ASX ANNOUNCEMENT

Actinogen presents to the Asian Society Against Dementia congress in Bandung, Indonesia

Sydney, 29 September 2023. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that its clinical scientist, Dr Jack Taylor, will present at the 17th international congress of the Asian Society Against Dementia (ASAD) in Bandung, Indonesia today.

Dr Taylor's presentation is titled: *The design of a state-of-the-art Phase 2b trial to evaluate the therapeutic potential of Xanamem,® a specific inhibitor of 11B-HSD1, in mild and moderate Alzheimer's Disease.*

The presentation provides an overview of the Xanamem therapeutic rationale, the positive results of two prior placebo-controlled trials and a biomarker trial that together validate the design of the Company's upcoming XanaMIA Phase 2b trial in mild-to-moderate Alzheimer's disease.

The presentation slides are attached to this announcement.

ENDS

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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

® Xanamem is a registered trademark of Actinogen Medical Limited

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 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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The design of a state-of-the-art Phase 2b trial to evaluate the therapeutic potential of Xanamem®, a specific inhibitor of 11β-HSD1, in mild and moderate Alzheimer's Disease

Jack Taylor PhD, Clinical Scientist

17th International Congress of The Asian Society Against Dementia

September 29, 2023

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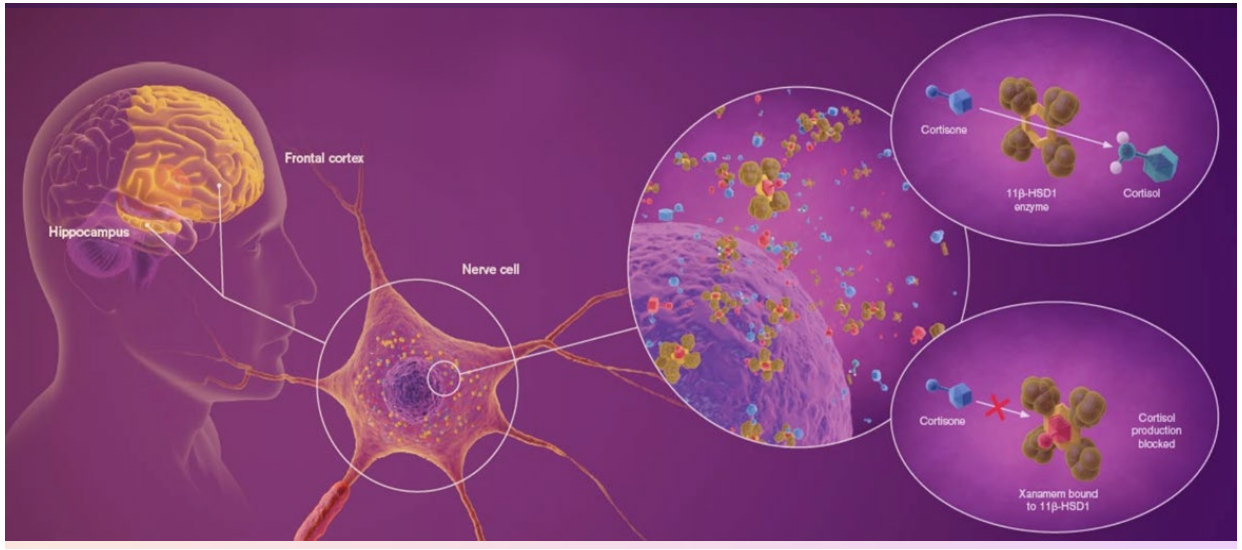
Xanamem: oral, low-dose, once-a-day treatment with a unique, non-amyloid/tau mechanism

Mouse experimental studies & clinical trials validate cortisol target for treatment of AD[1-4]

Brain penetrant 11β-HSD1 small molecule enzyme inhibitor **reduces cortisol inside brain** cells[3,4] - modulating signalling pathways and underlying disease processes

Potential to be:

- Rapidly **cognitive enhancing**
- **Disease-modifying** (slow or halt progression) in AD[1,3]
- **Anti-depressant**



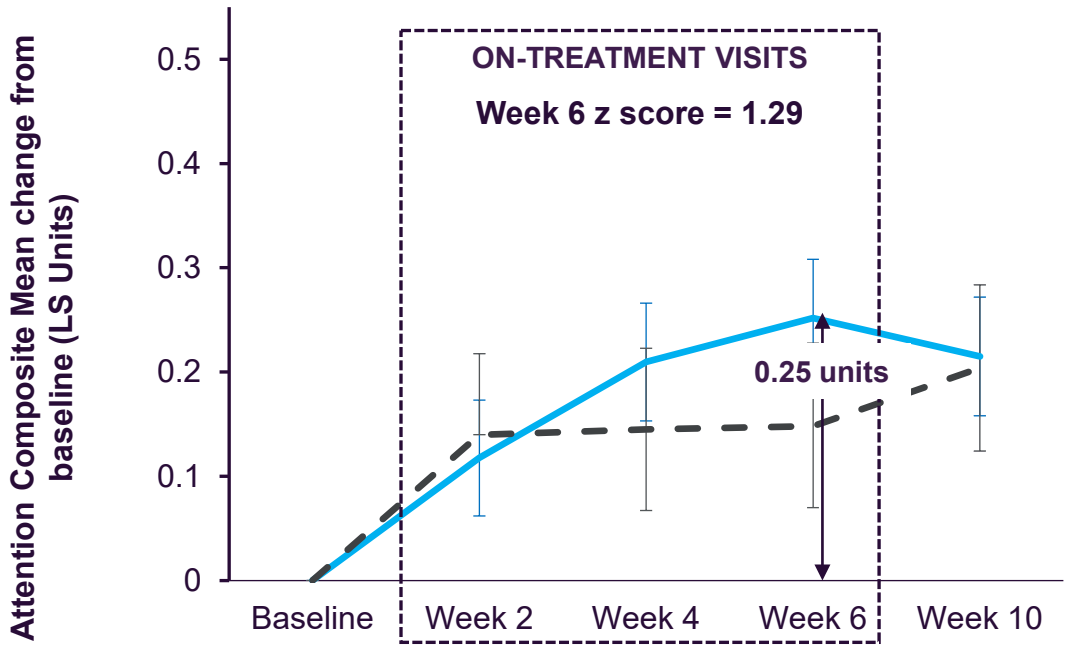
1. Sooy et al. 2015 showing effects on amyloid plaque reduction in an aged mouse model after 28 days associated with increases in insulin degrading enzyme – at 13 month cognitive protection was independent of continued amyloid deposition; 2. Popoli et al. 2011 microglial cell modulation in rats, effects on glutamate, cannabinoid and other signalling pathways; 3. Hilt, D. Oral symposium AD/PD International Conference 2023; Actinogen website: Actinogen – News; 4. based on human PET scan evidence (data on file), Webster et al. 2017 Selection and early clinical evaluation of the brain-penetrant 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) inhibitor UE2343 (Xanamem™)

Similar Xanamem effect on composite of working memory and attention* in two placebo-controlled trials

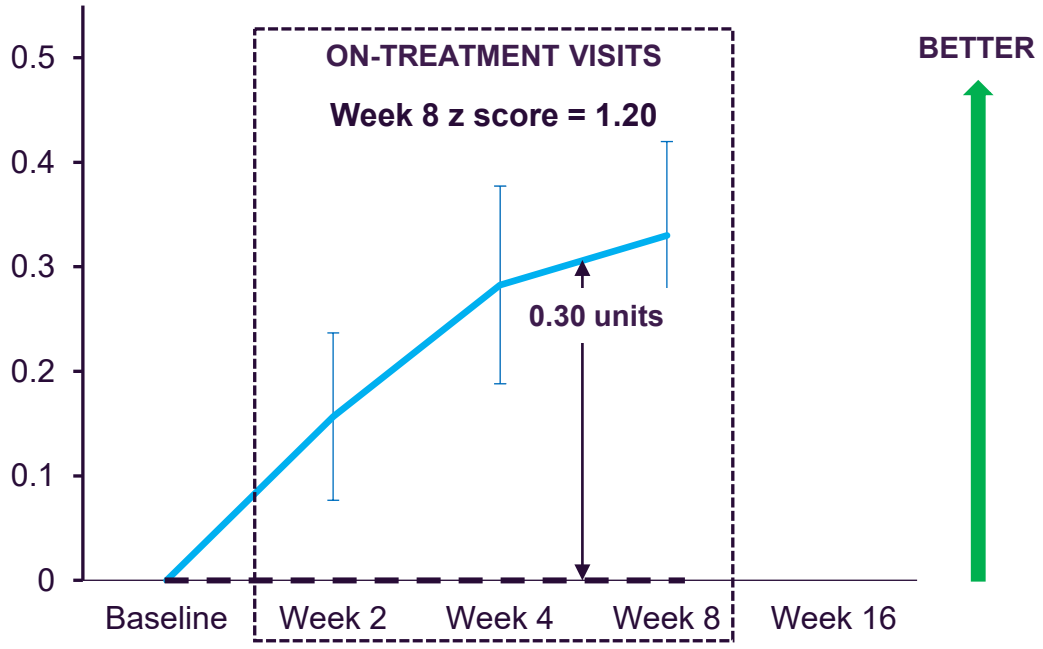
Actinogen

Consistent positive Cogstate effects in trials of older, cognitively normal people aged 50-80 years

XanaMIA Phase 1b trial (n=107, Xanamem 10 mg & 5 mg)[1]



XanaHES Phase 1b trial (n=42, Xanamem 20 mg)[2]



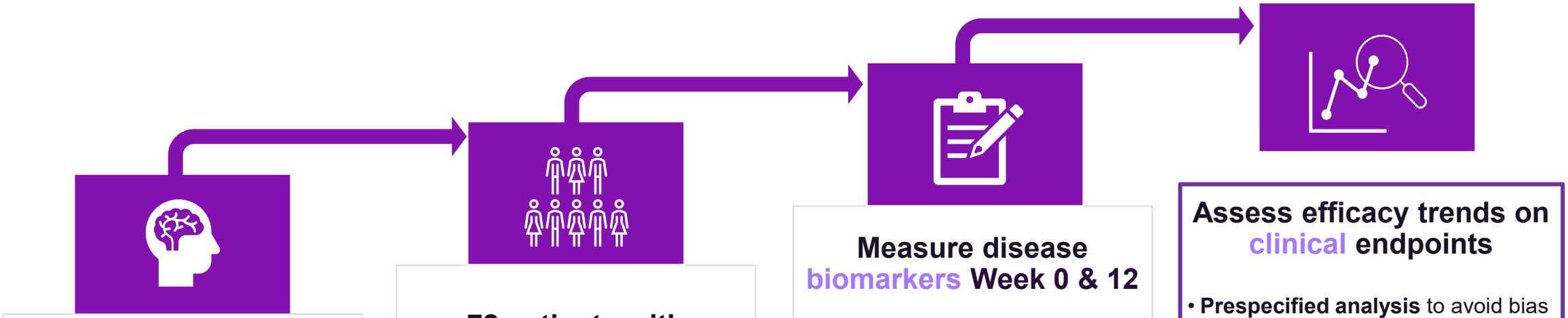
Attention composite improved in two independent, randomized trials

* "Attention composite" of working memory/visual attention/psychomotor speed (mean, SE), z score MMRM analysis Xanamem vs. placebo

1. Placebo n=32
2. Placebo group values were all below zero, not shown, n=12

2022: Phase 2a blood biomarker study design & methods

Uses a pre-specified protocol and analysis plan to avoid bias



Phase 2a trial (XanADu)

- **185 people with mild AD** (MMSE 20-26)
- Clinical diagnosis: no amyloid imaging or biomarkers
- Placebo-controlled
- 12 weeks
- 10 mg Xanamem vs. placebo

72 patients with stored blood samples

- Available plasma stored at -80°C
- Evaluated by expert biomarker laboratory blinded to treatment assignment

Measure disease biomarkers Week 0 & 12

- **pTau181**
- **Amyloid 42/40 ratio**
- **GFAP**
- **tTau (insufficient volume)**
- **NfL (insufficient volume)**

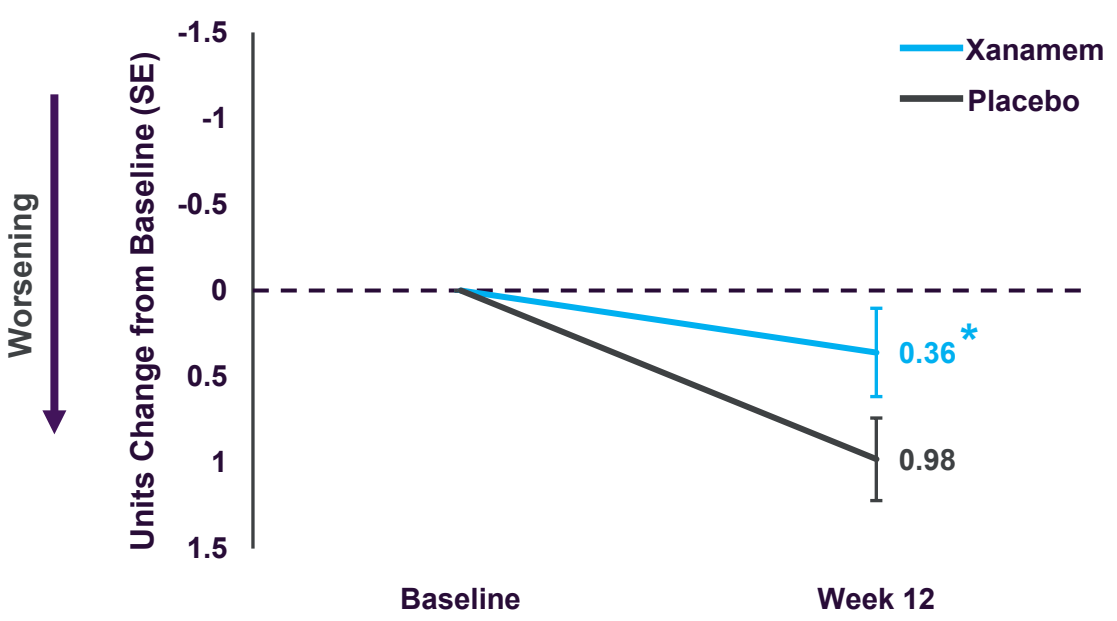
Assess efficacy trends on clinical endpoints

- **Prespecified analysis** to avoid bias
- Select by **baseline pTau181, MMSE and amyloid ratio levels to reassess** efficacy
- Focus on **endpoints most sensitive to change** in a MCI/mild AD population (**CDR-SB**)
- Cohen's d to measure clinical effect size with no correction of p values for multiple comparisons

Topline result from pre-specified analysis in AD patients with plasma pTau181 > median of 6.74 pg/mL

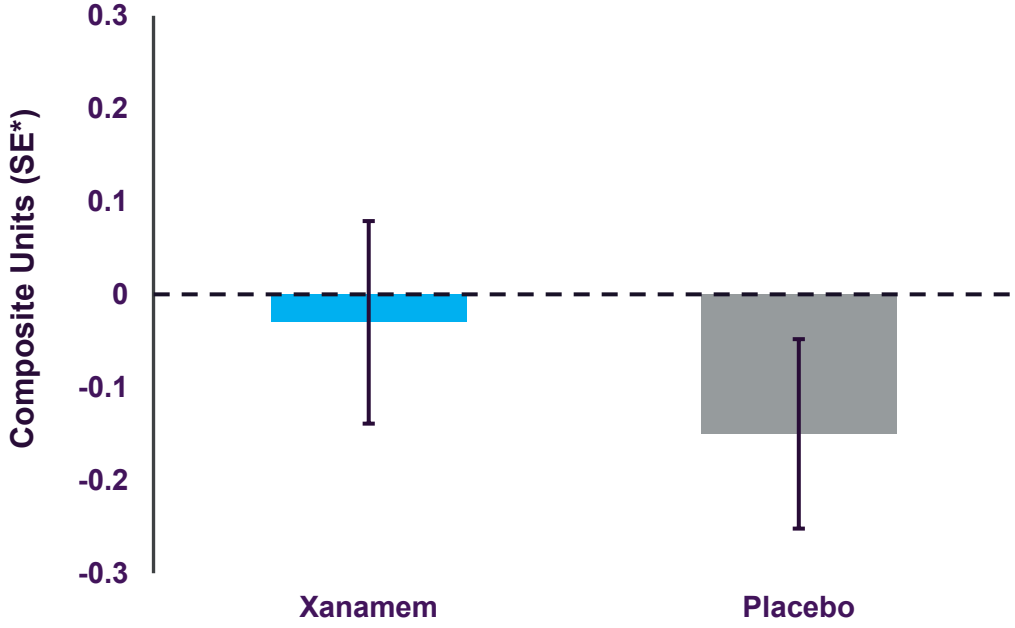
Using pre-specified protocol, statistical analysis plan and blinded biomarker analysis

CDR-SB change from baseline



* Difference vs. placebo: Cohen's d = 0.4, Mean 0.6 units, p = 0.09

Cognitive Composite† change from baseline



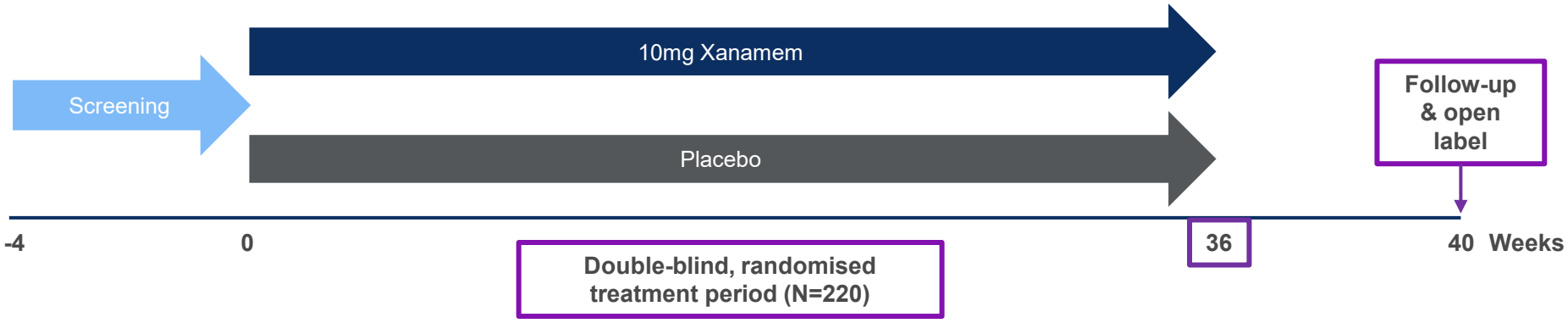
* Difference vs. placebo: Cohen's d = 0.19, Mean 0.12 units, p = 0.42

Oral Xanamem 10 mg largely prevented progression over 12 weeks

† "Cognitive composite" comprised equally weighted standardized change from baseline scores of three ADAS-Cog subscales the Word Recognition, Word Recall, and Orientation, the Controlled Oral Word Association Test (COWAT), and the category fluency test (CFT).

XanaMIA Phase 2b trial in Alzheimer's Disease

Matching patients and endpoints used in the positive Ph 2a analysis



Key inclusion/exclusion criteria	Primary Endpoints	Key Secondary Endpoints	Key Implementation Features
• Clinical diagnosis of **mild to moderate dementia** due to AD (NIA-AA, MMSE 18-26) • Blood **p-tau181** to confirm progressive AD diagnosis • Cognitive impairment test	• **Cognitive Test Battery (cognitive measures)**	• **CDR-SB (functional measure)** • **Amsterdam Activity of Daily Living** scale • Executive Function & Episodic Memory Function Composites • Care Giver questionnaire / Patient Global Improvement	• **Global** trial sites including US, AU, Asia, EU and other • **Actinogen "hands-on" operational model** • **Interim analysis H1 CY25**

NIA-AA=National Institute of Aging - Alzheimer's Association; CDR-SB Clinical Dementia Rating Scale – Sum of Boxes; MMSE – Mini-Mental State Examination

Clinical program to date supports Xanamem as a cognitive enhancer and potential disease modifier

- ✓ Improved attention and working memory in 2 independent randomized trials
- ✓ Clinical activity of Xanamem with large clinical effect size in mild AD
- ✓ Blood p-tau181 levels suitable to select patients for next XanMIA Phase 2b trial
- ✓ Global cognitive composite chosen as primary efficacy endpoint
- ✓ CDR-SB chosen to measure integrated cognition and function

Results from the XanaMIA Phase 2B trial are expected in 2025

Acknowledgements

Very special thank you to the participants and trial sites

Cognition Clinical Advisory Board

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Questions?