



## ASX ANNOUNCEMENT

### Actinogen presents at BIO International Convention in Boston

**Sydney, 16 June 2025.** Actinogen Medical ASX: ACW (“ACW” or “the Company”) is pleased to announce that its Chief Commercial Officer, Mr Andy Udell, and its Chief Medical Officer, Dr Dana Hilt MD, will be conducting meetings and delivering a company presentation at the BIO<sup>1</sup> International Convention (BIO 2025) in Boston, USA this week.

BIO 2025, running from June 16 to 19, is the world’s largest biotechnology event, bringing together industry leaders from around the world to learn, network, and build relationships.

Mr. Udell and Dr. Hilt will engage with international investors and potential biopharma partners throughout the conference to discuss Actinogen’s latest advancements and the potential of its lead asset, Xanamem®.

Actinogen is currently conducting a pivotal phase 2b/3 Alzheimer’s disease (AD) trial, the results of which could be transformational for the Company, and this is reflected in the meetings scheduled at the conference. The search for innovative therapies that could be used either alone or in combination for the treatment of Alzheimer’s is a significant priority for the pharma/biotech industry.

Mr. Udell and Dr. Hilt will deliver a corporate presentation in Room 153B at the Boston Convention & Exhibition Center at 4.45pm (US Eastern) Tuesday, June 17.

The presentation slides are attached to this announcement.

#### Mr Udell commented:

*“We are thrilled to share our progress at BIO 2025. Our ongoing Phase 2b/3 trial for Alzheimer’s disease marks a pivotal advancement in our commitment to pioneering transformative therapies. We have a full slate of meetings and look forward to engaging with industry leaders and potential partners to further our efforts.”*

**ENDS**

#### Investors

**Dr. Steven Gourlay**  
CEO & Managing Director  
P: +61 2 8964 7401  
E: [steven.gourlay@actinogen.com.au](mailto:steven.gourlay@actinogen.com.au)

**Michael Roberts**  
Investor Relations  
M: +61 423 866 231  
E: [michael.roberts@actinogen.com.au](mailto:michael.roberts@actinogen.com.au)

#### Media

**George Hazim**  
Media & Public Affairs Australia  
M: +61 417 516 262  
E: [georgehazim@mediaaffairs.com.au](mailto:georgehazim@mediaaffairs.com.au)

***Announcement authorised by the Board of Directors of Actinogen Medical***

<sup>1</sup> The Biotechnology Innovation Organization (BIO) is the world’s largest advocacy association for biotechnology and the producer of the convention.

® Xanamem is a registered trademark 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 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.

## 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 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 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. Initial results from an interim analysis triggered by the 100<sup>th</sup> participant reaching 24 weeks of treatment are anticipated in Q4 2025 and final results Q4 2026.

**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.

## About Xanamem (emestedastat)

Xanamem's novel mechanism of action is to control the level of cortisol in the brain through the inhibition of the cortisol synthesis enzyme, 11 $\beta$ -HSD1, without affecting production of cortisol by the adrenal glands. Xanamem is a first-in-class, once-a-day pill designed to deliver high levels of cortisol control in the brain.

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.

The Company has studied 11 $\beta$ -HSD1 inhibition by Xanamem in approximately 400 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.

## 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.

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



## Oral Xanamem<sup>®</sup> (emestedastat)

*Controlling brain cortisol to slow progression in Alzheimer's disease  
and treat depression*

BIO Partnering Meetings  
June 2025

# Xanamem is in advanced stages of development



## Novel 11 $\beta$ -HSD1 cortisol control mechanism, oral, attractive safety profile

- Brain cortisol has long been proposed as a pathogenic mechanism in Major Depressive Disorder (MDD) and Alzheimer's (AD)
- Unique brain-penetrant tissue cortisol synthesis inhibitor that leaves adrenal cortisol synthesis unaffected
- Over **400 people** treated with excellent safety and low drug interaction risk



## Positive phase 2 clinical data de-risk Xanamem program

- **Disease-modifying activity on CDR-SB** in phase 2a trial in biomarker-positive Alzheimer's patients
- **Phase 2a MDD trial showing clinically & statistically significant activity - benefits across multiple endpoints**
- Positive data from both trials read through to other indications in psychiatry and the dementias



## Patent/data protection and advanced manufacturing

- **Composition of matter protection** to 2031, and 2036 with extensions in major markets, newer patents in process
- **Data exclusivity protects Xanamem data** from use by others for 5 to 10 years from approval e.g. 10 years in EU
- **Manufacturing process scaled up and patented**, contractors Asymchem (China) & Catalent (US)



## Large clinical and commercial opportunities

- **No other brain-penetrant cortisol control drugs in development, first to be awarded INN and USAN names<sup>1</sup>**
- Anti-depressant market is currently ~\$20 billion, with major opportunities for novel mechanisms & better-tolerated drugs
- Alzheimer's market likely to be \$20 billion by 2030, with major opportunity for a safe & effective oral agent

1. Xanamem's International Nonproprietary Name (INN), emestedastat, was awarded by a naming committee of the World Health Organization: "stedastat" chosen for the first time for all 11 $\beta$ -HSD1 inhibitors; USAN (United States Adopted Name)



# Xanamem's unique mechanism of action

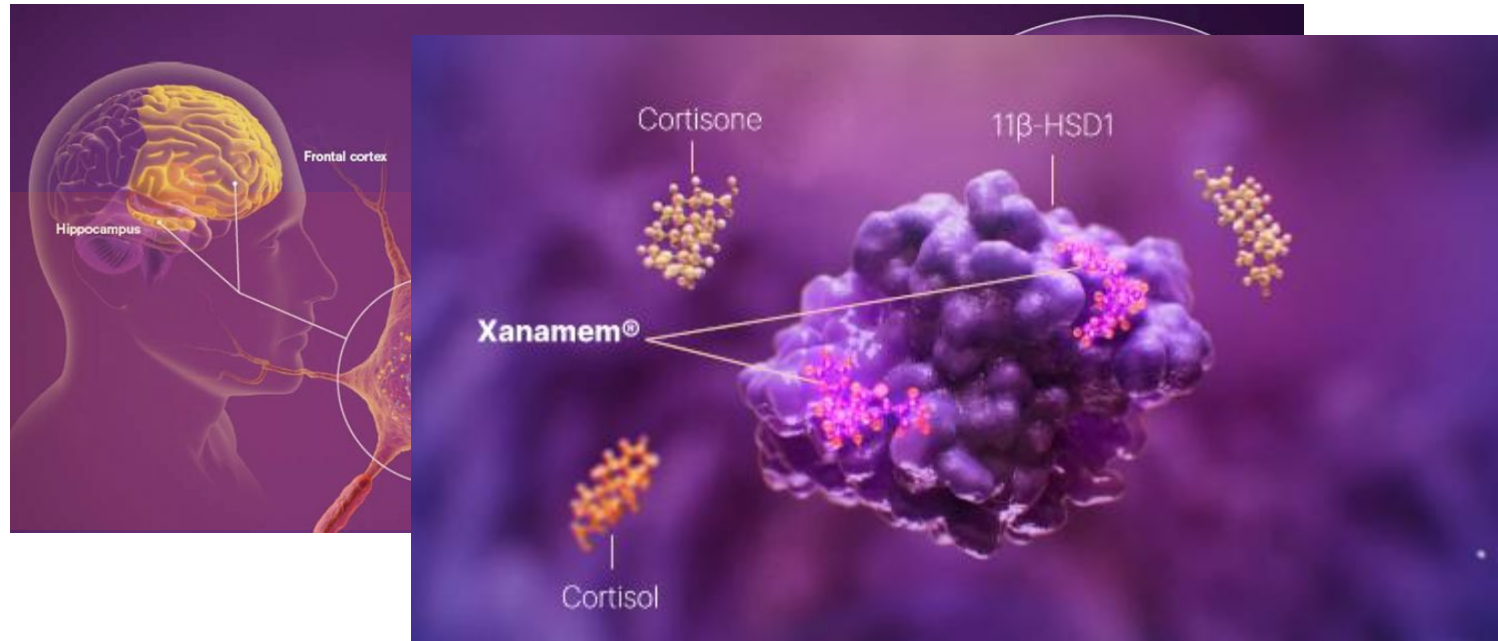
[Mechanism of Action video for Xanamem \(emestedastat\)](#)



# Once-daily oral treatment with a unique mechanism

Xanamem is a small molecule tissue cortisol synthesis inhibitor (11 $\beta$ -HSD1 enzyme)

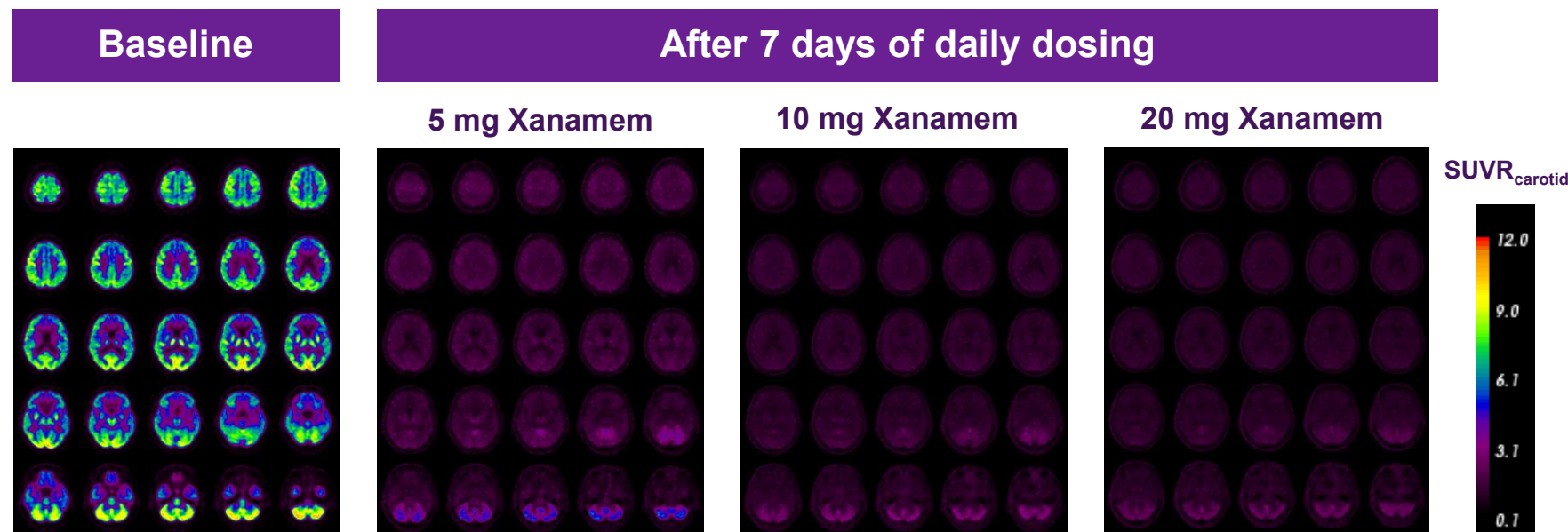
- ✓ Potentially disease-modifying in AD
- ✓ Anti-depressant activity in phase 2
- ✓ Brain-penetrant at low doses
- ✓ Good safety profile in ~400 treated
- ✓ Low drug interaction potential ideal for combination therapy



**Mouse experimental studies, brain cortisol levels & human clinical trials validate cortisol as a target for the treatment of AD**

# Human PET study shows full target engagement

Other 11 $\beta$ -HSD1 enzyme inhibitors have not achieved adequate brain levels



Xanamem extensively binds to the 11 $\beta$ -HSD1 enzyme throughout the brain, with high post-treatment effects (absence of color) after 7 days at all doses, slightly less at a 5 mg dose.

This is consistent with full hormonal pharmacodynamic activity seen in clinical trials with doses as low as 5 mg.

Journal of Alzheimer's Disease 97 (2024) 1463–1475  
 Brain 11-Hydroxysteroid Dehydrogenase Type 1 Occupancy by Xanamem™  
 Assessed by PET in Alzheimer's Disease and Cognitively Normal Individuals  
 Victor L. Villemagne, Vincent Dor, Lee Chong, Michael Kassiou, Rachel Mulligan,  
 Azadeh Feizpour, Jack Taylor, Miriam Roesner, Tamara Miller and Christopher C. Rowe



# Alzheimer's disease program

# Alzheimer's disease market is large and growing

Strong cortisol control scientific rationale to address huge unmet medical need

## Rationale

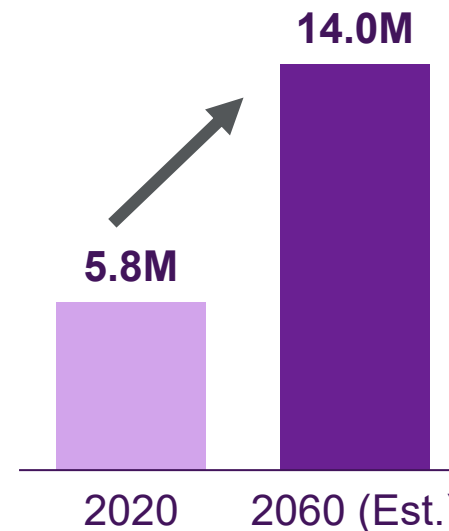
- Cortisol levels elevated in brain fluid in early AD
- Chronic corticosteroid treatment leads to hippocampal atrophy and cognitive impairment
- Elevated cortisol levels are associated with clinical progression
- Alzheimer's disease mouse model: 30–60% inhibition of 11 $\beta$ -HSD1 provides full neuroprotection
- AD phase 2a trial shows slowed disease progression in biomarker-positive patients
- ***Safe & effective oral therapy is “holy grail”***

## Growing Alzheimer's Disease market – U.S.

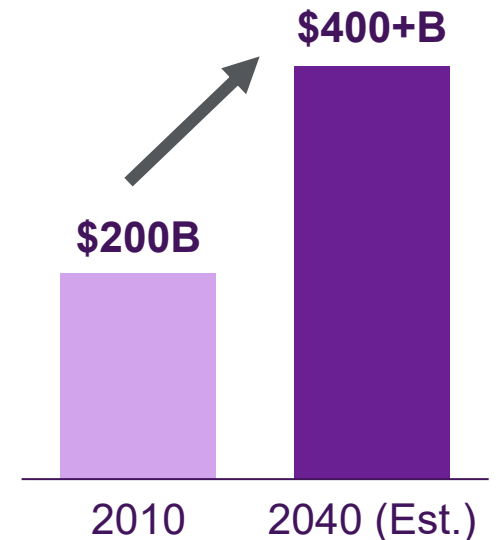
Large, unsatisfied and growing market



# of patients



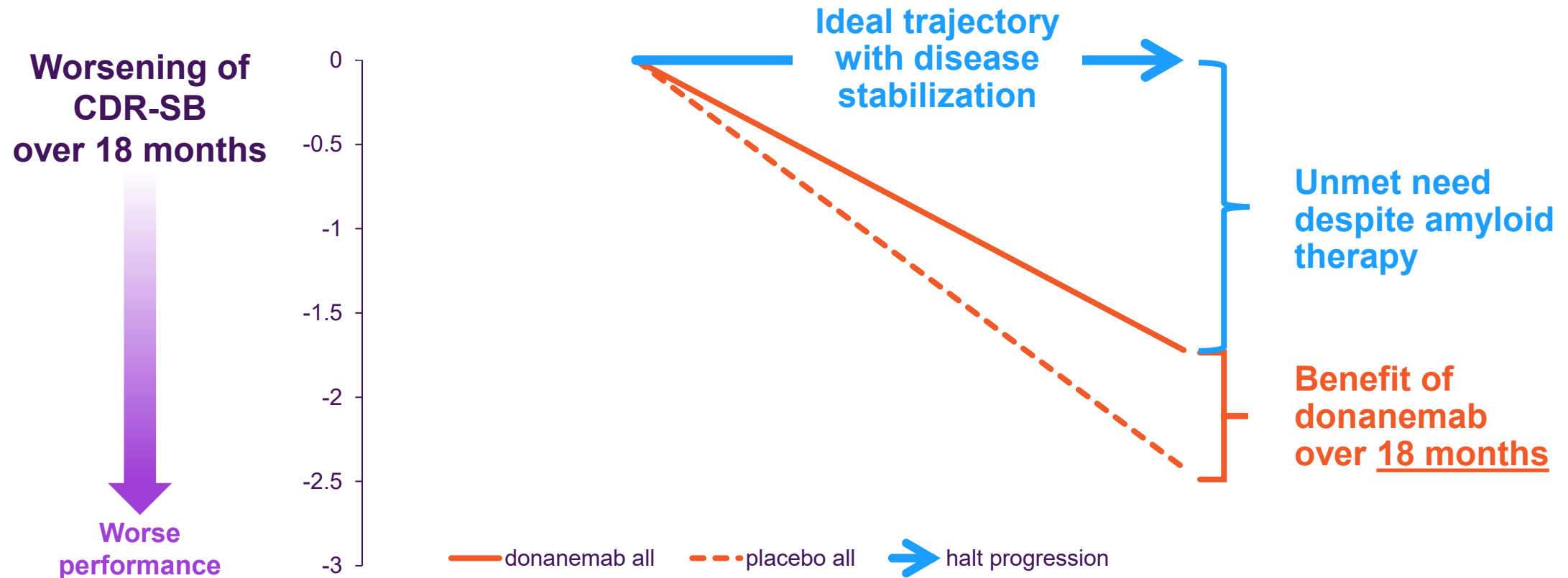
Cost to treat



# Anti-amyloid therapy modestly slows AD progression



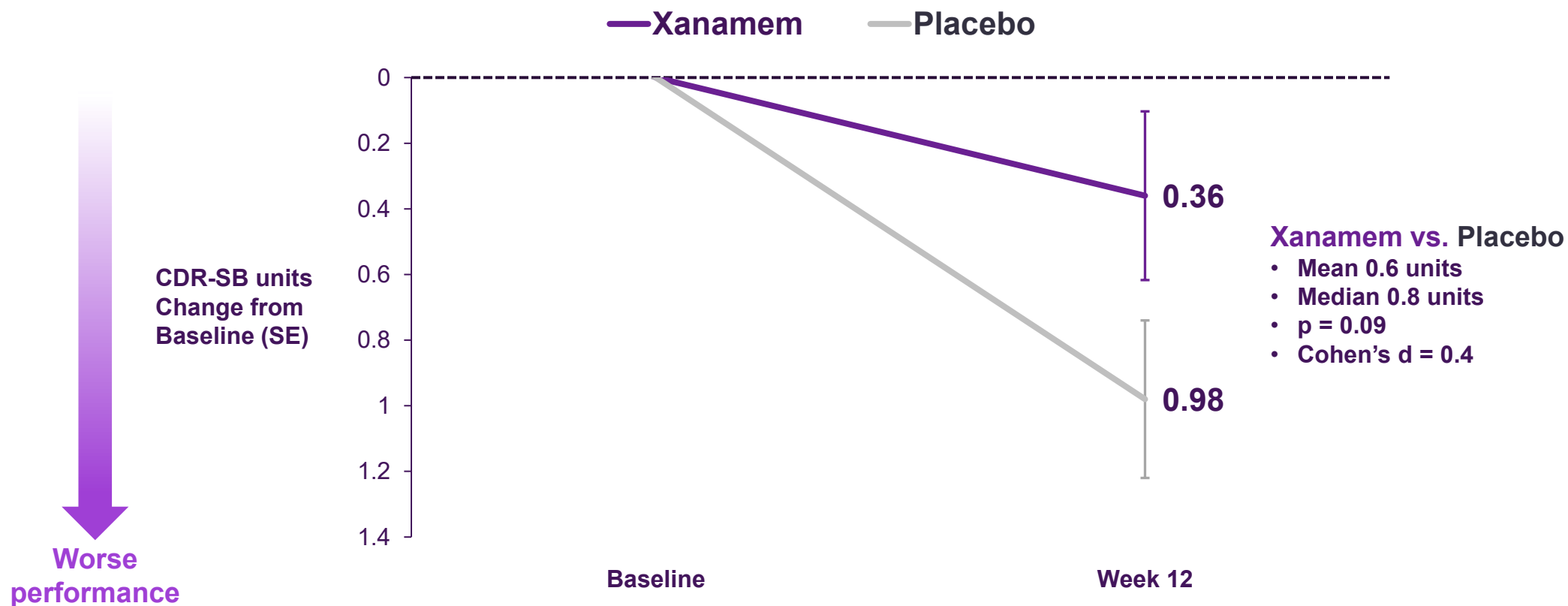
Ideally patients with AD would not worsen on treatment at all



Drugs targeting other mechanisms like Xanmem are needed

# Large Xanamem benefit in high pTau181 patients

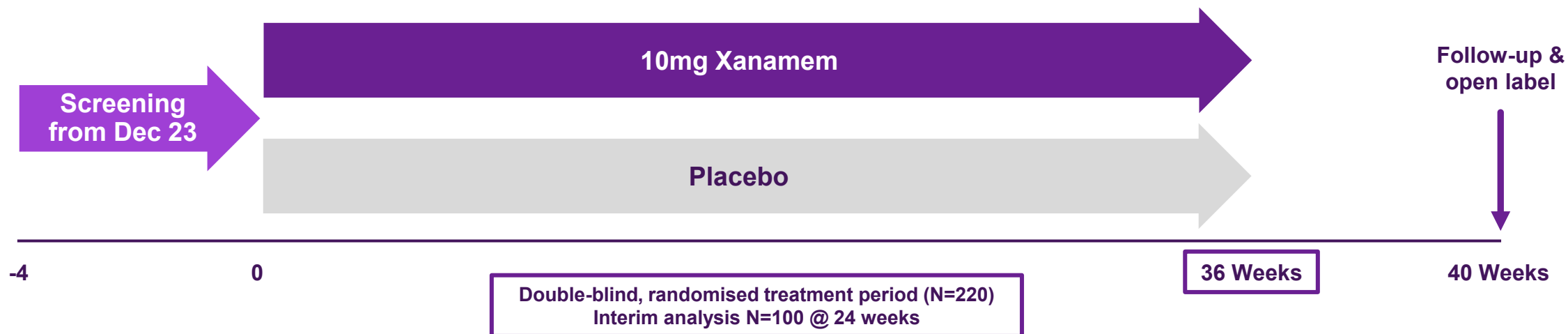
Phase 2a biomarker study: major slowing of CDR-SB decline over 12 weeks (n=34)



Journal of Alzheimer's Disease 100 (2024) 139–150  
 Plasma pTau181 Predicts Clinical Progression in a Phase 2 Randomized Controlled Trial of the 11-HSD1 Inhibitor Xanamem® for Mild Alzheimer's Disease  
 Jack Taylor, Mark Jaros, Christopher Chen, John Harrison and Dana Hilt

# XanaMIA phase 2b/3 trial in Alzheimer's disease

Initial, interim results in Q4 2025, final results Q4 2026



Key Inclusion Criteria	Primary Endpoint	Key Secondary Endpoints	Implementation
<ul style="list-style-type: none"> <li>Blood pTau biomarker positive</li> <li>Mild-moderate Alzheimer's by NIA-AA criteria</li> </ul>	<ul style="list-style-type: none"> <li><b>CDR-SB (functional and cognitive measure) @36 weeks</b></li> </ul>	<ul style="list-style-type: none"> <li>Cognitive Test Battery (7 cognitive measures well-validated in the Alzheimer's field)</li> <li>Amsterdam Activity of Daily Living (functional measure)</li> </ul>	<ul style="list-style-type: none"> <li>Enrolment at 15 Australian &amp; 20 US sites</li> <li>Interim analysis planned when ~100 people complete 24 weeks</li> </ul>



# Depression program



# There remains significant unmet need in depression

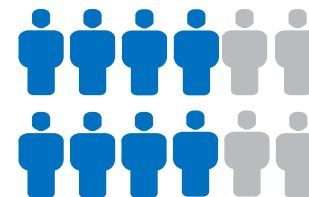
Xanamem's unique mechanism and safety differentiate it from older drugs

## Scientific rationale

- More than 50 years of research associates cortisol with depression
- Elevated CSF and plasma cortisol levels associated with diagnosis, treatment outcomes and relapse
- Positive effects of cortisol receptor antagonism reported with mifepristone<sup>3</sup>
- ***Now positive phase 2a data on depressive symptoms for Xanamem (MADRS, PGI-S)***

## U.S. Depression market large unmet need

- 21M patients have had  $\geq 1$  MDD episode



- Two-thirds with an episode **with severe impairment** in the past year
- 61% of all adults with MDD episodes receive treatment
- $\geq 365$  M prescriptions per year

**A safe, durably effective and combinable small molecule is a very attractive product profile for depression AND Alzheimer's**

# Phase 2a depression symptom benefits (2024) - major scientific and drug development achievement

Data support further MDD development and are a positive for Alzheimer's too

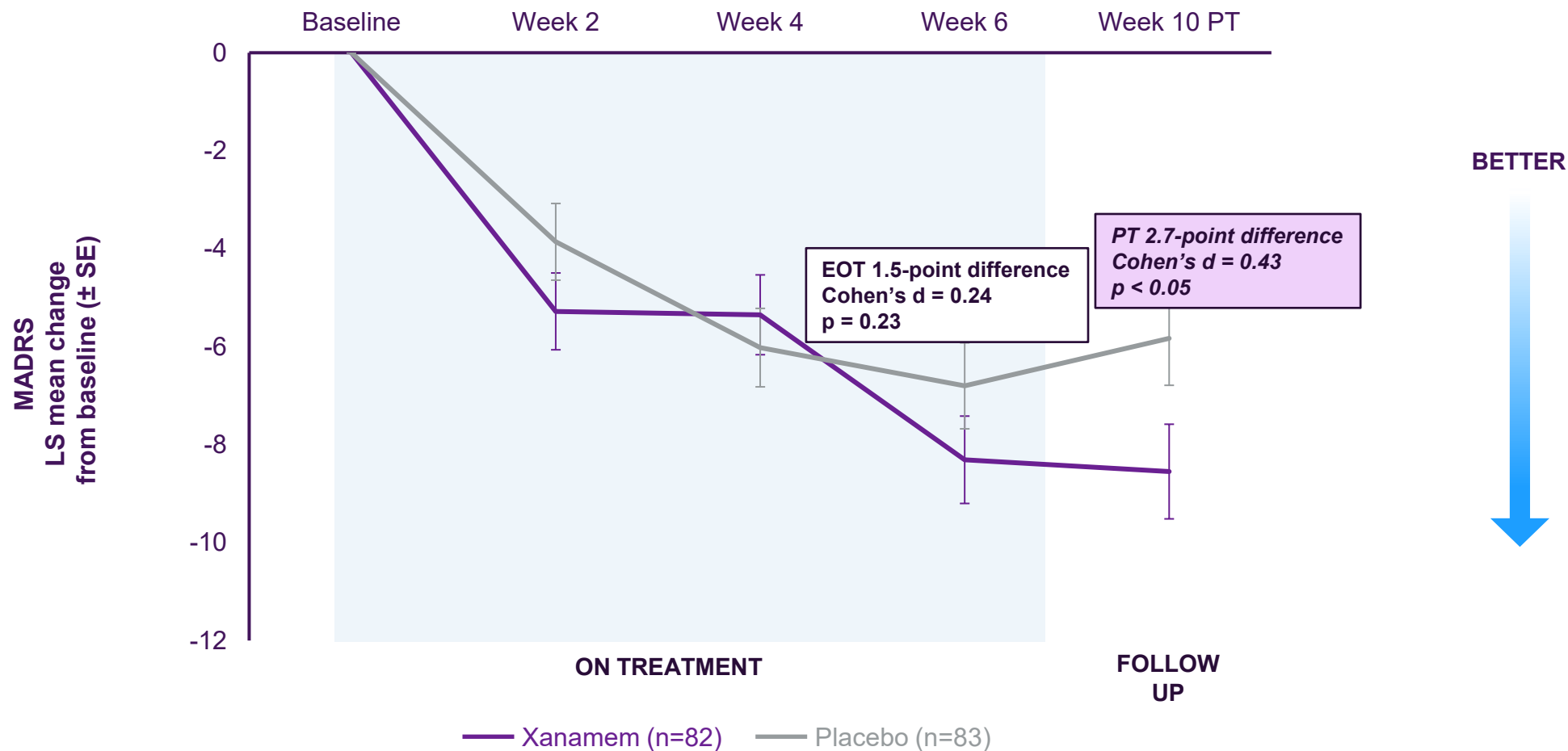


- ***Clinically and statistically significant treatment benefits on depressive symptoms for MADRS and patient-reported outcome of severity***
- Predominantly co-treated population with moderate MDD
- Consistent depression efficacy across subgroups
- Xanamem was safe and well tolerated (n=165 treated) with no observed suicide risk or withdrawal syndrome
- The trial was well-conducted with no major differences between Australia and the UK or at high enrolling clinical sites
- Benefits on depression are a desirable feature for an Alzheimer's drug
- Funding for the next depression trial being investigated with potential partners and/or granting bodies

# Xanamem MADRS improvement from Week 6 (n=165)

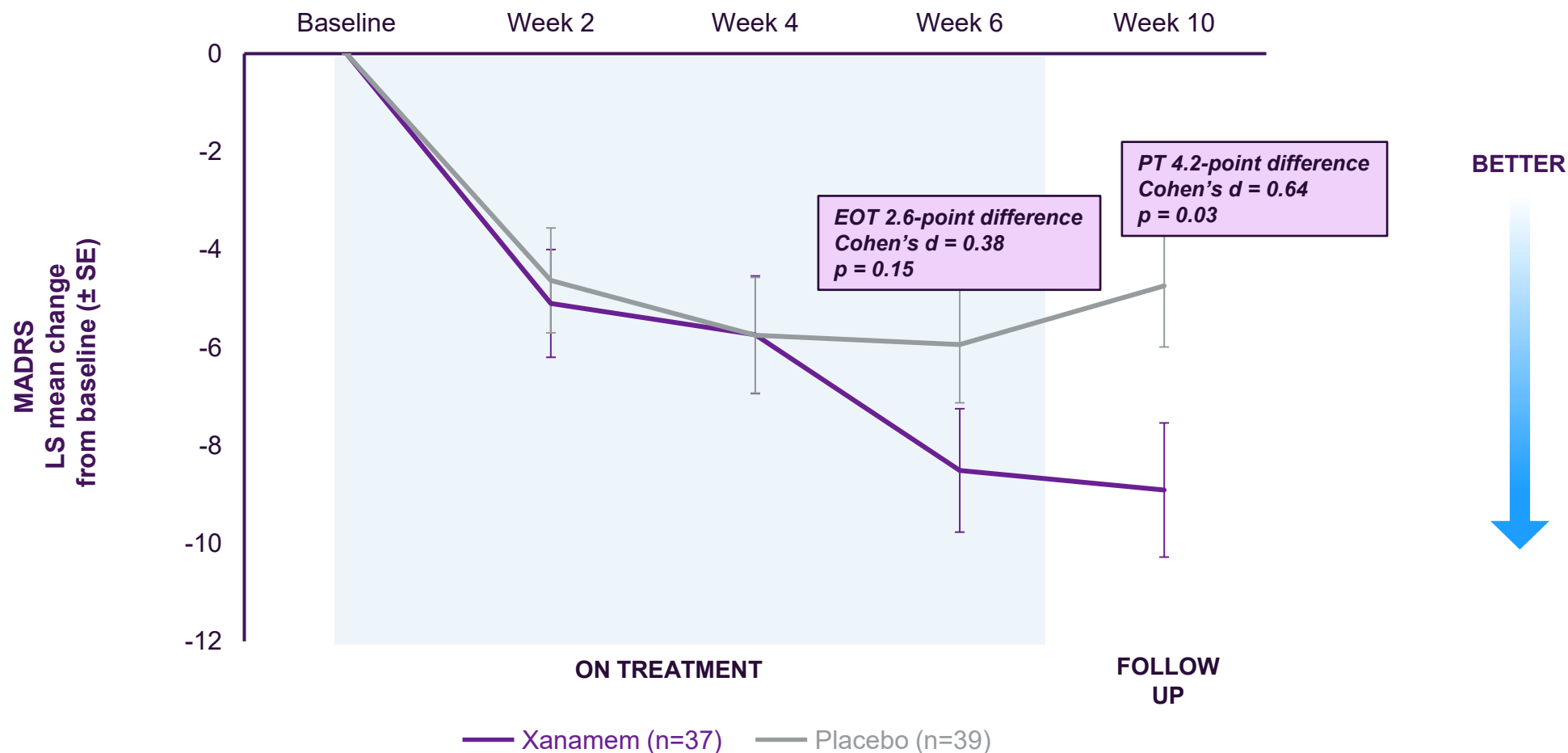


All randomized participants



# MADRS benefit in patients also taking SSRI (n=76)

Largest co-treatment subgroup





# Conclusion and Questions

# Building momentum toward Alzheimer's results

Numerous value-add milestones in 2025 and 2026 before final XanaMIA P2b results late 2026



- ***Xanamem has shown positive results in two Phase 2 trials: AD and MDD***
- ***Positive phase 2a MDD data validates multiple Xanamem programs***
  - ✓ Clinical activity of unique “cortisol control” mechanism of action
  - ✓ Clinical activity of the 10 mg daily dose being used in all trials
  - ✓ Reinforces the likelihood of seeing a disease-modifying effect in Alzheimer’s disease over 36 weeks in current XanaMIA trial
- ***Company funded to at least mid 2026***
- ***Commercial planning underway*** in preparation for early marketing approvals and potential partnership(s)
- ***Trial, regulatory, publication and presentation milestones*** in coming 18 months

# Contacts

## Steven Gourlay

CEO & Managing Director

P: +61 2 8964 7401

E. [steven.gourlay@actinogen.com.au](mailto:steven.gourlay@actinogen.com.au)

## Andrew Udell

Chief Commercial Officer

P: +1 203-912-3526

E. [andy.udell@actinogen.com.au](mailto:andy.udell@actinogen.com.au)

## Kristine Dorward

Head of Business Development

P: +1 514-618-0360

E. [kristine@pullanconsulting.com](mailto:kristine@pullanconsulting.com)