



ASX ANNOUNCEMENT

Actinogen presents a brief corporate presentation highlighting the Company, Xanamem and its strong scientific rationale in Alzheimer's disease based on human cortisol literature

Sydney, 06 August 2026. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce the 12-minute podium presentation entitled "Advancing Oral Xanamem in Alzheimer's disease" presented at the annual Bioshares Biotech Summit in Queenstown, NZ, today.

Highlights from the presentation are:

1. Xanamem® (emestedastat) is a promising, oral enzyme inhibitor designed to control elevated levels of the "stress hormone", cortisol, in the brain
2. Cortisol is synthesized from inactive cortisone in brain tissue by Xanamem's target enzyme, 11 β -HSD 1
3. The rationale for controlling cortisol in Alzheimer's disease (AD) via inhibition of its production by 11 β -HSD1 is strong:
 - a. The adverse effects in the brain of therapeutic cortisol or excess cortisol seen in diseases such as Cushing's syndrome include impairment of memory, learning and problem-solving, as well as psychiatric symptoms and shrinkage of brain tissue
 - b. Elevated cortisol levels in brain fluid are associated with AD
 - c. Elevated cortisol levels in brain fluid are also associated with the major genetic risk factor for AD, ApoE4
 - d. Genetic alterations of 11 β -HSD1 affect risk of cognitive decline: overexpression leads to decline while absence of expression is protective
 - e. Xanamem has shown preliminary activity in a trial of patients with mild AD and positive effects on attention and working memory in older volunteers.
4. The Company's first pivotal trial in 247 participants with AD will report topline, final results in November this year.

A copy of the presentation is attached to this announcement.

View this announcement on our InvestorHub: <https://investors.actinogen.com.au/link/eW1apP>

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Announcement authorised by the Disclosure Committee of Actinogen Medical Limited

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. It has also conducted a phase 2 trial in patients with cognitive impairment and depression and may 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.

Clinical Trials

The XanaMIA Phase 2b/3 Alzheimer's disease trial is a double-blind, 36-week treatment, placebo-controlled, parallel group design trial in 247 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 its ability to slow progression of Alzheimer's disease is assessed with a variety of endpoints. The primary endpoint of the trial is the internationally-recognized CDR-SB (Clinical Dementia Rating scale – Sum of Boxes). The trial is being conducted in Australia and the US and is now closed to participant recruitment. It has passed an independent Data Monitoring Committee safety and efficacy futility review and final topline results are expected in November 2026.

The XanaMIA-OLE Alzheimer's disease open-label extension is an open-label phase of up to 25 months treatment where all participants will receive active Xanamem 10 mg once daily. The trial evaluates safety and a limited number of efficacy endpoints such as the CDR-SB. The trial commenced in March 2026 and is open to all former and current participants in the XanaMIA Phase 2b/3 trial.

The XanaCIDD Phase 2a depression trial was a double-blind, six-week proof-of-concept, placebo-controlled, parallel group design trial in 167 patients with moderate, treatment-resistant depression and a degree of baseline cognitive impairment. Participants were evenly randomized to receive Xanamem 10 mg once daily or placebo, in most cases in addition to their existing antidepressant therapy, and effects on cognition and depression were assessed. Trial results were reported in August 2024 and showed clinically and statistically significant benefits on depression symptoms with positive effects on the MADRS scale (a validated scale of depression symptom measurement) and the PGI-S (a valid patient reported assessment of depression severity). Cognition improved markedly and to a similar extent in both Xanamem and placebo groups. The peer-reviewed publication relating to this trial can be accessed for free via this link: <https://tinyurl.com/ckm63z63>.

About Xanamem (emestedastat)

Xanamem's novel mechanism is to control elevated levels of cortisol (aka the "stress hormone") in the brain through the inhibition of the cortisol synthesis enzyme, 11 β -HSD1, without affecting production of cortisol by the adrenal glands which is essential for the body's normal functioning. Xanamem is a first-in-class, once-a-day pill designed to deliver high levels of cortisol control in key areas of the brain related to Alzheimer's and other diseases such as the hippocampus and frontal cortex. To view Xanamem's two-minute Mechanism of Action animation, [click here](#).

Chronically elevated cortisol is associated with progression in Alzheimer's Disease and excess cortisol is known to be toxic to brain cells. Cortisol itself is also associated with depressive symptoms and when targeted via other mechanisms has shown some promise in prior clinical trials. The recent XanaCIDD trial demonstrated clinically and sometimes statistically significant benefits on depressive symptoms, further validating the cortisol control mechanism for the Xanamem 10 mg oral daily dose.

The Company has studied 11 β -HSD1 inhibition by Xanamem in more than 500 volunteers and patients in eight clinical trials. Xanamem has a promising safety profile and has demonstrated clinical activity in patients with depression, patients with biomarker-positive Alzheimer's disease and cognitively normal volunteers. 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.

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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ACTINOGEN MEDICAL ENCOURAGES ALL CURRENT INVESTORS TO GO PAPERLESS BY REGISTERING THEIR DETAILS WITH THE DESIGNATED REGISTRY SERVICE PROVIDER, AUTOMIC GROUP.



Advancing oral Xanamem[®] in Alzheimer's Disease

Topline data from phase 2b/3 pivotal trial in November (n=247)

Potentially game-changing product profile

Strong scientific rationale for brain cortisol as a therapeutic target

Corporate Presentation, Bioshares 2026

August 6, 2026

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Corporate and Xanamem highlights



Potentially game-changing oral therapy in late-stage trials for Alzheimer's disease

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Validated 11 β -HSD1 mechanism with differentiated oral profile

- Xanamem is a novel oral therapy targeting elevated brain cortisol, a well-established risk factor for Alzheimer's disease and depression
- Oral administration and favorable safety profile support broad use

NEXT MAJOR VALUE INFLECTION
Pivotal trial topline results
November 2026



Biomarker-enriched pivotal trial with independent validation

- XanaMIA phase 2b/3 pivotal trial (n=247) fully enrolled; open-label extension commenced; topline results November 2026
- January 2026 independent Data Monitoring Committee recommended the trial continue unchanged following unblinded interim review of safety and efficacy futility



Regulatory clarity in the US and EU

- Current pivotal trial expected to form part of registrational package for Alzheimer's disease
- FDA and EMA guidance support a streamlined marketing approval path requiring only one additional pivotal trial following positive XanaMIA results



Strong capital position

- Company funded through mid 2027
- Resources focused on execution of the XanaMIA trial and its extension phase

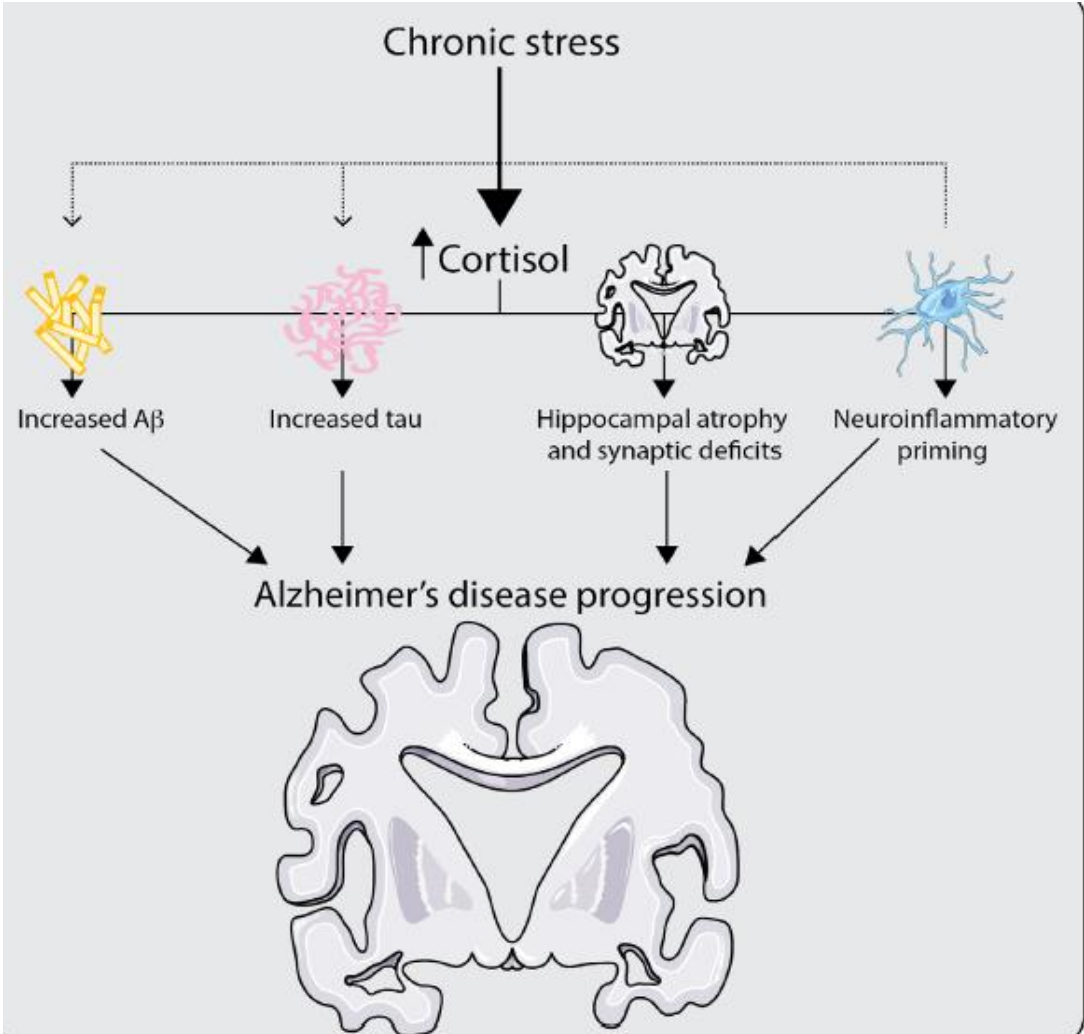
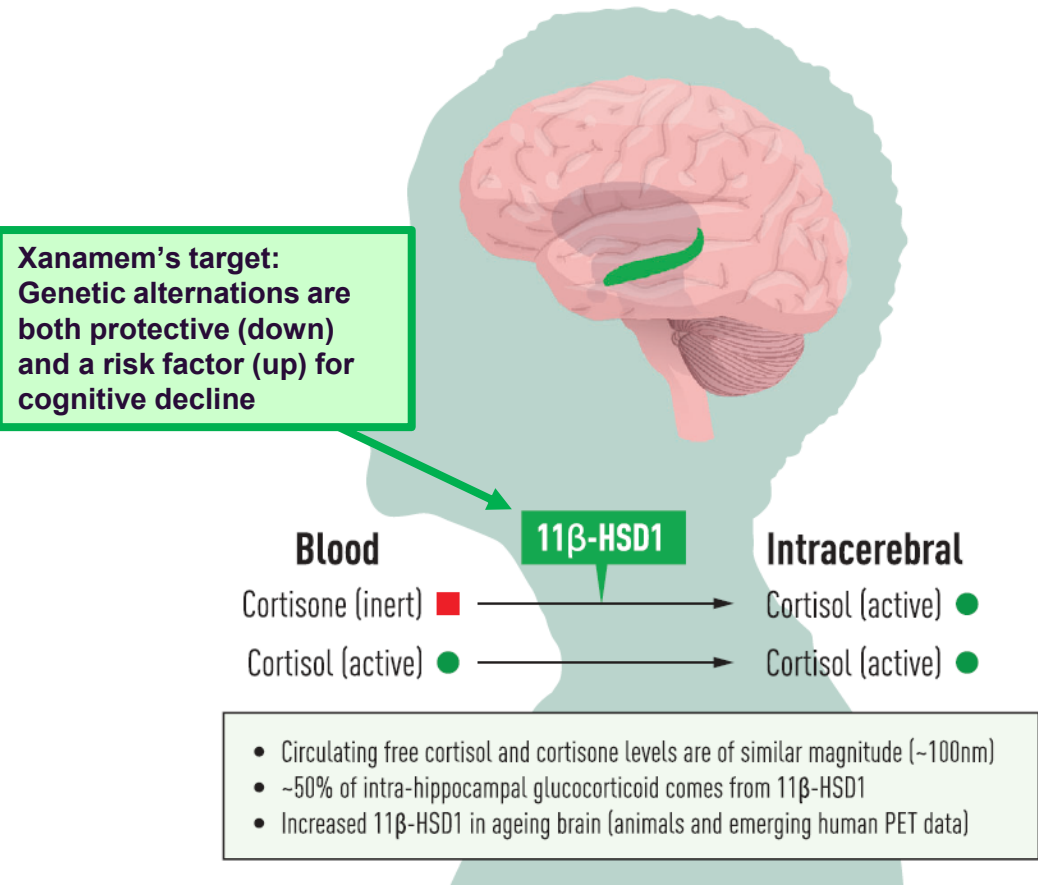
Why do we believe brain cortisol control with Xanamem can slow Alzheimer's disease (AD)?

Cortisol and the Alzheimer's brain



“Stress” and/or genetic factors may drive multiple AD mechanisms via cortisol

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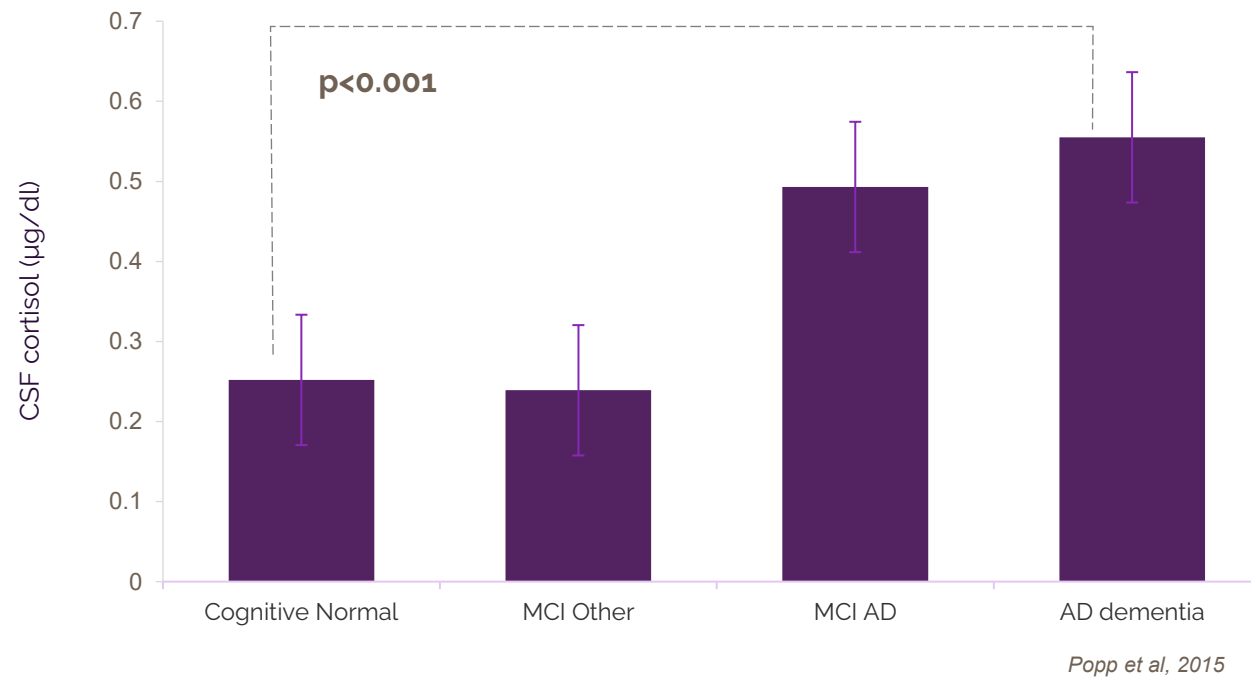


Elevated human brain cortisol levels linked to AD

Brain fluid cortisol measurements best reflect the tissue cortisol environment



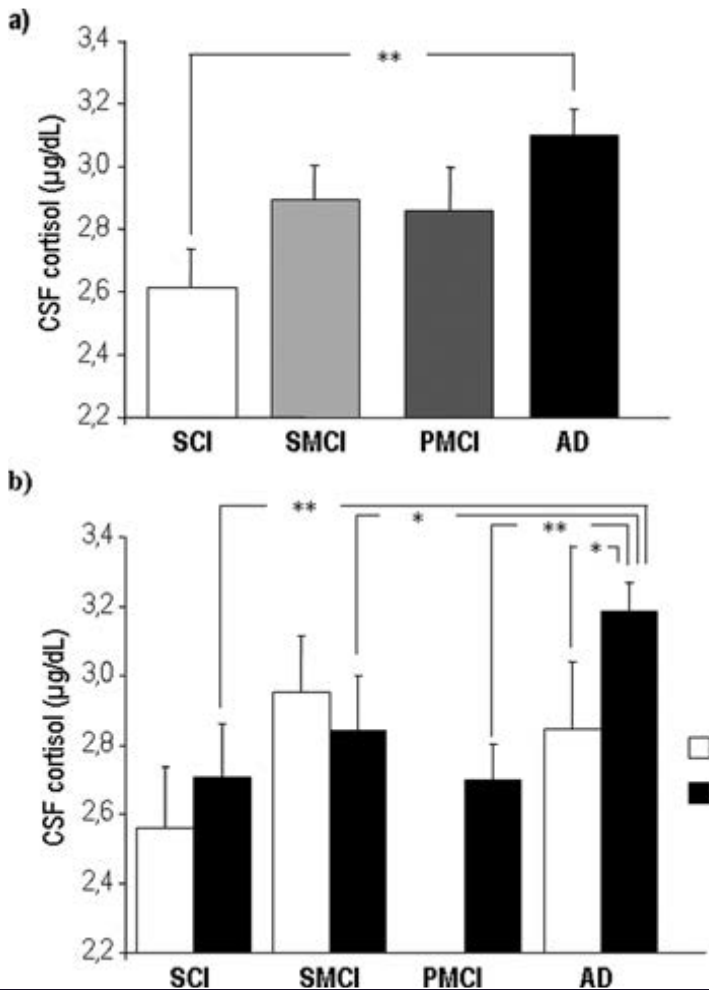
German Dementia Competency Network study



Major AD genetic risk factor of ApoE4 associated with elevated brain cortisol levels



~67% of patients in AD trials have one or two copies of the ApoE4 gene



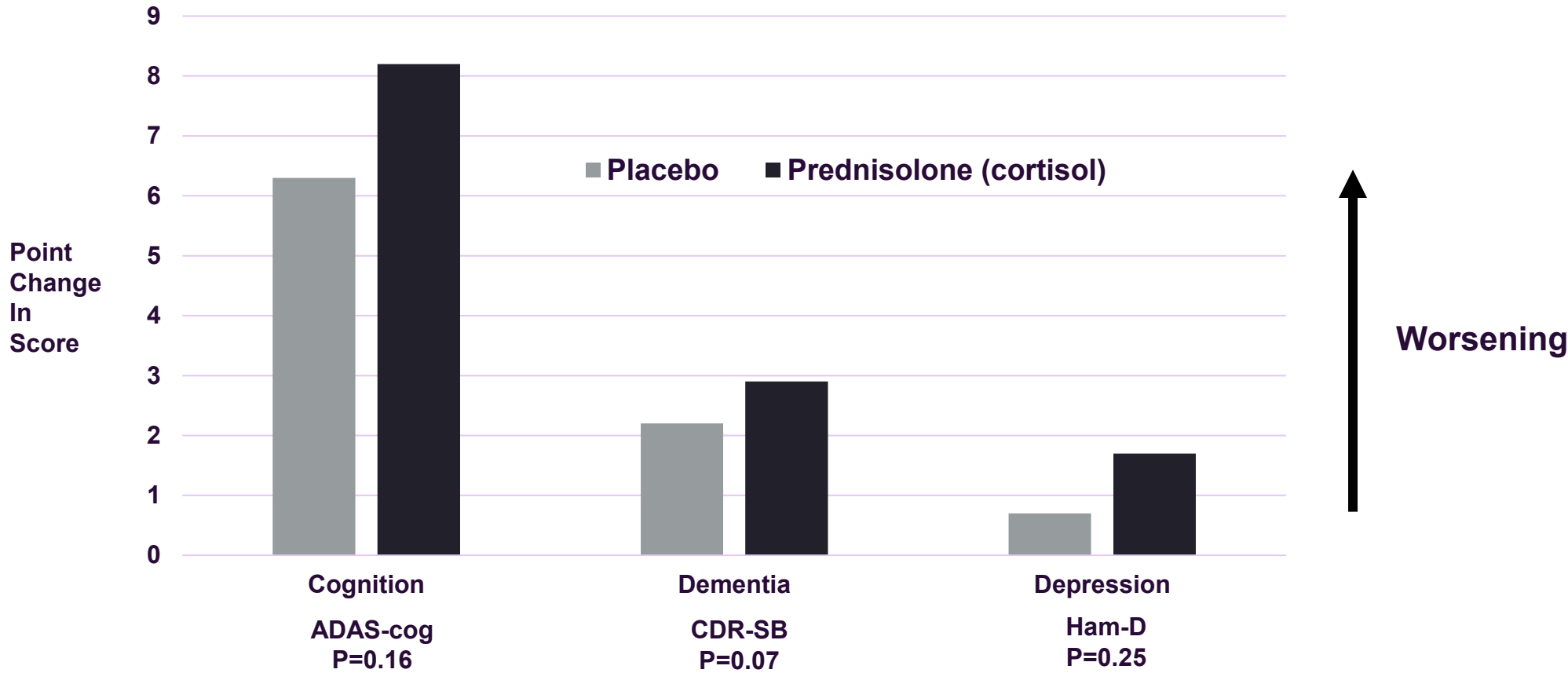
a) CSF cortisol level by disease classification (SCI: subjective cognitive impairment; SMCI stable mild cognitive impairment; PMCI progressive mild cognitive impairment; AD Alzheimer's disease)
b) As above by known ApoE4 genetic status (0 vs. 1-2 copies)

Therapeutic cortisol worsened AD over 12 months

Historical trial of 10mg prednisolone in patients with mild to moderate disease (n=138)



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Aisen et al. Neurology 54:Feb 2000; dropouts were more common in the prednisolone group

Cortisol excess is toxic to the brain



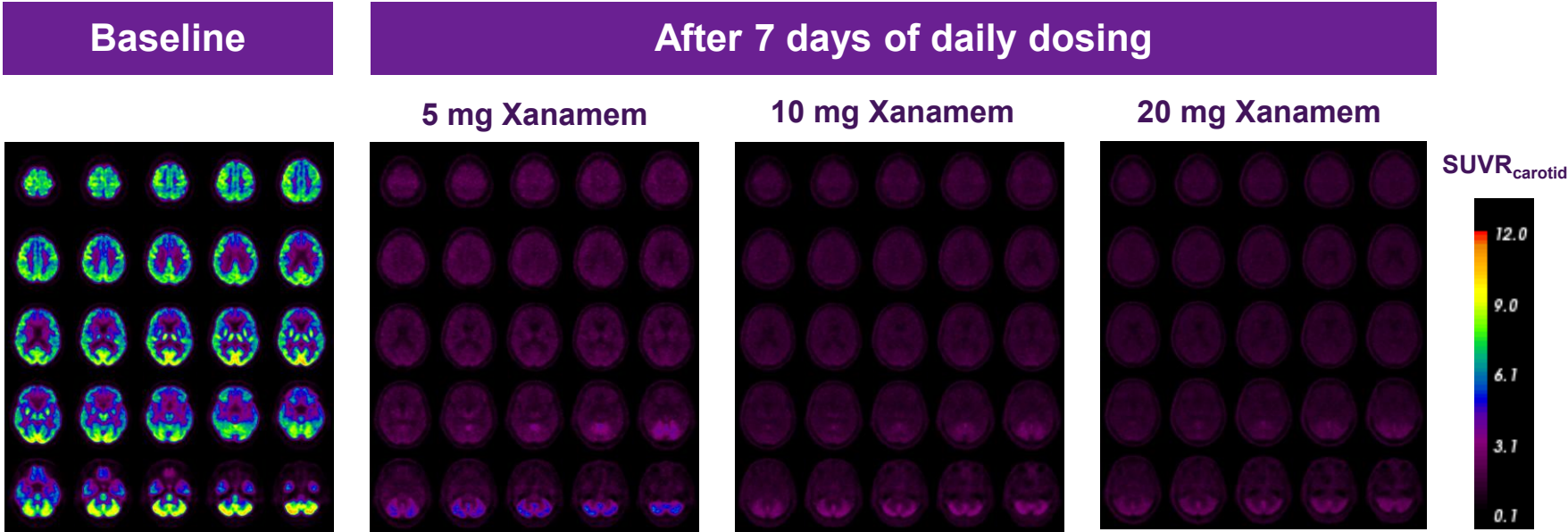
Literature from clinical use as a therapeutic and excess cortisol in Cushing’s syndrome

Symptom or sign of brain toxicity
Trends to worsening Alzheimer’s disease
Shrinkage to hippocampus
General brain shrinkage
Memory impairment
Executive function impairment
Difficulty learning
Poor concentration
Anxiety
Depression

Xanamem achieves high brain target occupancy



Distribution of cortisol synthesis enzyme 11 β -HSD1 shown in left panel



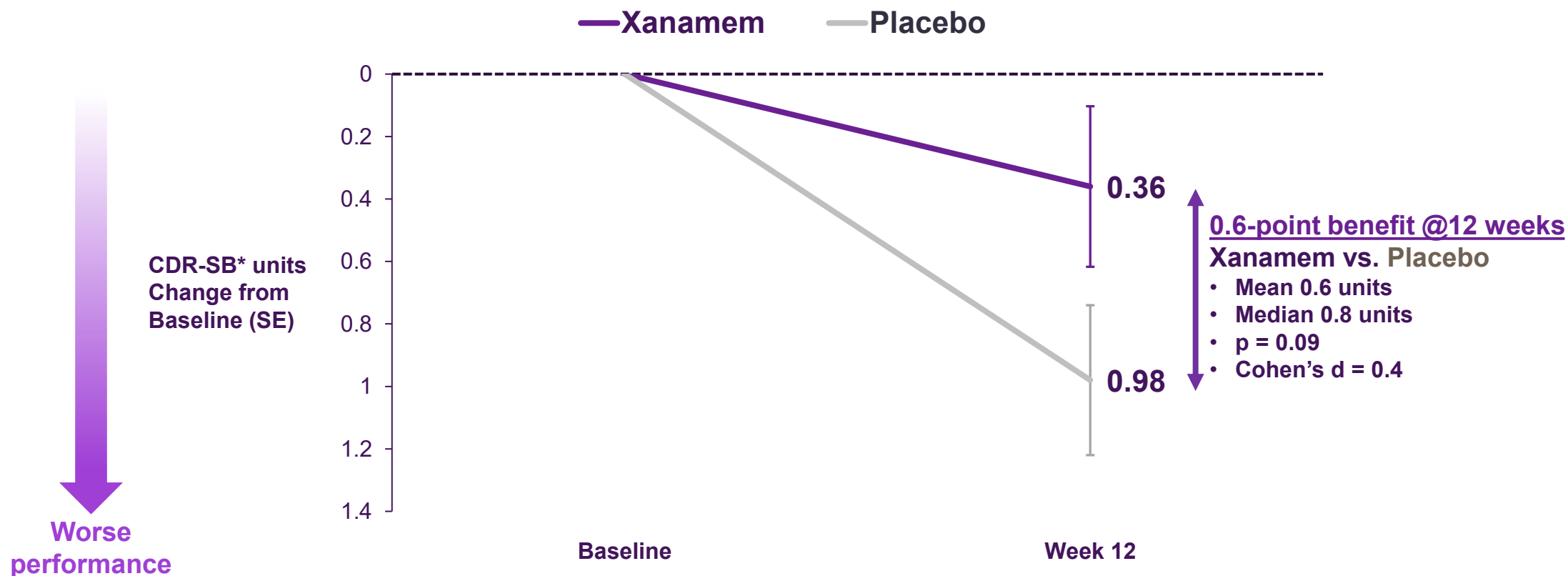
**Reduction in tracer signal (loss of color) indicates high 11 β -HSD1 occupancy -
Strong occupancy observed across evaluated clinical doses**

Xanamem data in patients with mild Alzheimer's



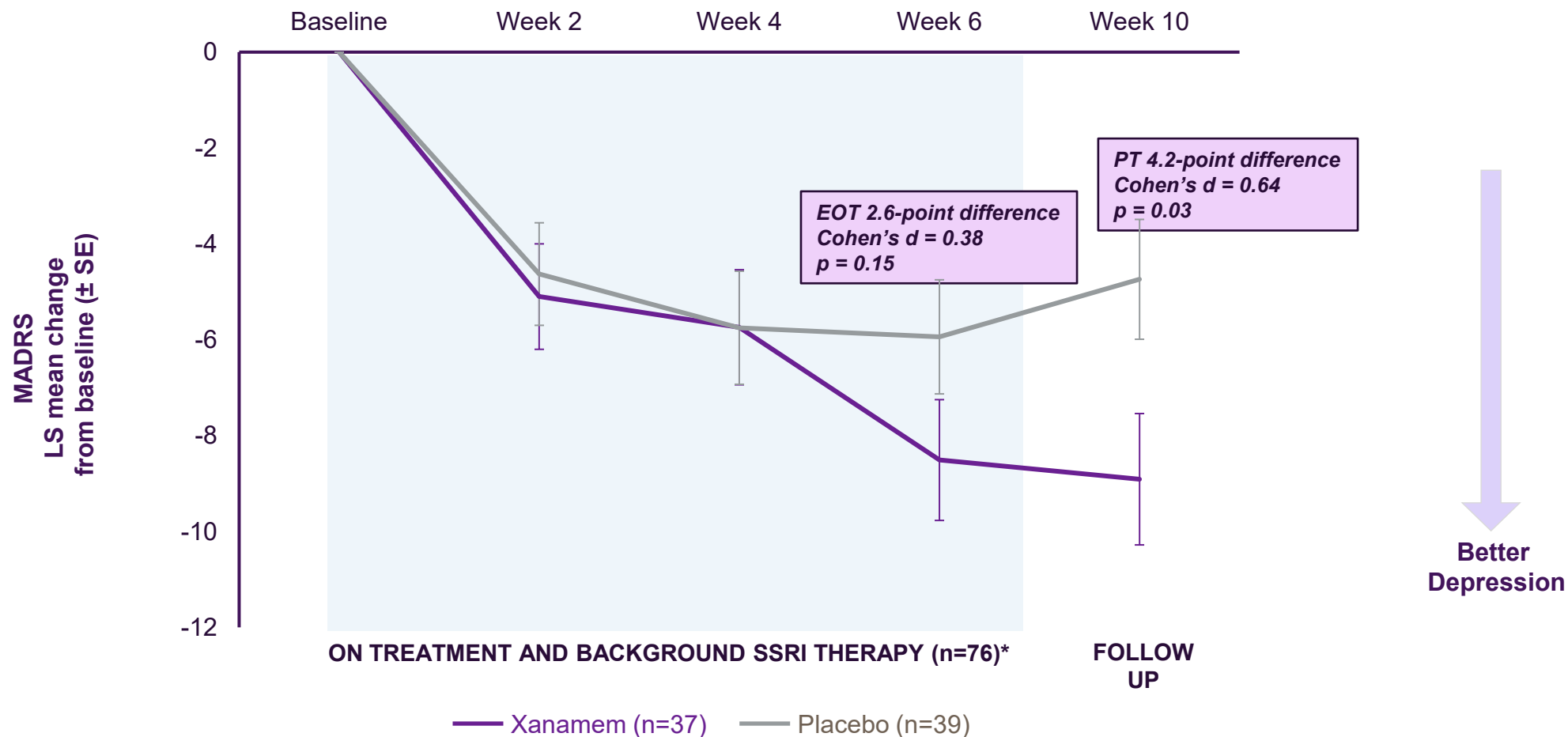
Phase 2a data showed slowing of decline over 12 weeks (n=34 with high pTau181)

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Durable activity in phase 2 depression trial

Separation from placebo overall and on background SSRI therapy



Abbreviations: SSRI, selective serotonin reuptake inhibitor.

*Planned phase 3 population

What we hope to see in November: much greater ability to slow disease than existing treatments



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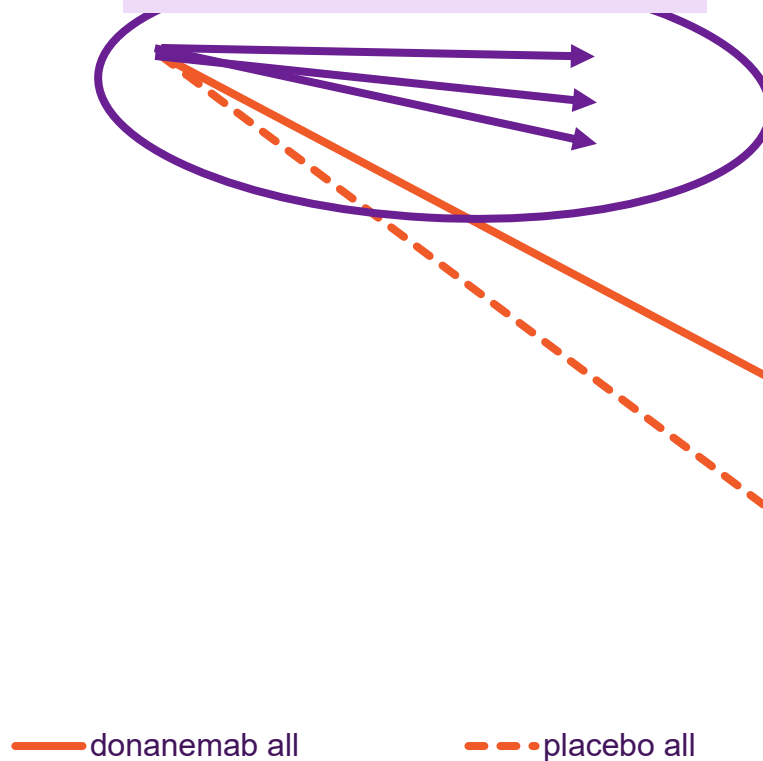
Worsening of
CDR-SB
over 18 months



Worse
performance



SIMULATED PHASE 2B/3 DATA



Xanomem phase 2a p-tau-positive patients showed near-stabilization

Modest benefit of donanemab (Kisunla) over 18 months¹

Xanomem may stabilize or slow CDR-SB progression more than other therapies

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