



ASX ANNOUNCEMENT

ACW progress update and Q&A webinar today

Sydney, 28 October 2025. Actinogen Medical ASX: ACW (“ACW” or “the Company”) is pleased to announce that it will be holding a live webinar at 11am (Sydney time) today, 28 October 2025. The leadership team, led by CEO, Dr Steven Gourlay, will outline the company's significant progress over recent months and discuss key upcoming milestones. Other members of the leadership team participating are Dr Dana Hilt, Dr Fujun Li, Andy Udell, Will Souter and Michael Roberts.

Pre-register now or register and join at 11am (Sydney time):

https://actinogenmedical.zoom.us/webinar/register/WN_L_TOuTmaR4qYvYnXrNzfDQ

A copy of the webinar presentation is attached to this announcement. At the conclusion of the presentation, there will be an opportunity for questions from webinar attendees.

A recording of the webinar will be made available as soon as possible after the conclusion of the event on the Company's YouTube channel and links to the recording will be provided on the Company's Investorhub: <https://investors.actinogen.com.au/>, website: <https://actinogen.com.au/> and social media platforms.

View this announcement on our InvestorHub: <https://investors.actinogen.com.au/link/r6Vq0r>

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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, 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 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 11 β -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.



Oral Xanamem® (emestedastat)

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

Webinar Presentation

28 October 2025

Agenda



- Introduction & Overview, Dr Steve Gourlay, CEO
- Xanamem Clinical & Regulatory, Dr Dana Hilt, CMO
- Manufacturing & Quality, Dr Fujun Li, Head of Manufacturing
- Commercial readiness, Mr Andy Udell, CCO
- Business Development & Partnering, Mr Andy Udell, CCO
- Financials, Mr Will Souter, CFO
- InvestorHub facility, Mr Michael Roberts, Head of Communications & Investor Relations
- Conclusion and Q &A, Dr Steve Gourlay, CEO

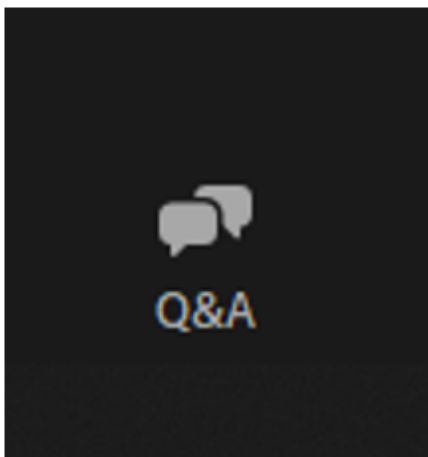
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Online Q&A

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Overview

Dr Steve Gourlay, CEO & MD



Xanamem: Clear pathway to Alzheimer's approval

Phase 2b/3 pivotal trial on track, FDA agreement streamlines development



- FDA confirms streamlined development pathway to US marketing approval
 - ✓ One additional pivotal trial of 10 mg vs. placebo and open-label safety studies
 - ✓ Clear guidance on minimal ancillary nonclinical and clinical pharmacology work
 - ✓ Agreement on key manufacturing items
- Ongoing XanaMIA pivotal phase 2b/3 clinical trial
 - ✓ Accelerated enrolment at 35 clinical centers in US and Australia – screening closes Oct 31
 - ✓ Excellent safety profile maintained
 - ✓ Interim analysis of safety and efficacy futility late January 2026
 - ✓ On-track for topline final results mid Q4 2026
 - ✓ Open-label extension phase opens Q1 2026
- Phase 3 planning commencing in parallel with discussions re potential partnerships

Experienced board and management team



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



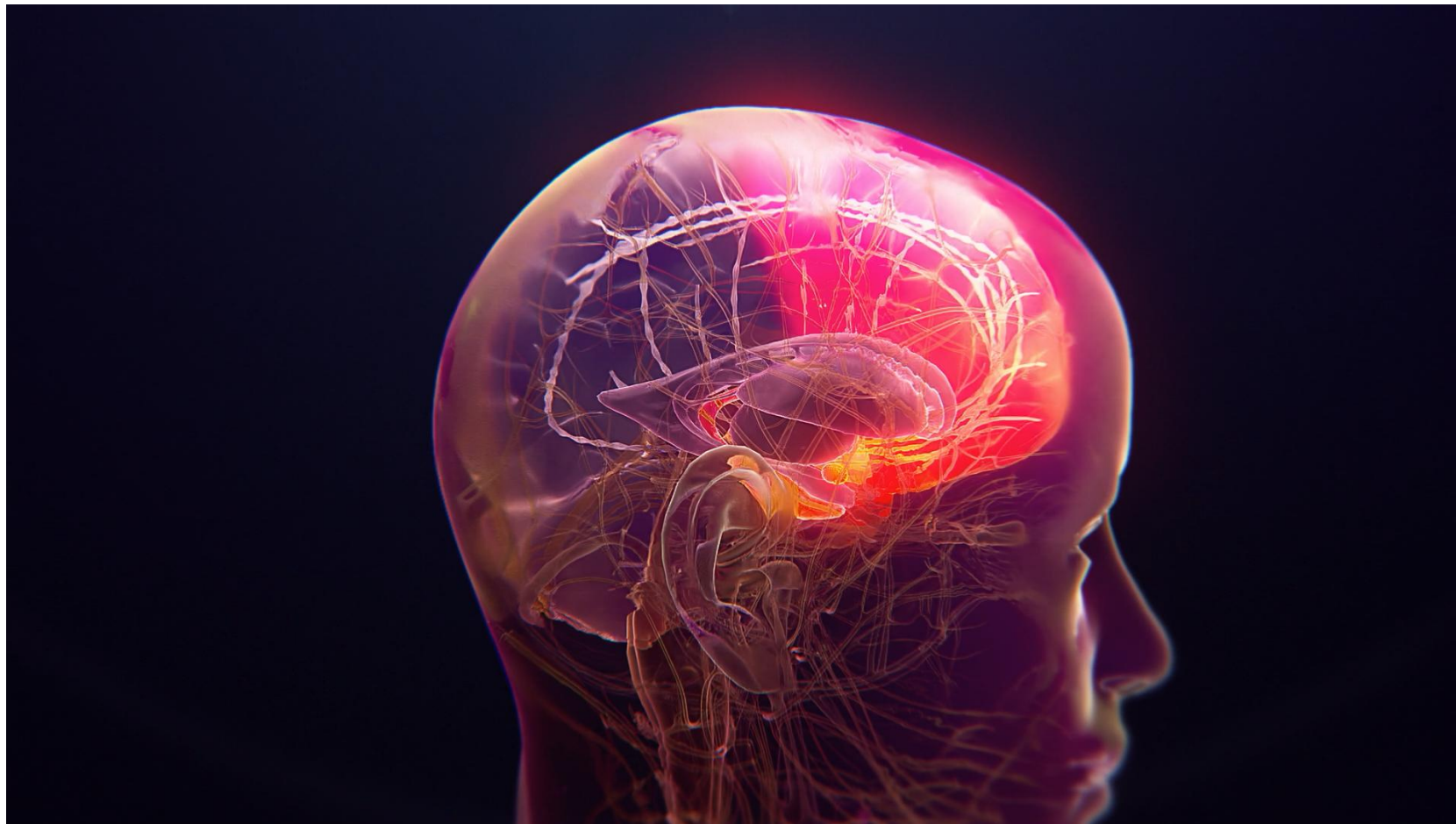
Fujun Li
Head of Manufacturing
PhD



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



Xanamem's unique mechanism of action animation



[Click here for animation video](#)

Xanamem Clinical & Regulatory

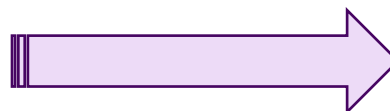
Dr Dana Hilt, CMO

Xanamem controls cortisol by inhibition of 11 β -HSD1¹

Controlling brain cortisol² has potential durable benefits

Reduction of “stress response” in brain

RAPID changes in kinases, cell function, neurotransmitters over hours to days lead to short-term “low stress” settings



“Lower stress” shorter term e.g.

- Reducing inflammation
- Improving neurotransmitter balance
- Decreasing cell death

SLOW changes in gene expression and protein synthesis over days to weeks lead to durable “low stress” settings

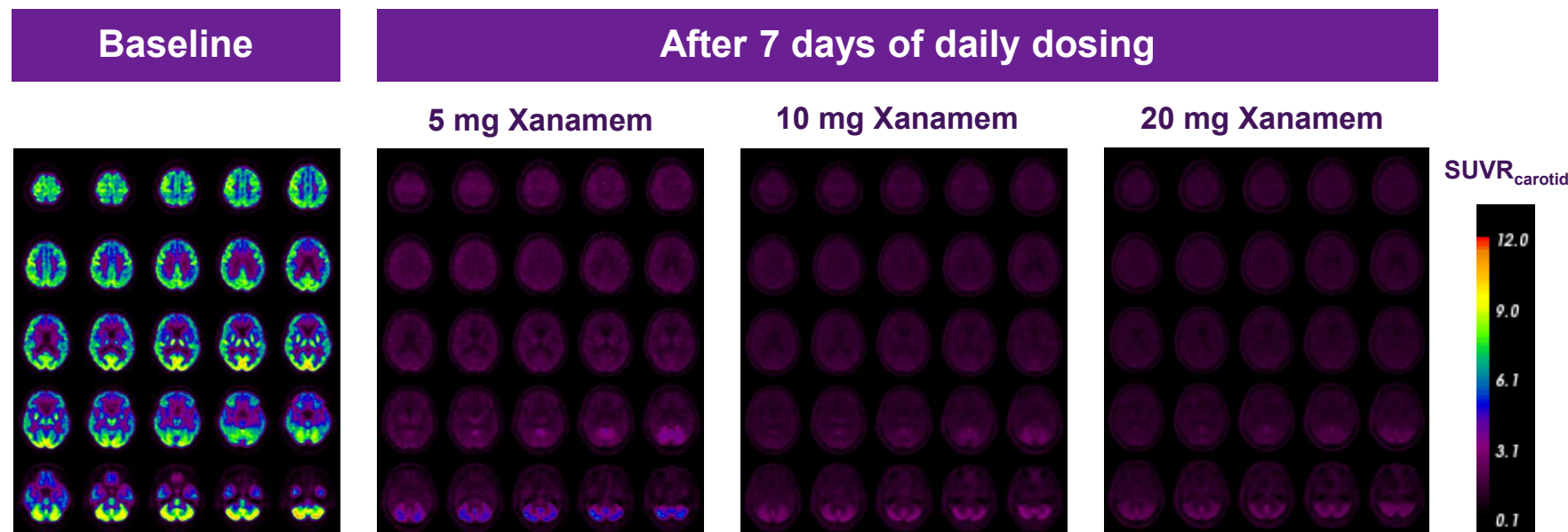


“Lower stress” longer term e.g.

- Improving neural circuitry
- Generating new brain cells
- Ideal receptor configurations

Human PET study shows full target engagement

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



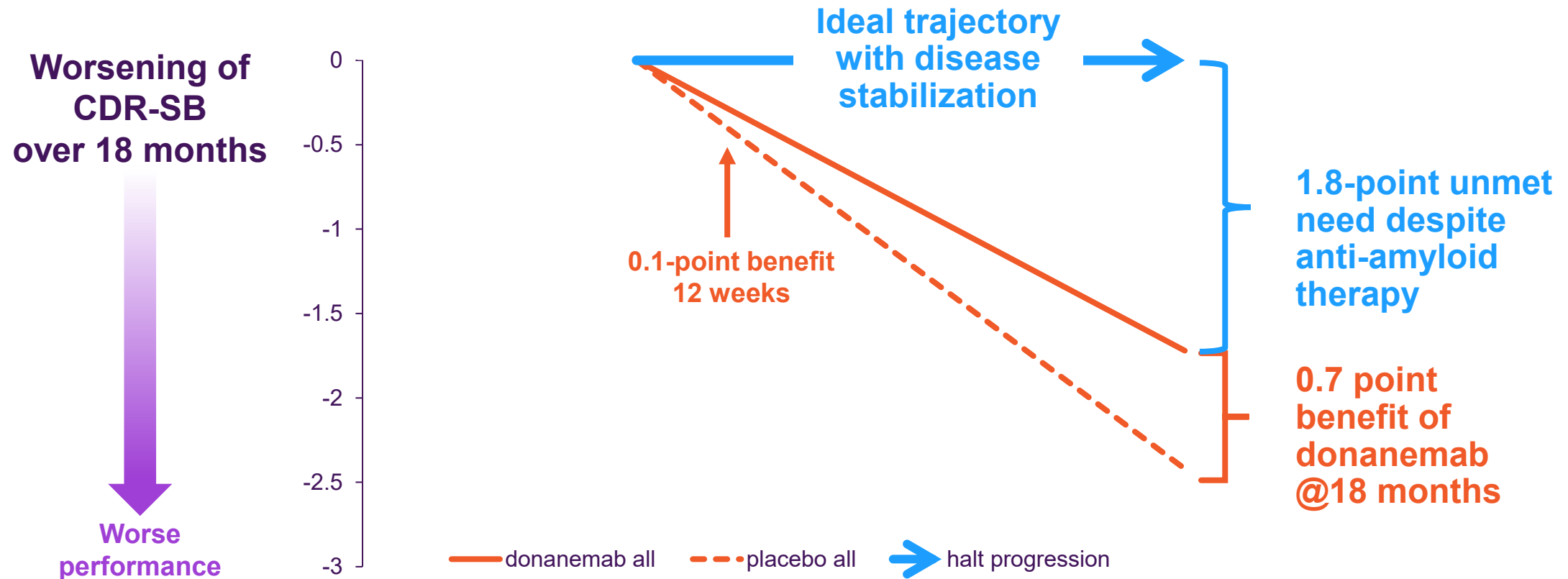
Xanamem extensively binds to the 11 β -HSD1 enzyme throughout the brain, with high post-treatment effects (absence of color) after 7 days at all doses, slightly less at a 5 mg dose.

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

Anti-amyloid therapy modestly slows AD progression

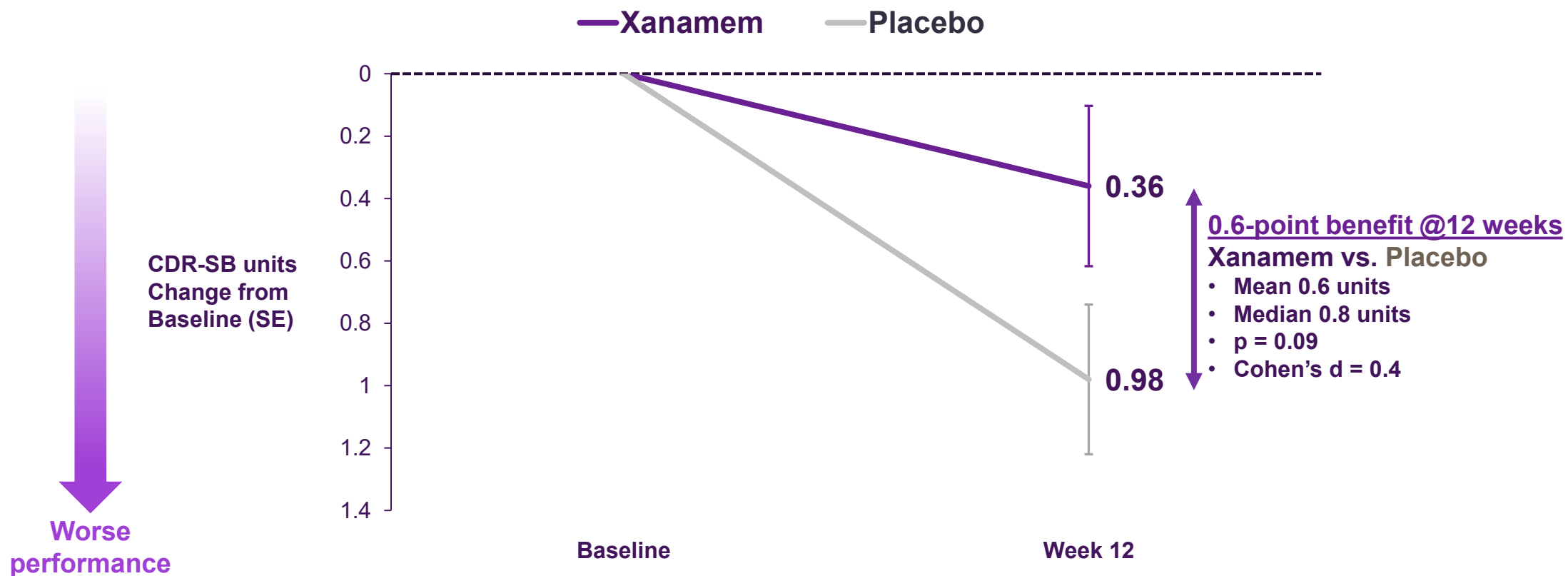
Ideally patients with AD would not worsen on treatment at all



Drugs targeting other mechanisms like Xanomem are needed

Large Xanamem benefit in high pTau181 patients

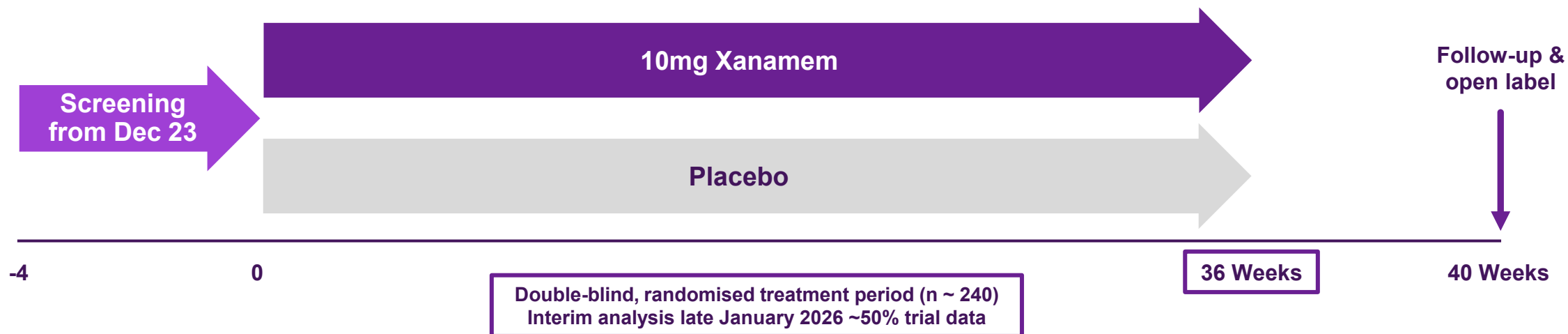
Phase 2a biomarker study: major slowing of CDR-SB decline over 12 weeks (n=34)



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

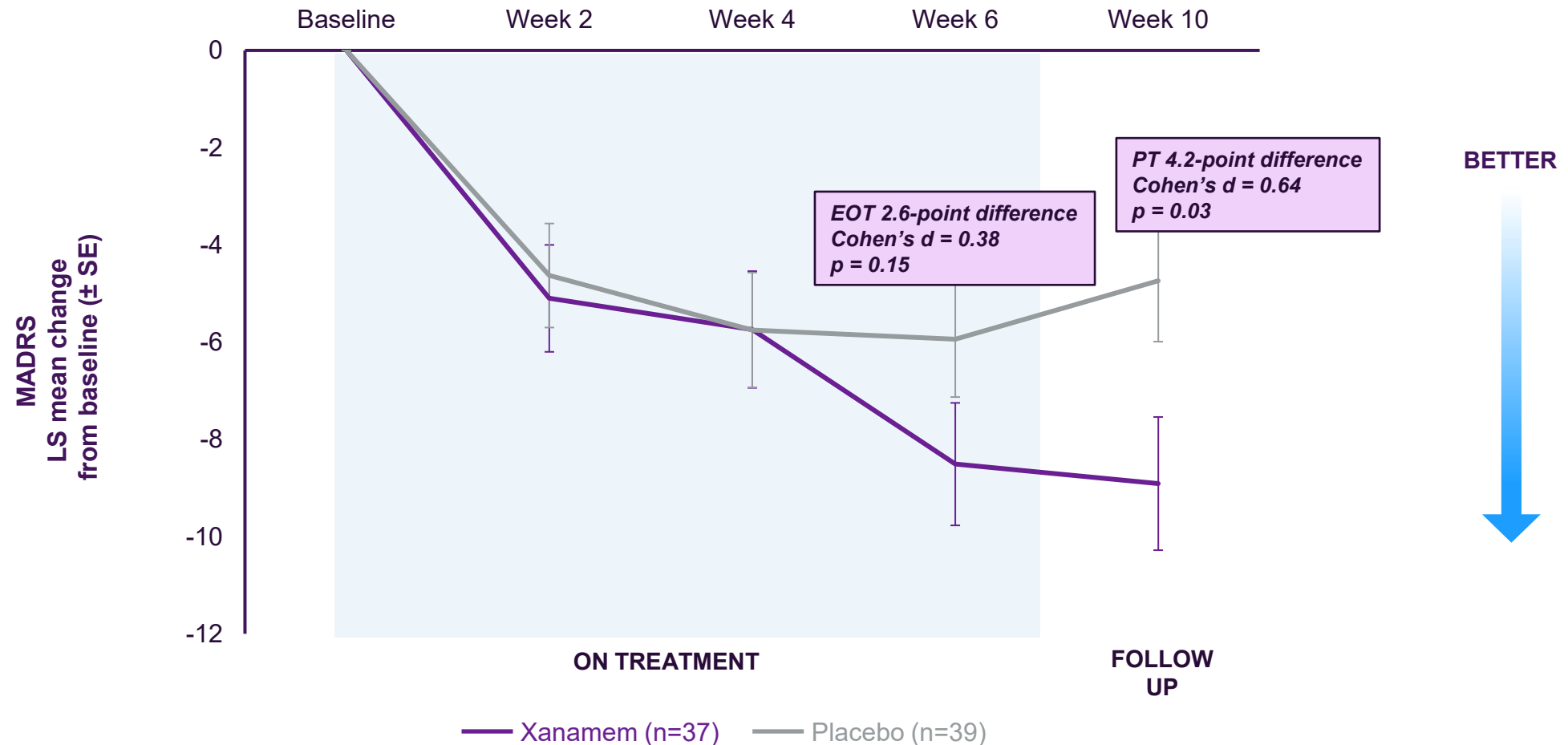
XanaMIA phase 2b/3 trial in Alzheimer's disease

Initial, interim analysis late January 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)	- Enrolment at 15 Australian & 20 US sites - Likely final enrolment ~240 (was 220) Q4 2025 - Interim analysis late Jan 2026 for safety & efficacy futility - Open-label extension Q1 2026

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



Regulatory progress de-risks Xanamem program



- UK ILAP innovation passport status awarded in 2024
- Recent FDA meeting confirms streamlined development pathway to US marketing approval
 - ✓ One additional pivotal trial of 10 mg vs. placebo and open-label safety studies
 - ✓ ICH¹ guideline standard safety database of 1500 individuals
 - ✓ Clear guidance on minimal ancillary nonclinical and clinical pharmacology work
- Similar European Medicines Authority meeting in 2026
- Additional pathways to speed US and other approvals will be used at the earliest opportunity

1. ICH: the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. An initiative that brings together regulatory authorities and the pharmaceutical industry to develop guidelines and standards aimed at harmonizing the drug development and registration process globally, ensuring the safety, efficacy, and quality of medicines.

Manufacturing & Quality

Dr Fujun Li, Head of Manufacturing

Successful scale-up of drug substance and tablet manufacturing



- ***Successful scale-up production of Xanamem drug substance***
 - ✓ Asymchem in China – high quality global supplier to large and small pharma
 - ✓ Patent protection in process
- ***On-going scaled-up tablet production***
 - ✓ Catalent in USA
 - ✓ No tariff issues on import of drug substance from China for clinical trial material manufacturing
 - ✓ Patent protection in process
- **FDA agreement on “regulatory starting materials”**
 - ✓ Agreed designation of the regulatory starting materials confirms synthesis pathway being used
- **Successful clinical pharmacology trial confirms 10 mg tablet performance and daily dose**
- **Quality oversight**
 - ✓ Careful quality oversight by Actinogen for both Asymchem and Catalent

Commercial readiness

Andy Udell, CCO



Alzheimer's disease market is large and growing

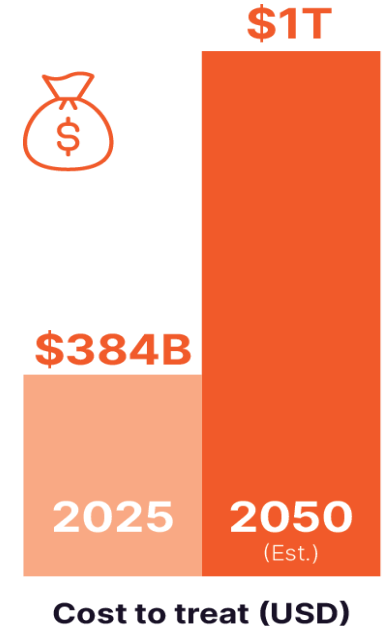
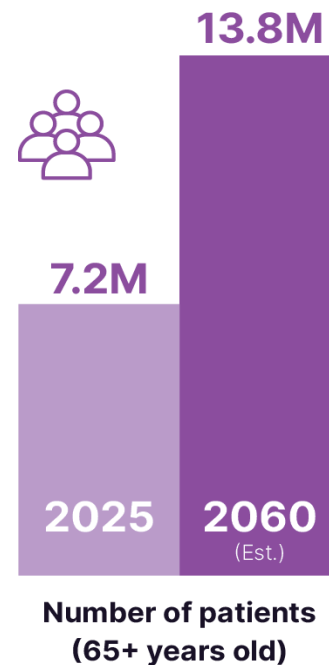
Strong cortisol control scientific rationale to address huge unmet medical need

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 β -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



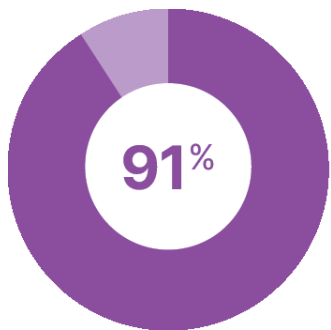
Direct insights from the front line of Alzheimer's care



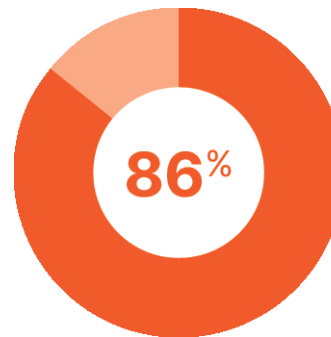
Physician perspectives on current practice, unmet needs, and future therapies¹

- Market research with over 100 general neurologists and dementia/geriatric specialists
- Representative of the AD-treating physician population as it relates to geography and practice type, and:
 - 18 mean years in practice
 - 94% of time in clinical practice setting
 - Mean of 222 Alzheimer's patients (median: 175) under personal care (per physician)

Current Market Perceptions:



of neurologists agree there is a **high unmet need** for **DMTs** for **early AD**



of neurologists expect their **approach to treating early AD** will **change over the next 5 years** as **novel DMTs** launch

*"I think eventually what will happen is that we're **not going to be just treating patients with an amyloid remover**, but also **anti-neuroinflammation, mitochondrial enhancers, synaptic enhancers** and so on and so on, in order to actually stop or substantially **slow down the progression of the disease**."*

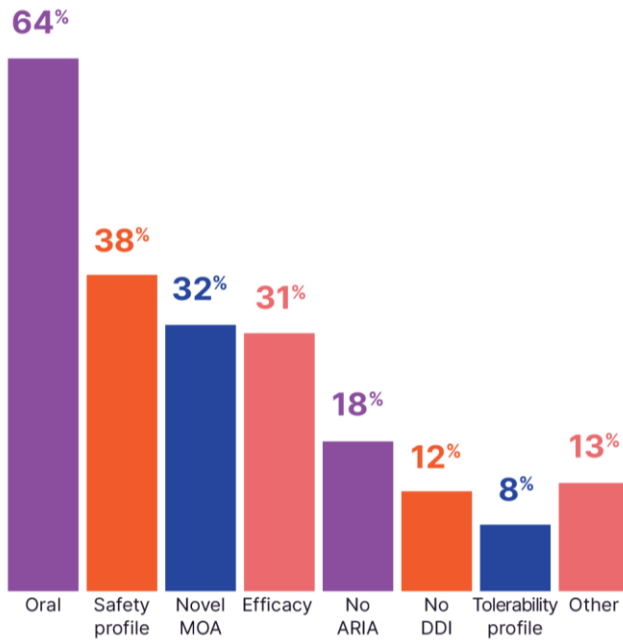
Strong physician response to Xanamem's target profile



Over half of their current AD patients fall within Xanamem's addressable market

Positive reaction to Xanamem's potential advantages per clinician feedback

Advantages of Xanamem (Unaided) % of respondents



"Oral agent with distinctive mechanism of action, no safety concern."

"More efficacious, oral, no concern for ARIA, can be used in more advanced AD."

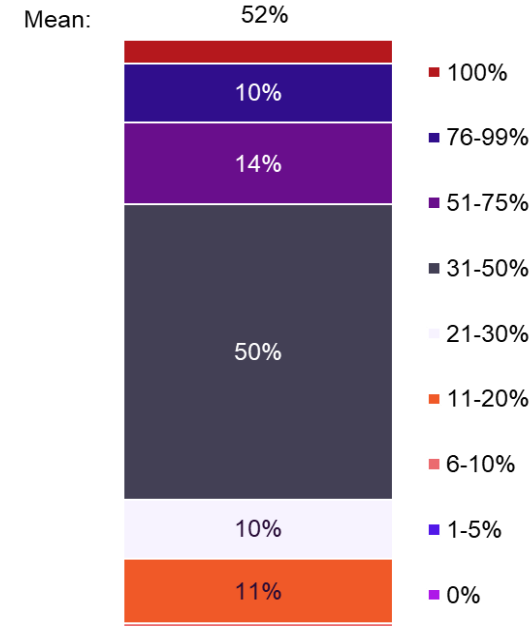
"It appears to be quite safe. There is little work to be done on the part of the clinician or the patient (dosing, labs, titration, etc.)"

Above and right: Spherix Global Insights: Market Dynamix Early Alzheimer's Disease (US) Q2 2025 (n=101) and Custom Quantitative Analysis (US) July/August 2025 (n=91)

DMTs: Disease modifying therapies
ARIA: Amyloid-related imaging abnormalities

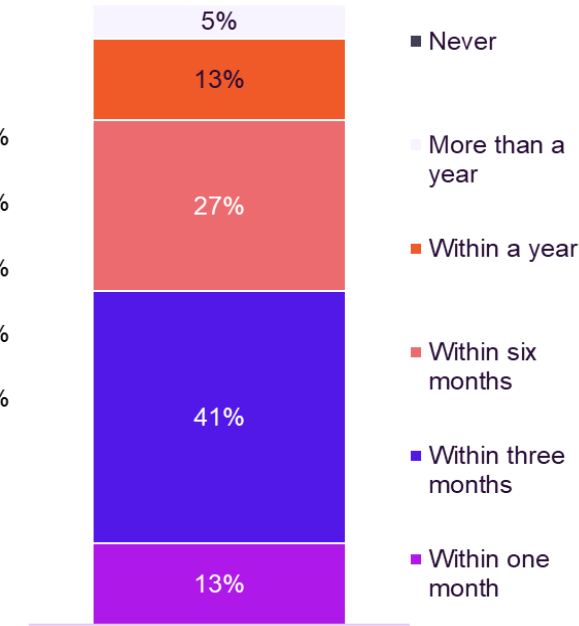
Xanamem Patient Candidacy

% of respondents



Anticipated Timeline to Prescribe

% of respondents



Driving awareness of Xanamem and cortisol biology



Expanding education, engagement and visibility



- **Educational need identified:** Qualitative research and advisory boards revealed limited physician understanding of the role of cortisol in the brain and its link to Alzheimer's pathology
- **Action taken:** Developed a concise two-minute animation explaining Xanamem's unique "cortisol control" mechanism of action
- **Scientific presence:** Active participation at major Alzheimer's conferences, including a booth at AAIC and presence at CTAD and other key global meetings
- **KOL engagement:** Ongoing collaboration with leading neurologists and psychiatrists through advisory boards, 1:1 discussions, and planning for future review papers and publications
- **Broader awareness:** Continuing to elevate Xanamem's visibility and differentiation through consistent medical, scientific, and educational initiative

Business Development & Partnering

Andy Udell, CCO

Increased level of partnering interest and activity



- Well-established relationships with major and mid-sized pharma interested in neurodegeneration/Alzheimer's
 - ✓ Meetings at multiple annual Alzheimer's conferences
 - ✓ Sachs Neuroscience conference during JP Morgan week
- Pullan consulting retained to drive outreach and partnering processes
- BIO meetings
 - ✓ BIO June 2025 generated a higher level of interest than previously
 - ✓ BIO Europe November 2025
- Increased dataroom diligence activities in recent months
- Company focus on value-add regional partner(s)

Finances

Will Souter, CFO



Cash runway to at least mid 2026



- Proforma cash position of \$12.9m providing runway well into 2026
- As full enrolment nears, cash burn plateaus
- Other sources of funding include:
 - Conversion of options – 2 unlisted tranches at \$0.0375 worth ~\$6m
 - Further R&D loan funding with increased R&D spend
 - Potential upfront funding from a partnership deal
- Considerable increase in interest from the investment community as key milestones approach, including from retail, HNW, institutional generalist and specialist investors, local and international investment banks and expert biotech analysts
- Xanamem program represents enormous upside in potential valuation compared to Actinogen's current market capitalization and the size of the opportunity in AD and other diseases

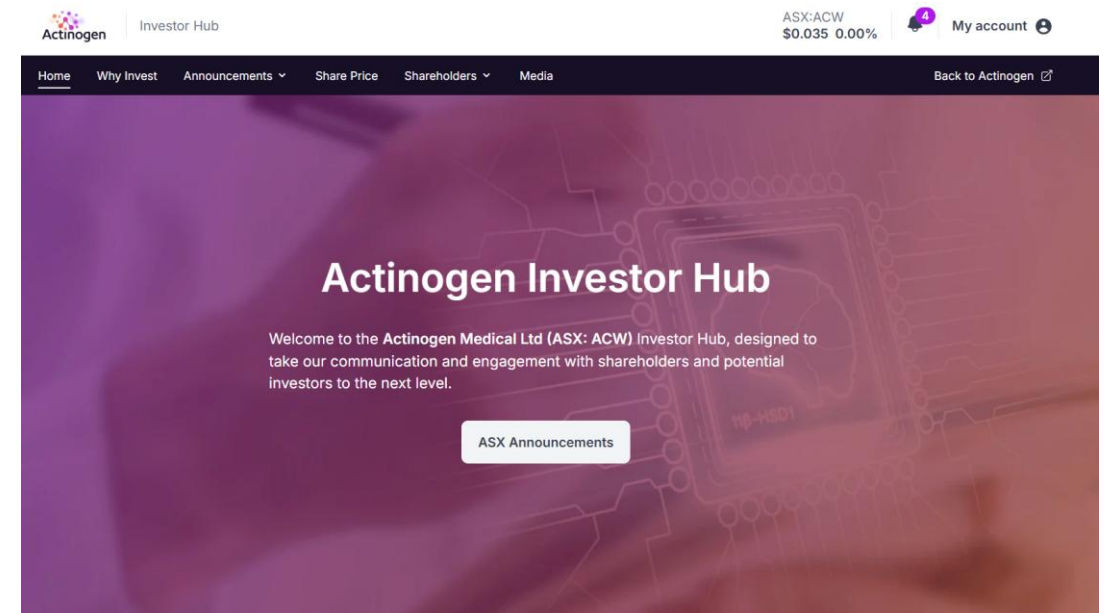
InvestorHub facility

Michael Roberts, Head of Investor Relations
& Communications

InvestorHub provides investors with enhanced functionality & direct engagement with ACW



- Consistent & familiar format for investors across all companies using InvestorHub
- Direct interaction with ACW management via Q&A function associated with each announcement
- Immediate distribution of price-sensitive ASX announcements
- Summary text & video attached to key announcements
- Ability to identify & register as 'High Net Worth' investor
- Regular enhanced functionality updates



[Click here to access the Actinogen InvestorHub](#)

Conclusion



On track to deliver transformative Alzheimer's data

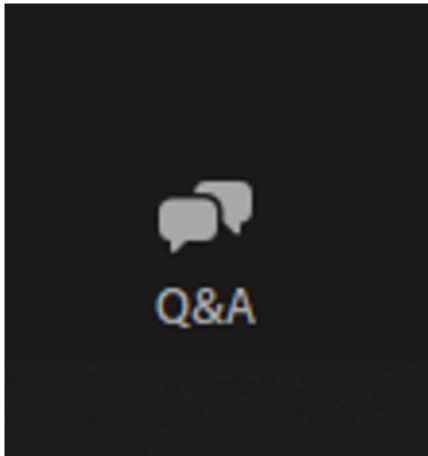
Multiple catalysts ahead as Xanamem advances towards pivotal results



- ***On-track with program in patients with mild-moderate Alzheimer's disease***
 - ✓ FDA confirms development pathway to US marketing approval
 - ✓ Full enrolment of ~240 XanaMIA pivotal trial participants in Q4 2025
 - ✓ Formal interim analysis of safety & efficacy futility late Jan 2026, topline final results Q4 2026
- ***Positive phase 2a depression data validates Xanamem clinical activity in the brain***
 - ✓ Further validates “cortisol control” mechanism of action in the brain and 10 mg dose
 - ✓ Reinforces the likelihood of seeing a disease-modifying effect in Alzheimer's disease
 - ✓ Peer-reviewed journal publication pending, further depression trials partner-dependent
- ***Scaled up manufacturing***
- ***Commercial & partnership planning underway***
- ***Company funded to at least mid 2026***
- ***Other trial, regulatory, publication and presentation milestones***

Online Q&A

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Appendix



Multiple near-term milestones in coming year

Milestone	Likely Timing
Screening activities close, XanaMIAAD trial	Q4 25
Full enrolment, ~240 patients with AD, XanaMIAAD trial	Late Q4 25
XanaCIDD MDD peer-reviewed journal publication	Q4 25 / Q1 26
CTAD conference AD presentation in San Diego	Q4 25
Sach's Neuroscience conference	Mid Jan 26
Meetings at JP Morgan Healthcare conference week, San Francisco	Mid Jan 26
Interim analysis XanaMIAAD trial	Late Jan 26
ADPD conference AD presentation 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
Final results, XanaMIAAD trial	Mid Q4 26

Key references

Other references see also <https://actinogen.com.au/xanamem>



11 β -HSD1 inhibition

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Currencies

- Currencies are in Australian dollars unless otherwise stated

Selected Glossary 1

- **11 β -HSD1** – 11 beta HydroxySteroid Dehydrogenase-1 enzyme. Selectively expressed in brain, liver, adipose.
- **A β** – Amyloid beta – a type of amyloid protein associated with Alzheimer's Disease, 42 and 40 are different forms
- **ACTH** – Adrenocorticotrophic hormone that regulates blood levels of cortisol
- **AD** – Alzheimer's disease
- **ADAS-Cog** – Alzheimer's Disease Assessment Score - Cognition
- **ApoE4** – Apoprotein genotype associated with genetic risk of Alzheimer's Disease
- **ATN** – Amyloid, Tau, Neurodegeneration
- **Clinical Scales** – Measure how a patient feels, performs and functions
- **CDR-SB** – Clinical Dementia Rating "Sum of Boxes" scale measuring cognition and function on an 18-point scale (high worse)
- **CNS** – Central nervous system
- **CSF** – Cerebrospinal fluid
- **CTAD** – Clinical Trials on Alzheimer's Disease (conference)
- **CTB** – Cognitive Test Battery of computerized tests
- **Double-blind** – Investigators, participants and company do not know who has active vs placebo treatment during a trial
- **EMA** – European Medicines Agency
- **FDA** – US Food & Drug Administration
- **Filamen A** – A protein believed to relate to amyloid toxicity
- **GFAP** – Glial Fibrillary Acidic Protein – a marker of microglial cell activation in the brain
- **IDSST** – International Digit Symbol Substitution Test of cognition

Selected Glossary 2

- **IQCODE** – Informant Questionnaire on Cognitive Decline in the Elderly
- **MCI** – Mild Cognitive Impairment – memory, executive function deterioration with retained functional abilities
- **MDD** – Major Depressive Disorder
- **MMSE** – Mini Mental State Examination – a 30-point scale of simple questions to assess mental abilities
- **NfL** – Neurofilament Light – a nerve protein in the brain and rest of the body too
- **NIA-AA** – National Institutes of Aging and Alzheimer’s Association
- **NMDA** – A type of receptor for glutamate in the brain
- **NPI** – Neuropsychiatric Inventory to assess psychiatric symptoms
- **NTB** – A Neurologic Test Battery, in this presentation one designed to measure executive function aspects of cognition
- **PET** – Positron Emission Tomography – a type of body scan
- **Placebo controlled** – Non-active treatment for double-blind design
- **p-Tau181 or 217 AD** – Biomarker of phosphorylated Tau protein
- **QPCT** – Glutaminyl-peptide cyclotransferase is an enzyme proposed to create toxic amyloid species
- **RAVLT** – Rey Auditory Visual Learning Test
- **RBANS** – Repeatable Battery for the Assessment of Neuropsychological Status (a test of mental abilities)
- **ROC AUC** – Receiver Operating Curve Area Under the Curve (1.0 ideal) – a type of statistical test to compared two methods of measurement
- **SSRI** – selective serotonin reuptake inhibitor
- **Tau** – A brain protein
- **Ttau** – Total tau levels including both phosphorylated and non-phosphorylated tau

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