ASX ANNOUNCEMENT

Professor Paul Maruff joins Actinogen CMO, Dr Dana Hilt, today in a 'fireside chat' to review progress in evaluation of cognition, Alzheimer's disease and Xanamem's® clinical data

Prof Paul Maruff & Dr Dana Hilt neuroscience webinar: 11am today, 31 August 2023
Event registration: https://us02web.zoom.us/webinar/register/WN_TparOd53TUWkFUGeobwgTw

Sydney, 31 August 2023. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that one of the world's leading neuroscience authorities and cognition experts, Professor Paul Maruff, will join Actinogen's Chief Medical Officer and neurologist Dr Dana Hilt MD to discuss recent progress in the Alzheimer's disease (AD) field and cognitive impairment associated with depressive disorder (CIDD) at **11am today, Thursday 31 August 2023**.

This highly informative 'plain English' interview and discussion will focus on interpreting the various testing methods that have been applied to cognition in AD and CIDD and used to evaluate the efficacy of new drugs such as Xanamem.

Xanamem is ACW's promising novel once-a-day oral medication, currently under clinical development in a Phase 2a trial in patients with CIDD, and about to enter a new Phase 2b trial in patients with mild to moderate AD. It works on lowering brain cortisol and is one of only a few development programs that has demonstrated clinical activity in tests of cognition. Xanamem has positive data from three independent, controlled clinical trials to date.

Register now for today's event at 11am:
https://us02web.zoom.us/webinar/register/WN_TparOd53TUWkFUGeobwgTw

A copy of some presentation slides to be used as reference points for today's conversation is attached to this announcement. Other slides previously used in presentations and on the Actinogen website may also be shown if helpful to facilitate the discussion. As soon as practicable after the conclusion of the webinar a full recording will be made available on the company's website: www.actinogen.com.au.

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 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 330 patients with mild to moderate AD and progressive disease, determined by clinical criteria and confirmed by an elevated level of pTau181 protein in blood. Patients receive Xanamem 5 mg or 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.

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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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Xanamem® : Potential for Benefit in a Number of CNS conditions

Phase 2 studies to be conducted in MDD (Major depressive disorder) and mild/moderate AD

Dana C Hilt MD, CMO Actinogen Medical

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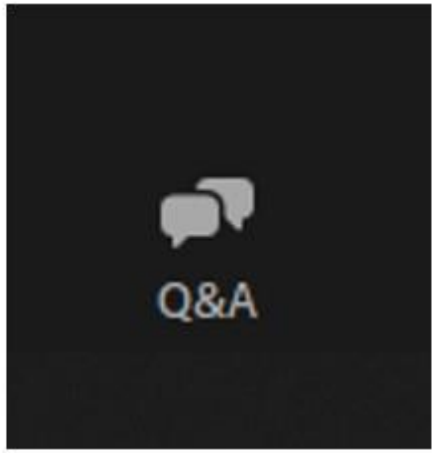
Introduction and welcome

Dr Steven Gourlay
MBBS FRACP PhD MBA
Chief Executive Officer

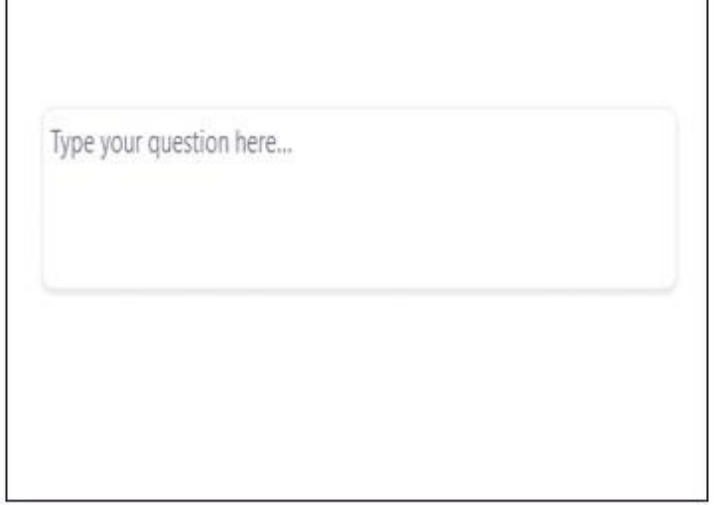
Dr Dana Hilt
MD
Chief Medical Officer

Online Q&A

1. Click on the Q&A icon



2. Type your question in the new Q&A window



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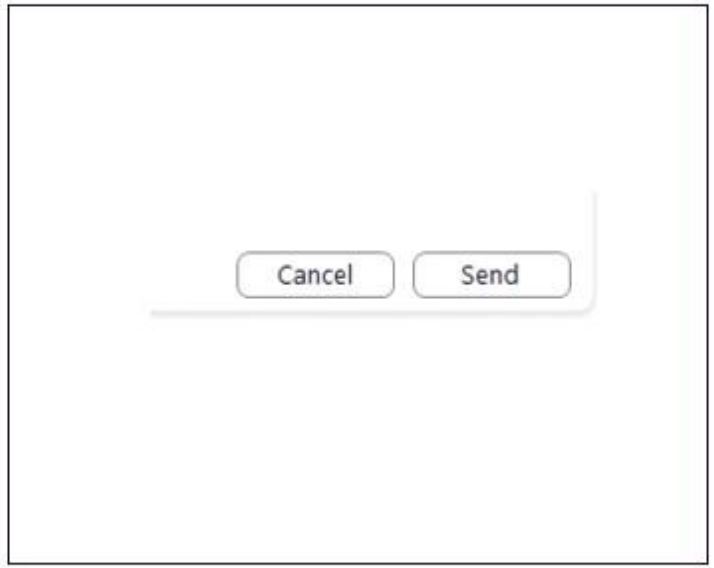

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Agenda

Welcome		**Michael Roberts** Investor Relations
Introduction		**Dr Steven Gourlay** Chief Executive Officer
Progress in evaluation of cognition, Alzheimer's disease and Xanamem's clinical data		**Professor Paul Maruff** Prof. Neuroscience and Co-Founder, Cogstate Ltd
Xanamem® : Potential for Benefit in a Number of CNS conditions – Phase 2 trials in progress		**Dr Dana Hilt** Chief Medical Officer
Summary	Moderator	**Dr Steven Gourlay**
Questions and wrap-up	Moderator	**Dr Steven Gourlay**

“Fireside chat” format discussion

Professor Maruff & Dr Hilt MD

Xanamem: Oral, low dose, once-a-day treatment with a unique (mainly) non-amyloid/tau mechanism

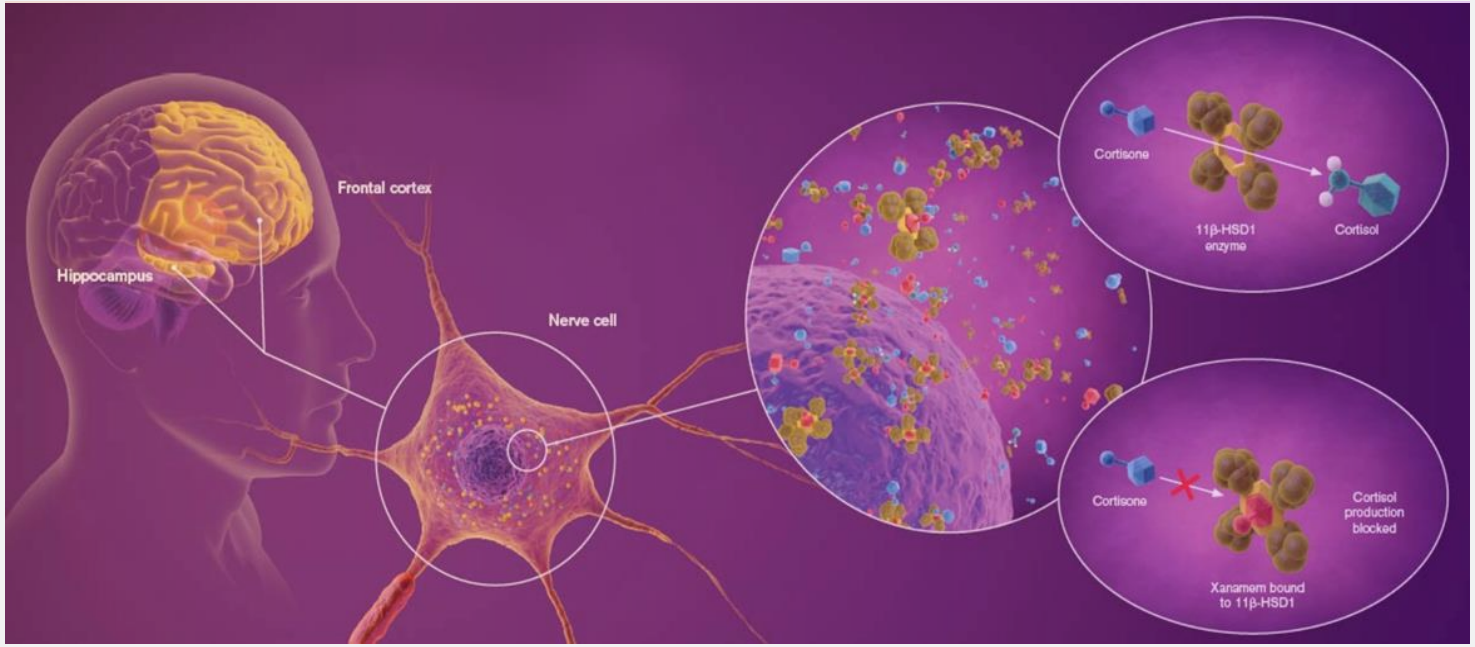
Only known brain penetrant 11β-HSD1 small molecule enzyme inhibitor

Reduces cortisol in brain - modulating signalling pathways and potentially underlying disease processes[1,2]

11β-HSD1 is preferentially expressed in brain and liver but minimally expressed in endocrine tissues

Xanamem may have potential to:

- ***Enhance cognition independent of disease condition/mechanism***
- ***Slow progression or produce durable delay in symptoms progression in AD***
- ***Anti-depressant/procognitive effects in depression with cognitive impairment***



1. Xanamem® is a CNS (Central Nervous System) penetrant small molecule based on human PET scan evidence and cerebrospinal fluid (CSF) measurements
2. 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; Popoli et al. 2011 microglial cell modulation in rats, effects on glutamate, cannabinoid and other signalling pathways

Xanamem Clinical data

Two separate normal volunteer studies have shown procognitive effects of Xanamem: Attention, working memory, and executive function

Re-analysis of the Phase 2 XanADu AD study shows procognitive and potentially clinical benefit in high pTau subgroup of AD patients

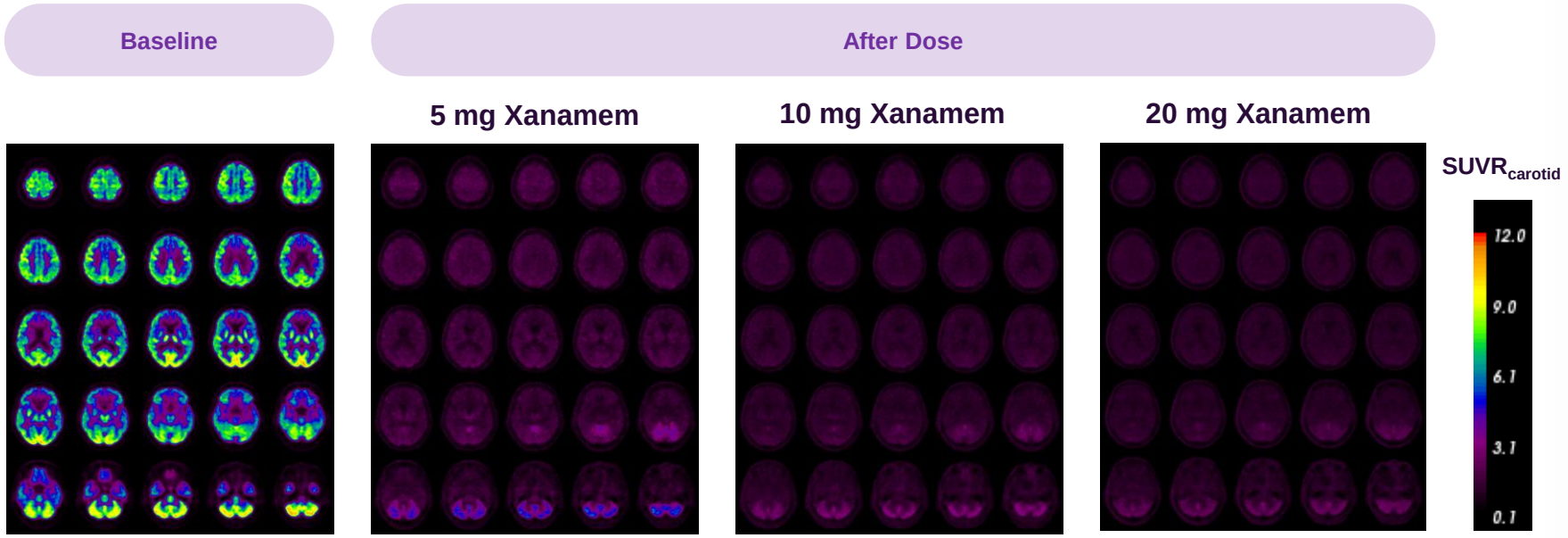
These data taken together support further studies of Xanamem as a procognitive and potential disease-course altering drug in a number of conditions

Two large Phase 2 studies will be conducted

- **Depression (MDD) with cognitive impairment (XanaCIDD)**
- **Mild/moderate AD with elevated pTau (XanaMIA)**

Xanamem gets into the brain and binds to its target at safe and well tolerated doses

Previous molecules to this target have <u>not</u> achieved adequate brain concentrations as they were poorly CNS penetrant



PET data demonstrates that Xanamem extensively binds to the 11β-HSD1 enzyme throughout the brain, with high post-treatment effects (absence of colour) after 7 days at all doses, slightly less at a 5 mg dose.

This is consistent with full hormonal pharmacodynamic activity seen with 10 mg in clinical trials. 5 and 10 mg show excellent clinical tolerability and safety and minimal systemic endocrine effects.

Note: Study population consisted of ~50% healthy older subjects who were cognitively normal and ~50% with Alzheimer's disease. Subjects dosed for seven days.
Baseline: Mean of baseline scans of patients in that dose group; After dose: Mean of post-dosing (7 days) scans in that dose group.

Xanamem in normal volunteers: Improves attention cognition domains in XanaHES* study by Week 4

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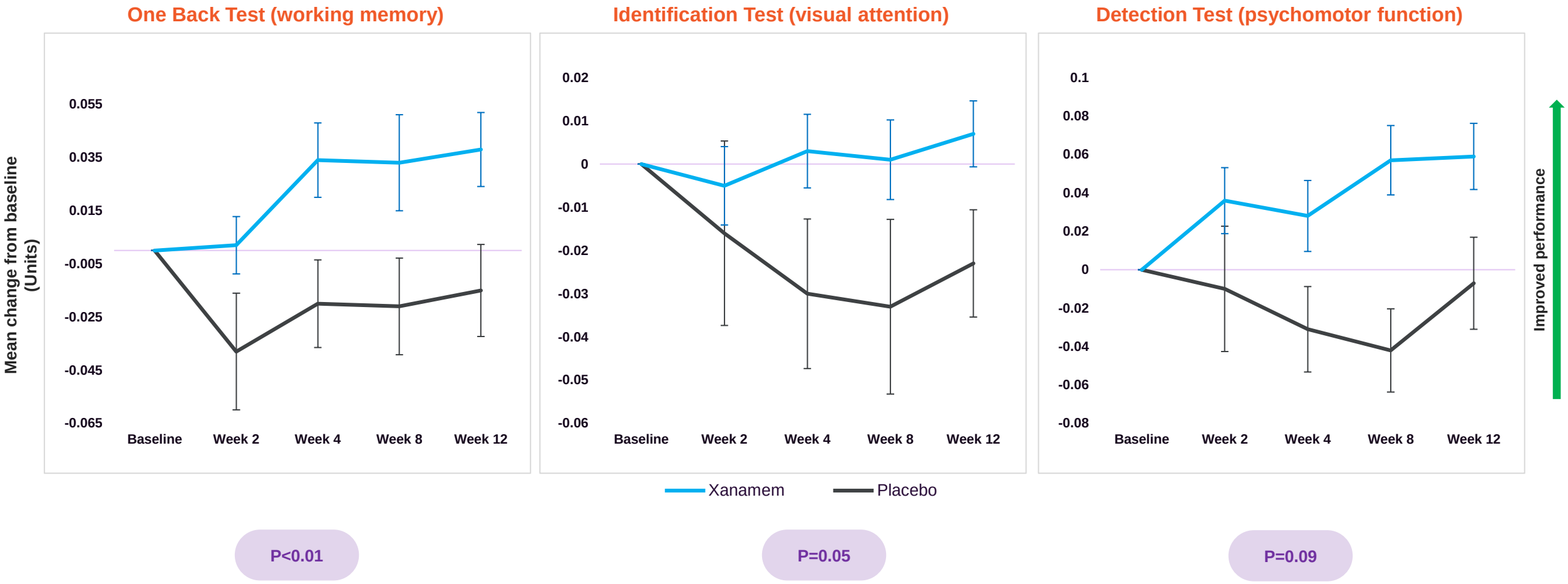

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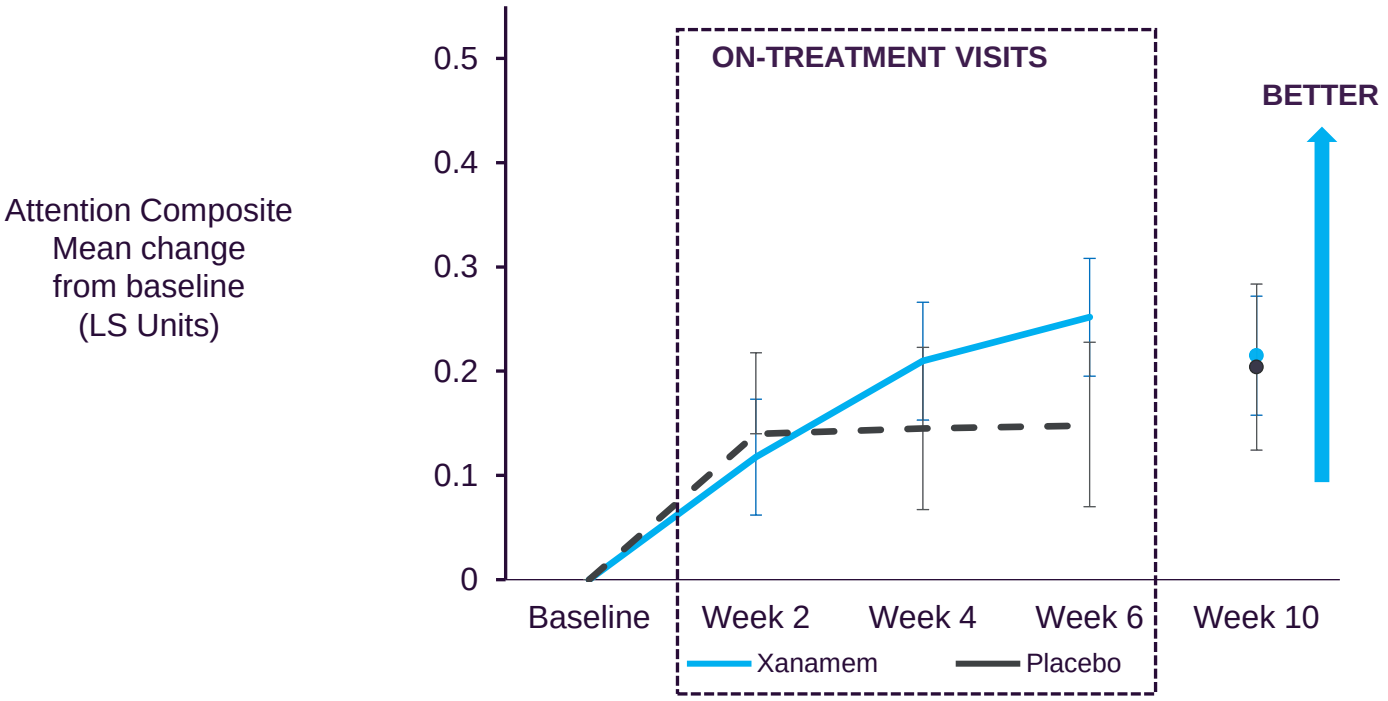
* n = 30 Xanamem 20mg vs n = 12 Placebo (Actinogen data on file)

Xanamem confirms improved attention/working memory by 4-6 weeks at lower doses in second trial

Computerized Cogstate test battery positive results in cognitively normal older people

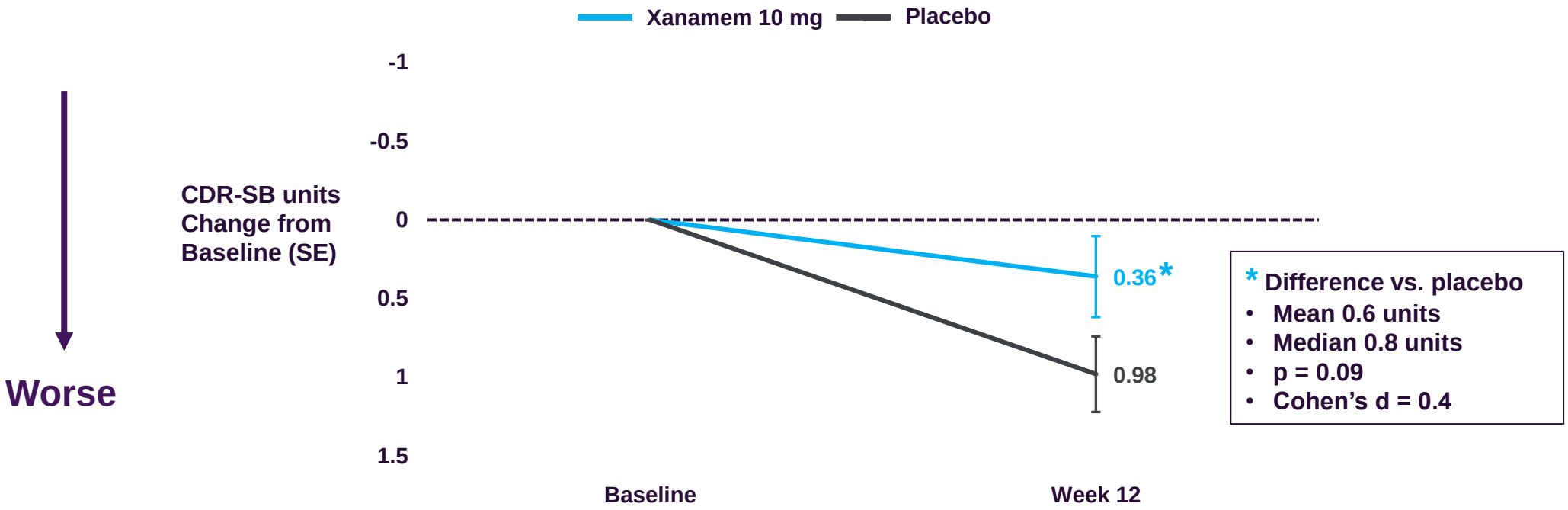
XanaMIA Phase 1b trial (n=107, Xanamem 10 mg & 5 mg)



Procognitive effects of Xanamem confirmed in second randomized trial

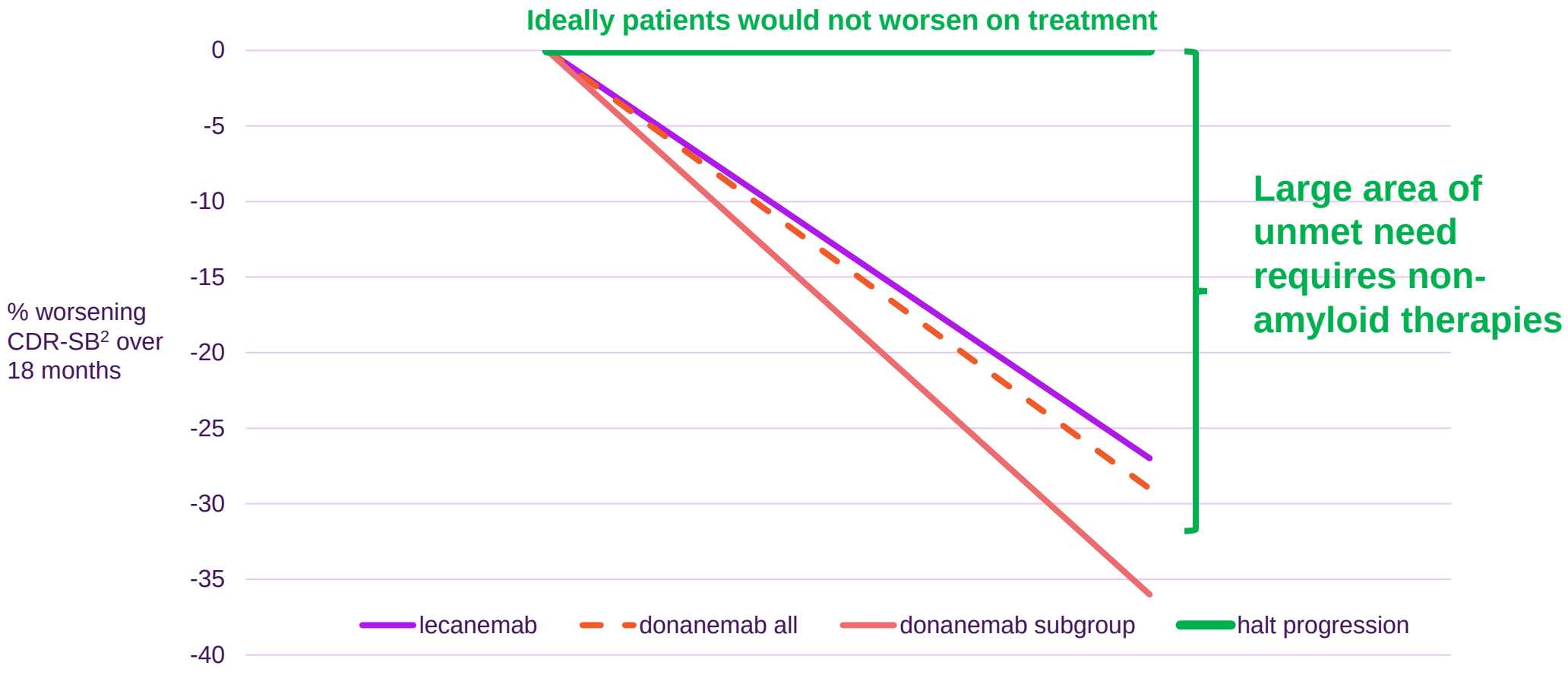
Xanamem prevents clinical decline in p-Tau181 elevated AD patients: Positive clinical effects

In trial participants with p-Tau181 > 6.74 pg/mL, Xanamem demonstrates disease stabilization on CDR-SB



Xanamem largely prevented clinical progression in AD over 12 weeks

Newer anti-amyloid antibodies shown to slow but not halt progression of AD[1]



Drugs targeting other mechanisms like Xanamem are needed

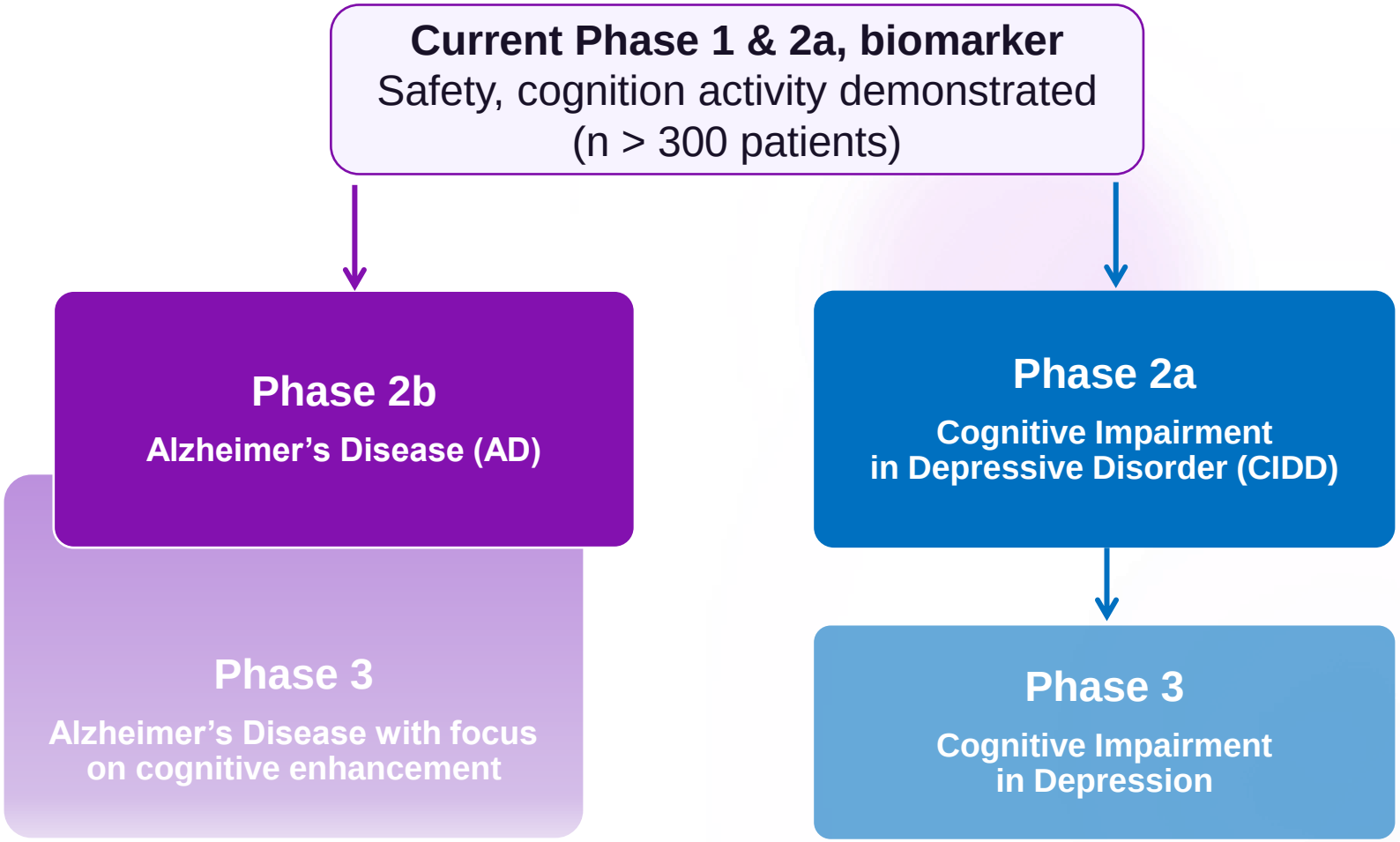
1. Lecanemab and donamemab are anti-amyloid antibodies given as an intravenous infusion every 2 or 4 weeks (van Dyck et al. 2022; DOI: 10.1056/NEJMoa2212948 n=1795 and Sims JR at al. *JAMA*. Published online July 17, 2023. doi:10.1001/jama.2023.13239
2. CDR-SB is an 18-point scale measuring functional status and was the primary endpoint for lecanemab and a secondary endpoint for donanemab

Xanamem moving to POC Phase 2 studies: AD and Cognitive Impairment in Depression

Biomarker trial data validate & simulate the planned Phase 2b protocol in patients with mild to moderate AD and elevated blood pTau

Xanamem Phase 2 & 3 program

Building on three independent Phase 1 and 2 studies showing safety and procognitive activity



Questions

Online Q&A

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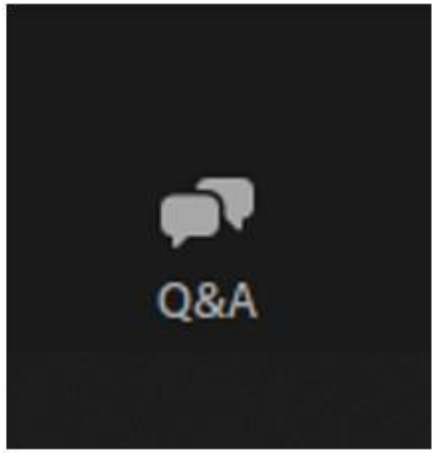

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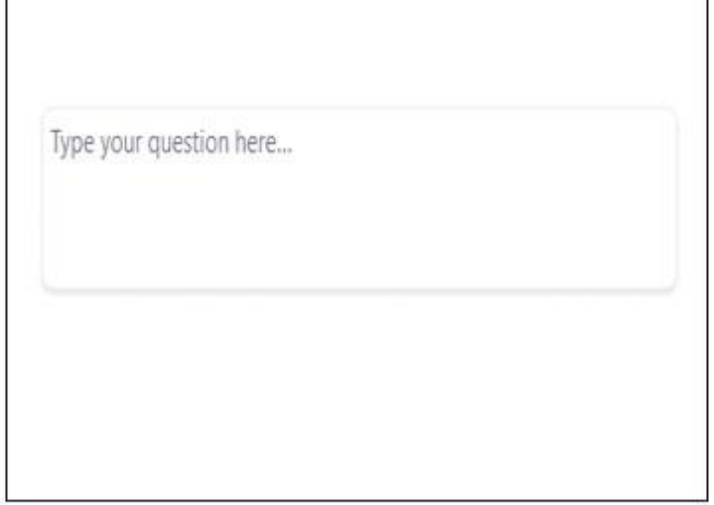

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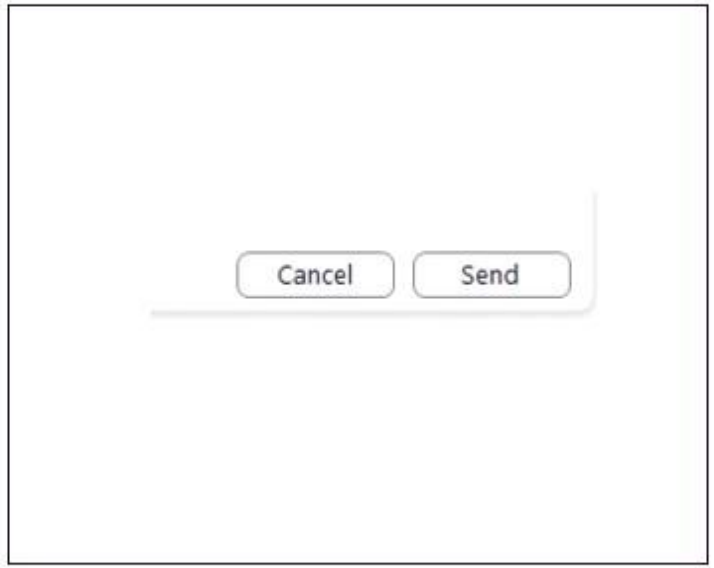

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Thank you

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