ASX ANNOUNCEMENT

Actinogen CEO & CFO present at Bell Potter Healthcare Conference 2025

Sydney, 19 November 2025. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that its CEO, Dr Steven Gourlay and CFO, Mr Will Souter, will present at the Bell Potter Healthcare Conference 2025 today.

The Company's presentation is titled *Oral Xanamem®: Controlling brain cortisol to slow progression in Alzheimer's disease and treat depression*. A copy of the presentation is attached to this announcement.

Shareholders interested in viewing the Company's presentation at the conference commencing at 1:00 pm can gain online access using the following link: https://bellpotterevent.com.au/healthcare-2025-ext/

View this announcement on our InvestorHub: https://investors.actinogen.com.au/link/eY2aWr

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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 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. The trial will be fully enrolled by the end of 2025 with initial results from an interim analysis in late January 2026 and final topline results in mid Q4 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 will evaluate safety and a limited number of efficacy endpoints such as the CDR-SB. The trial will commence in Q1 2026 and be 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.

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, 11β-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 video, 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 11β-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.

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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.

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

Actinogen

Oral Xanamem®

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

Bell Potter Healthcare Conference 2025

Dr Steven Gourlay, CEO

Mr Will Souter, CFO

19 November 2025

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Experience matters

Board of Directors

Dr. Geoff Brooke
Chairman
MBBS; MBA

Dr. Steven Gourlay
CEO & MD
MBBS; FRACP; PhD; MBA

Mr. Malcolm McComas
Non-Executive Director
BEc, LLB; FAICD; SF Fin

Dr. George Morstyn
Non-Executive Director
MBBS; PhD; FRACP CD

Dr. Nicki Vasquez
Non-Executive Director
PhD

Management Team

Dr. Steven Gourlay
CEO & MD

Dr. Dana Hilt
Chief Medical Officer
MD

Will Souter
Chief Financial Officer
BComm, LLB

Andrew Udell
Chief Commercial Officer
MBA

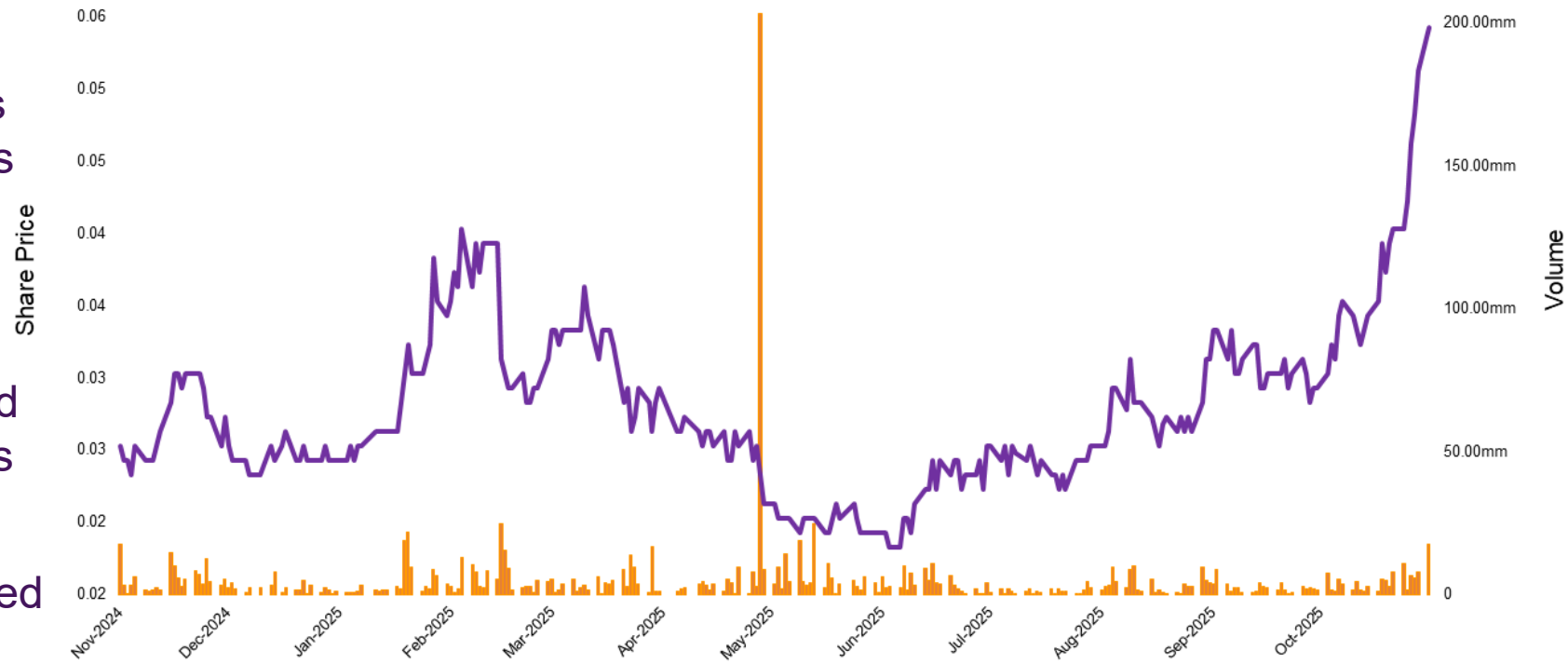
Cheryl Townsend
VP Clinical Operations
RN, M Health Law

Fujun Li
Head of Manufacturing
PhD

Michael Roberts
Head of IR & Comms
B.Ec (Hons), CPA, FFIN

ACW corporate snapshot*

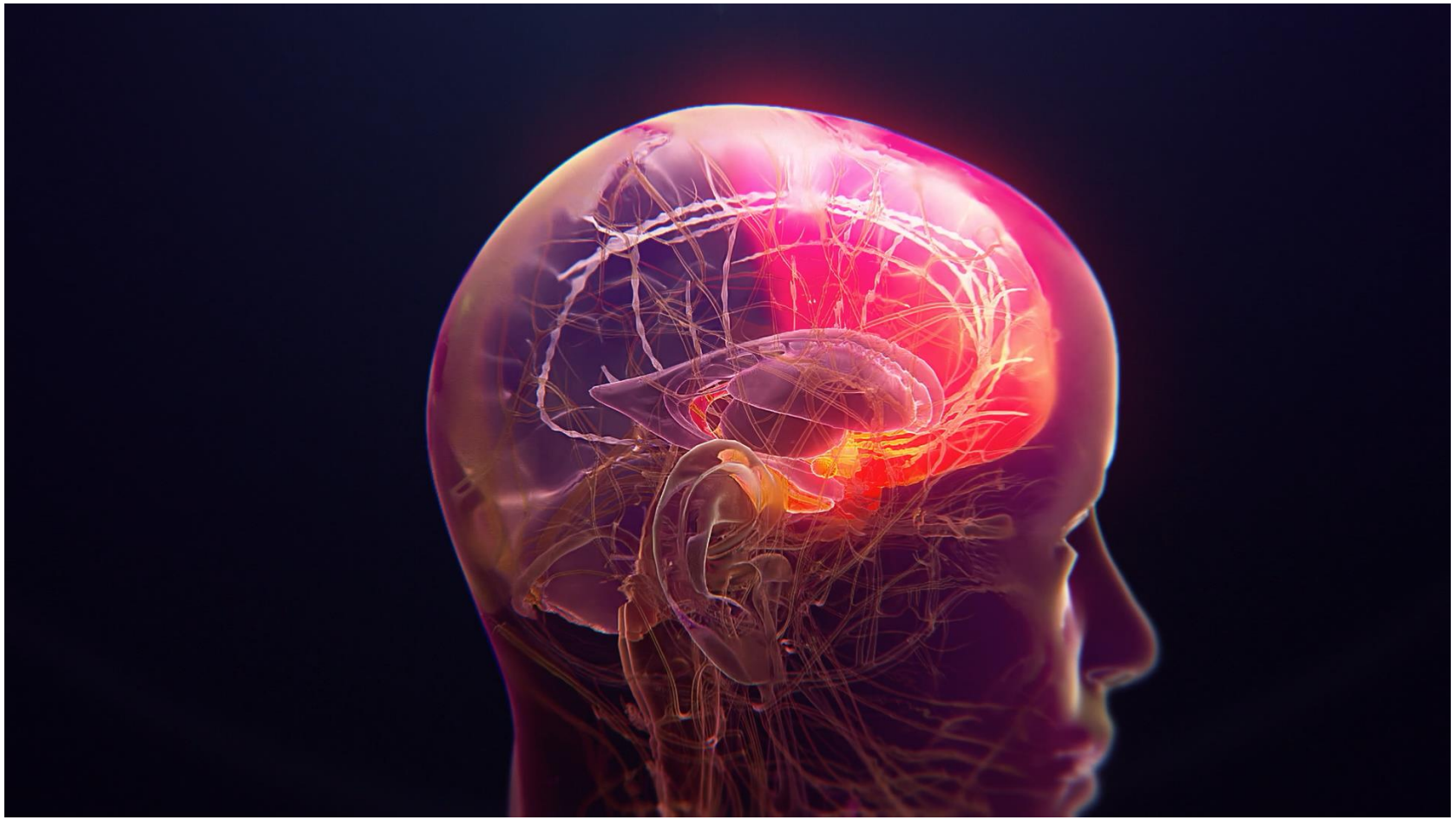
- Market cap of ~$175m significantly understates valuation upside in the success case for the current Alzheimer's disease trial
- Buyers have dominated ACW trading in CY25 following the removal of an overhang created by US fund BVF exiting all of its ASX positions including ACW
- CEO Steve Gourlay has invested $2m personally to become the major shareholder with ~5%



- Tight top 30% of the register comprising institutional and high net worth investors have continued to support the company through its pathway to this near-term value inflection point
- Significant support from other high net worth and retail investors who recognize the value upside potential

*ASX:ACW share price and volume trading chart 12 months to 17 November 2025

Xanamem's unique mechanism of action

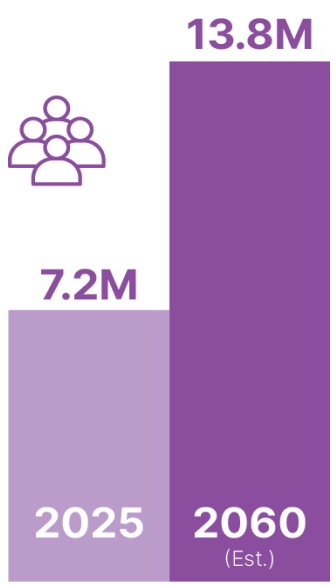


Click here for animation video

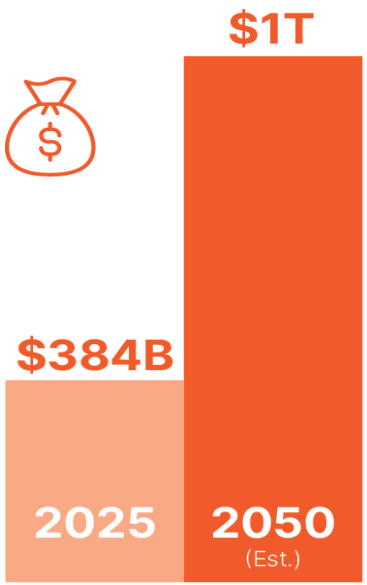
Alzheimer's disease market is large and growing

Growing Alzheimer's Disease market – U.S.

Large, unsatisfied and growing market



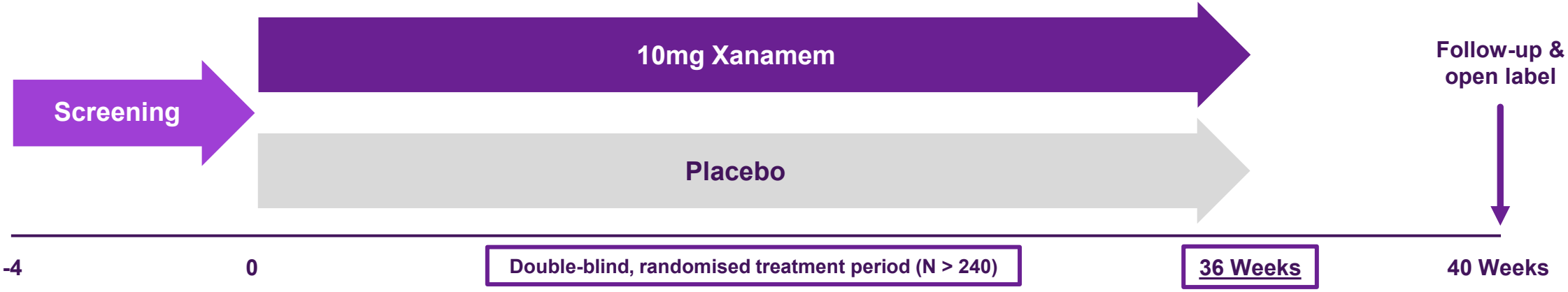
Number of patients (65+ years old)



Cost to treat (USD)

Optimal pivotal trial design & patient selection

Interim XanaMIA results in late Jan 2026, topline final results mid Q4 2026



Key Inclusion Criteria	Primary Endpoint	Key Secondary Endpoints	Implementation
• **Blood pTau biomarker positive** • Mild-moderate Alzheimer's by NIA-AA criteria	• **CDR-SB (functional and cognitive measure) @36 weeks**	• Cognitive Test Battery (7 cognitive measures well-validated in the Alzheimer's field) • Amsterdam Activity of Daily Living (functional measure)	• Full enrolment at 15 Australian & 20 US sites > 240 participants by end 2025 • Interim analysis late Jan 2026 (efficacy futility & safety)

NIA-AA=National Institute of Aging - Alzheimer's Association; **CDR-SB** Clinical Dementia Rating Scale – Sum of Boxes

Xanamem: Clear pathway to Alzheimer's approval

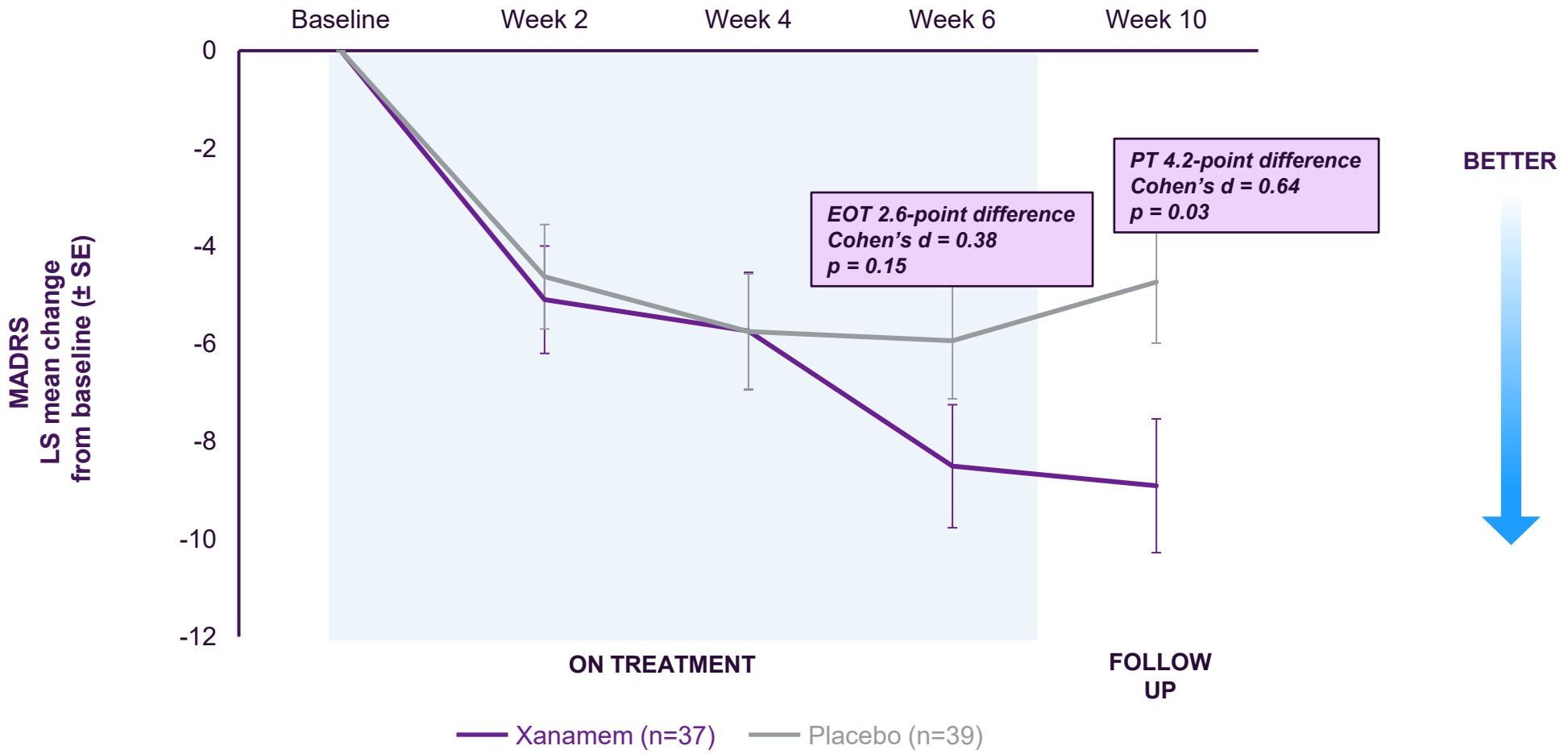
Phase 2b/3 trial on track, FDA agreement streamlines development, EMA meeting 2026

- Recent FDA agreement confirms development pathway to US marketing approval using one additional pivotal trial of 10 mg vs. placebo and open-label safety studies
- Clear guidance on manufacturing, ancillary studies
- Ongoing XanaMIA pivotal clinical trial:
  - Brisk enrolment in US and Australia, full enrolment Dec 2025
  - Excellent safety profile maintained, positive first Data Monitoring Committee review
  - Interim analysis of safety and efficacy futility in late Jan 2026
  - On-track for final results in mid Q4 2026
- Phase 3 planning commencing in parallel with discussions re potential partnerships

Previous results that give the company confidence in a positive phase 2b/3 trial outcome in Alzheimer's

1. Clinical benefit on depression symptoms in phase 2 (n = 165)
2. Large clinical benefit in pTau biomarker-positive Alzheimer's patients (n = 34)
3. Human PET study showing high brain target engagement (n = 40)
4. Very strong cortisol scientific rationale in Alzheimer's

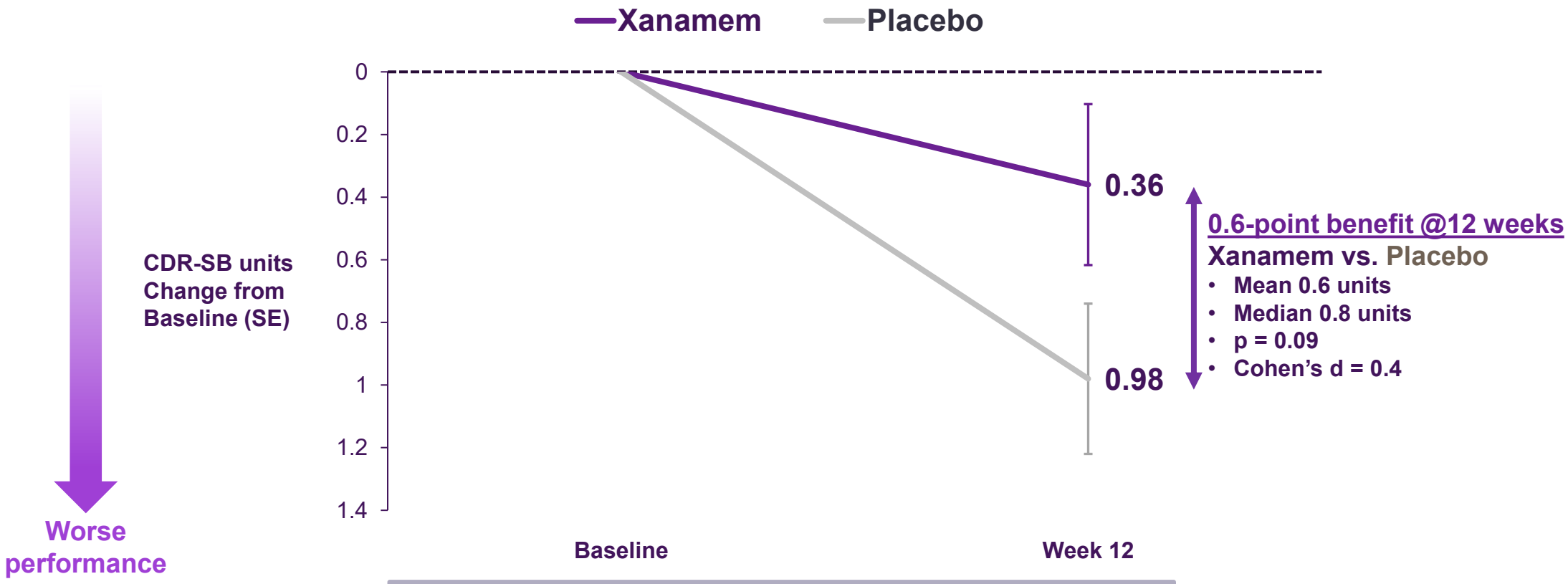
Major depressive disorder phase 2a: benefit also seen in patients taking background SSRI anti-depressant (n=76)



Abbreviations: SSRI, selective serotonin reuptake inhibitor

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

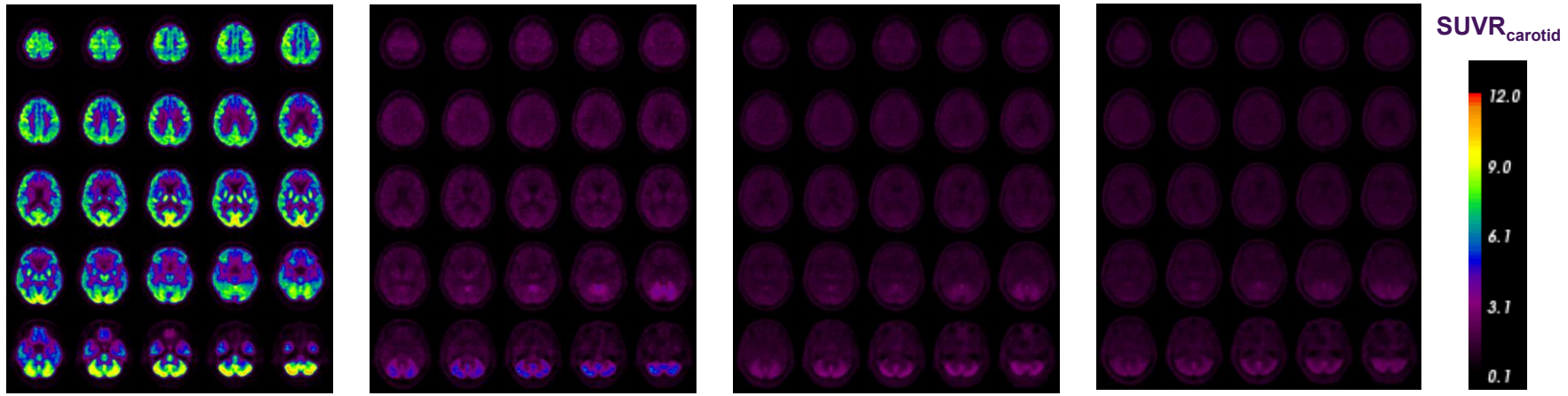
3. Human PET study shows full target engagement

Other 11β-HSD1 enzyme inhibitors have not achieved adequate brain levels

Baseline

After 7 days of daily dosing

5 mg Xanamem | **10 mg Xanamem** | **20 mg Xanamem**



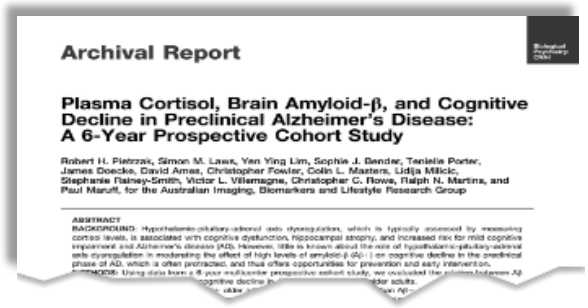
Xanamem extensively binds to the 11β-HSD1 enzyme throughout the brain, with high post-treatment effects (absence of color) after 7 days at all doses, slightly less at a 5 mg dose.

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

4. Very strong cortisol scientific rationale in Alzheimer's

- ✓ Compelling evidence provided by the Australian Imaging, Biomarker & Lifestyle Study of Ageing (AIBL) study (2017)[1]
  - Higher plasma cortisol leads to a much greater risk of developing AD
  - Accelerated effect of Aβ+ on decline in global cognition, episodic memory, and attention
- ✓ Individuals with the APOE-ε4 allele have higher CSF cortisol[2]
- ✓ Multiple other studies support the association between cortisol and AD development and progression[3-6]
- ✓ High cortisol and low folate predict probable Alzheimer's disease after age 75[7]
- ✓ Higher CSF cortisol levels in AD patients are associated with more rapid clinical worsening and cognitive impairment[8,9]

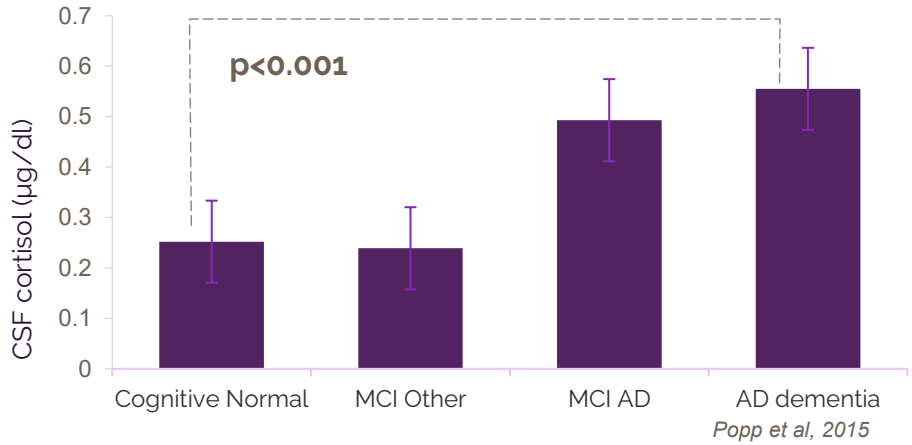

Archival Report

Plasma Cortisol, Brain Amyloid-β, and Cognitive Decline in Preclinical Alzheimer's Disease: A 6-Year Prospective Cohort Study

aibl

The Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing

MEAN CSF CORTISOL LEVELS



Popp et al, 2015

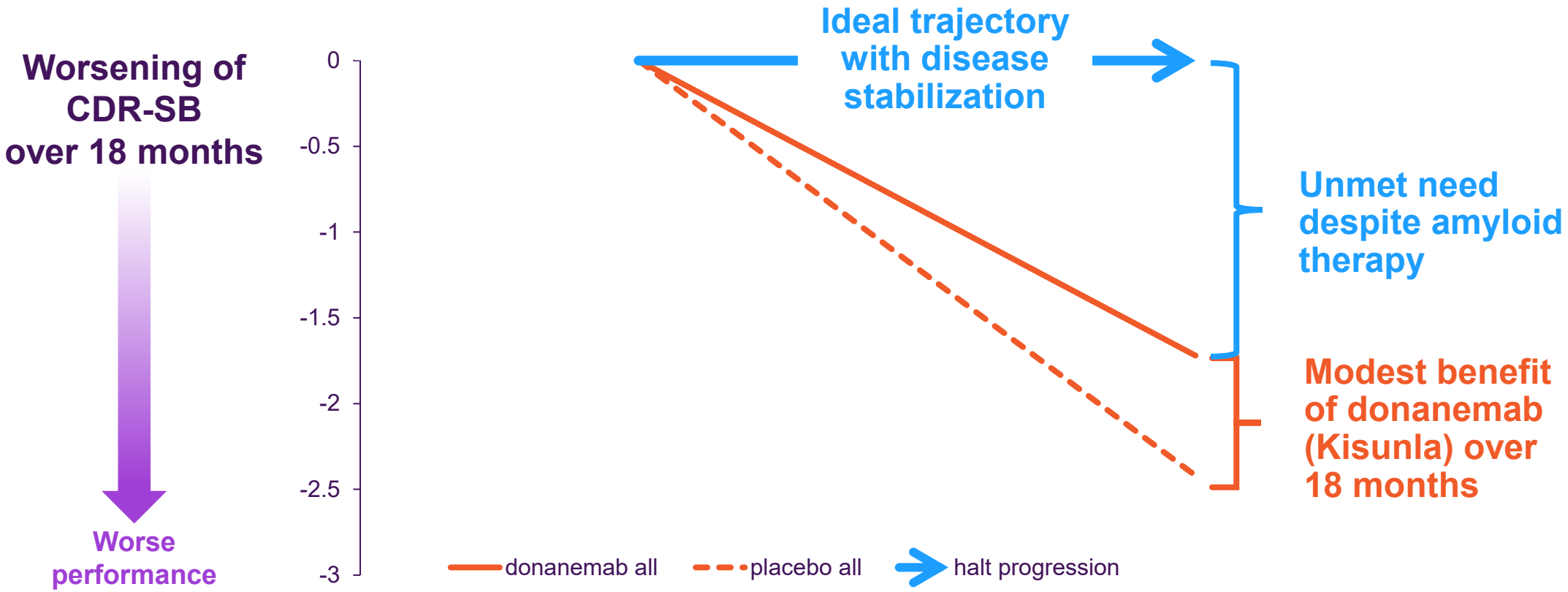
[1] Pietrzak et al., 2017, Biol Psychiatry: Cognitive Neuroscience and Neuroimagery, [2] Lupien et al., 1998, Nat Neurosci 1:69–73; [3] Geerlings et al., 2015, Neurology 85: 1-8; [4] Lehallier et al., 2016, JAMA Neurology 73(2), 203-212; [5] Popp et al., 2015, Neurobiol. Aging 36:601–607; [6] Ennis et al., 2017, Neurology 88(4):371-378; 2:45-52; [6] Lupien et al., 2009, Nat Rev Neurosci 10:434–445; [7] Hinterberger et al., J Am Ger Soc 2013 61(4):648-651; [8] Cernansky et al., 2006, Am J Psychiatry 163:2164-2169; [9] Kornhuber & Jensen, 2015, Neurobiol Aging 36:601-607;

Strategic insights about commercialization and partnering in AD

1. Anti-amyloid infusions have a borderline risk-benefit profile
2. Xanamem is being developed with a better risk-benefit and ease-of-use profile aimed at stabilizing the disease safely
3. Desired Xanamem benefits include multiple aspects of cognition and life functioning – ideally to halt Alzheimer's decline completely
4. XanaMIA has potential to be a catalyst for commercial and partnering interest

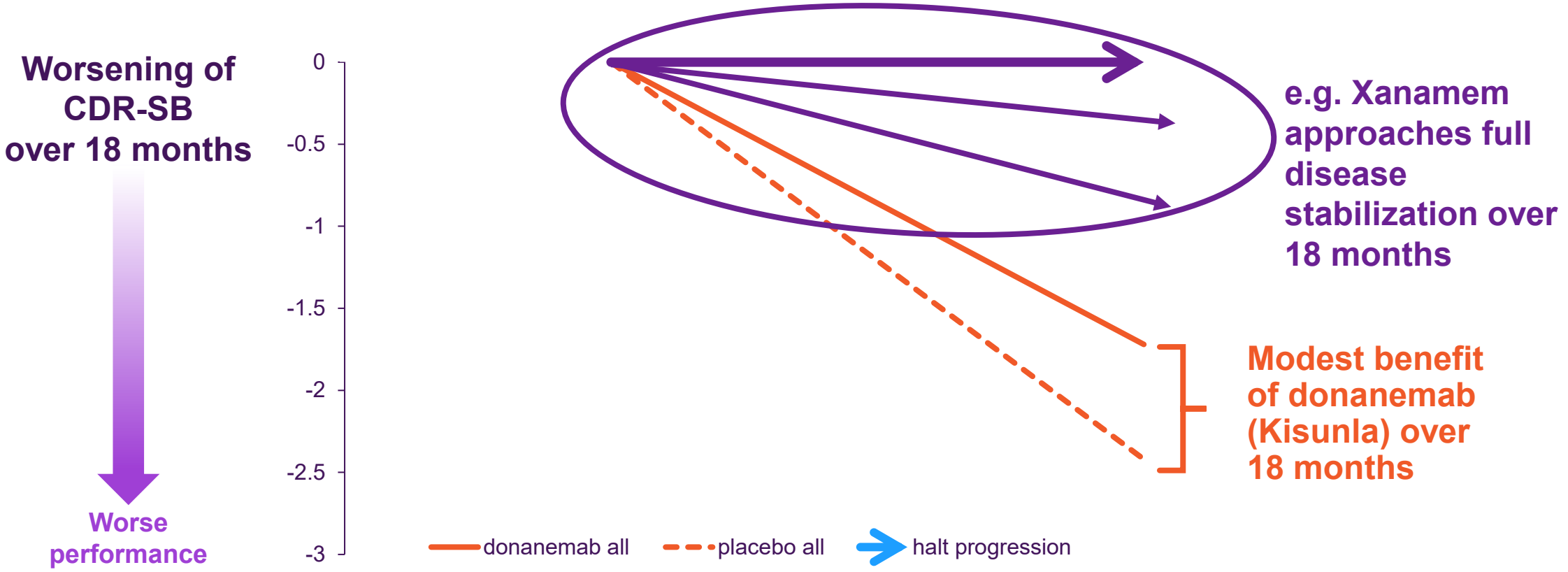
1. Anti-amyloid drugs only modestly slow disease

Ideally patients with AD would not worsen on treatment at all



Drugs targeting other mechanisms like Xanamem are needed

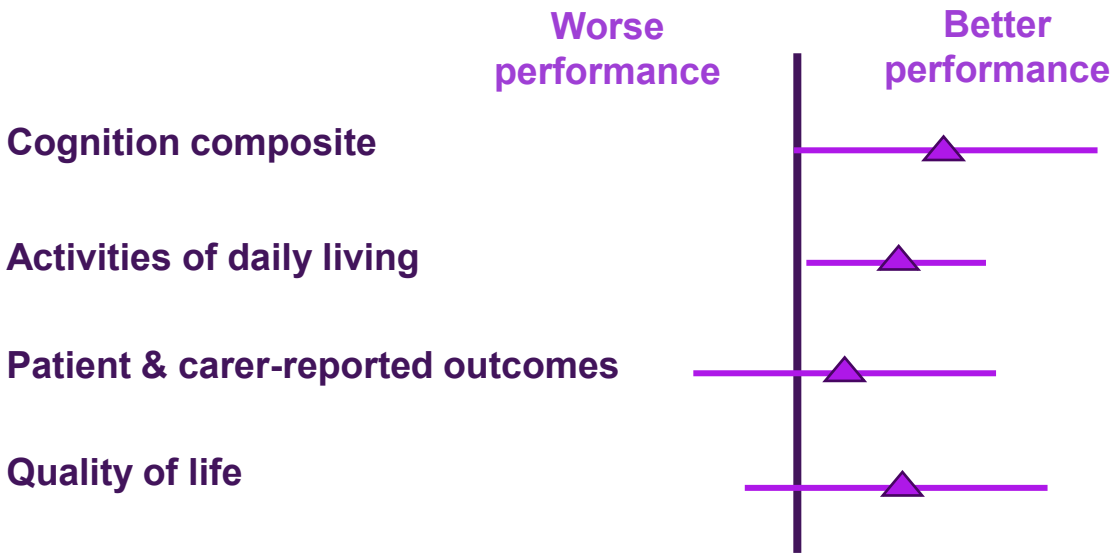
2. Potential for Xanamem to beat existing approved treatments on CDR-SB primary endpoint



If results are good, Xanamem could be many times more effective than other drugs

3. Opportunity for consistent benefit across safety and key secondary measures

Safety[1]: No serious adverse events related to Xanamem (n ~ 500)



EXAMPLE SECONDARY ENDPOINT DATA (MEAN, 95%C.I.)[2]

1. No serious adverse events related to Xanamem have been reported across all clinical trials to date; various other safety data are reported in peer reviewed publications (see https://actinogen.com.au/xanamem/) 2. Example means shown by triangles; where example 95% confidence interval (C.I.) lines cross the midline, it means the p values would > 0.05

4. XanaMIA catalyst for commercial & partnering events

We know the commercial opportunity is huge:

- ✓ US Neurologists treating AD love the idea of a safe and effective, oral drug and indicate that uptake would be rapid in the first year
- ✓ Xanamem could easily move to first line therapy and displace many existing treatments
- ✓ Combinability with other small molecules and biologics a major plus
- ✓ Multiple potential commercialization partners are reviewing our confidential data

We are planning for:

- ✓ Completing one or more regional partnership deals
- ✓ Final results that are good enough to excite multiple, global partnership bids
- ✓ Final results that are good enough for regulators to seriously consider expedited approvals

Conclusion

Building momentum toward Alzheimer's results

Numerous value-add near-term milestones

- ***On-track with XanaMIA pivotal trial for mild-moderate Alzheimer's disease***
  - ✓ Full enrolment of > 240 participants in XanaMIA pivotal trial Q4 2025
  - ✓ Interim results late January 2026, topline final results mid Q4 2026
- ***Highly positive market research with about 100 US Alzheimer's physicians***
  - ✓ More than 50% of their patients are good Xanamem candidates
  - ✓ And 80% of physicians would prescribe Xanamem in the first 6 months
- ***FDA agreement on streamlined path to Xanamem approval***
  - ✓ One other pivotal trial of 10 mg vs. placebo
  - ✓ Standard clinical pharmacology and safety database requirements
- ***IP portfolio strengthened with the prosecution of multiple new patents***
- ***Increased partnership interest and dataroom activity***
- ***Company funded beyond mid 2026***

Multiple near-term milestones in coming year

Milestone	Likely Timing
Screening activities close, XanaMIA AD trial	Oct 25
Full enrolment, 220 patients with AD, XanaMIA AD trial	Dec 25
XanaCIDD MDD peer-reviewed journal publication	Q4 25 / Q1 26
CTAD AD conference in San Diego	ad
Meetings at JP Morgan Healthcare conference week, San Francisco	Mid Jan 26
Interim analysis XanaMIA AD trial	Late Jan 26
ADPD AD conference in Copenhagen	Q1 26
EMA Scientific Advice meeting for AD	Q2 26
Clinical Trials Science Forum – focus on commercial planning	Q2 26
BIO conference in San Diego	Q2 26
AAIC AD conference in London	Q3 26
Last patient completes 36-week treatment, 4 week follow-up	Oct 25
Final results, XanaMIA AD trial	Mid Q4 26

Q & A

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