Week 6 of ~3.5 units without reduction upon treatment cessation.

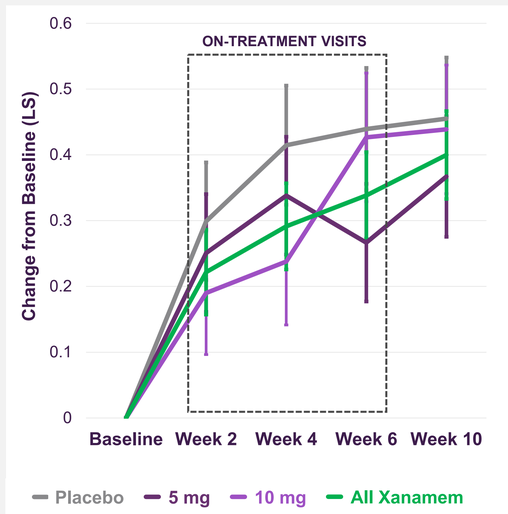

Fig 3: Mean (LS) change from baseline in scores in the Memory Composite of the CTB. Error bars represent ± SE.

Conclusions

- **In cognitively unimpaired older adults six weeks treatment with Xanamem 5 and 10 mg was associated with clinically important improvement in attention.**
- **Xanamem related improvement in attention was qualitatively and quantitatively consistent with that observed in a previous study using a 20 mg dose.**
- **Xanamem was safe and well tolerated.**
- **A larger Phase 2b trial in patients with MCI / mild Alzheimer's Disease is planned for commencement in 2023.**