



Advancing oral Xanamem® in Alzheimer's disease

XanaMIA Phase 2b/3 pivotal trial final participant visit complete

Topline Alzheimer's data November 2026

Potentially game-changing product profile in CNS diseases

Corporate Presentation

October 2026

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Corporate and Xanamem highlights



Potentially game-changing oral therapy for CNS diseases in late-stage trials



Validated 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

Pivotal Alzheimer's results
November 2026



Biomarker-enriched pivotal trial with independent validation

- XanaMIA phase 2b/3 pivotal trial (n=247) completed its final participant visit; open-label extension commenced; topline results remain on track for 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 beyond late 2027
- Resources focused on execution of the XanaMIA trial and preparation for 2027

Experienced leadership

Proven experience in clinical development, manufacturing, regulatory & commercialization

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Chairman
MBBS; MBA



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VP Clinical Operations
RN, M Health Law



Fujun Li
Head of Manufacturing
PhD



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



Positioned to meet a huge unmet medical need in Alzheimer's disease

Strong physician interest and demand for Xanamem

Global Alzheimer's therapeutic market expected to exceed US\$20B by 2030

Quantitative survey of 91 U.S. neurologists treating Alzheimer's disease (June 2025)

Respondents each manage ~250 AD patients on average

Rapid adoption expected

~80% expect to prescribe within 6 months

- 13% within first month
- 41% within three months

Early uptake anticipated among high-volume AD prescribers

Significant market share potential

~50% projected peak share

- 43% estimate 31–50% peak share
- 14% estimate >50% peak share

Broad eligibility supports substantial utilization

Expected role in management

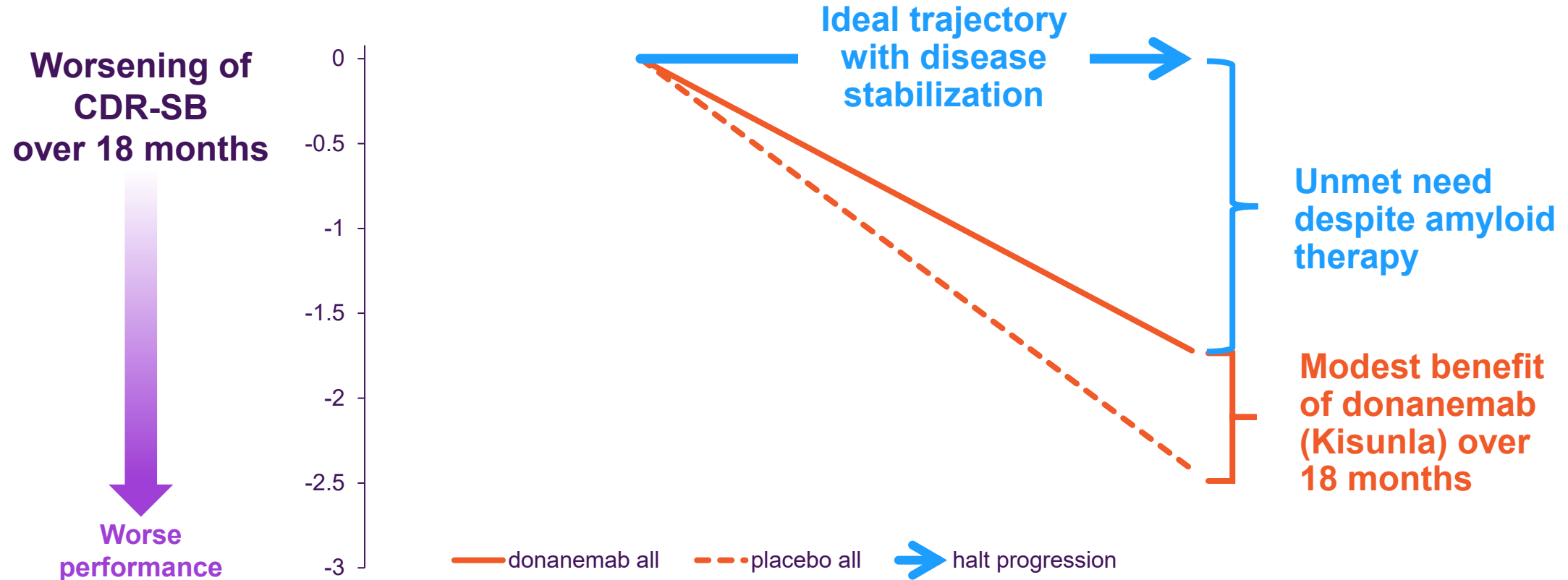
92% anticipate leading / definite role

- 30% expect top-two agent
- 0% indicate no role

Oral profile and safety drive enthusiasm

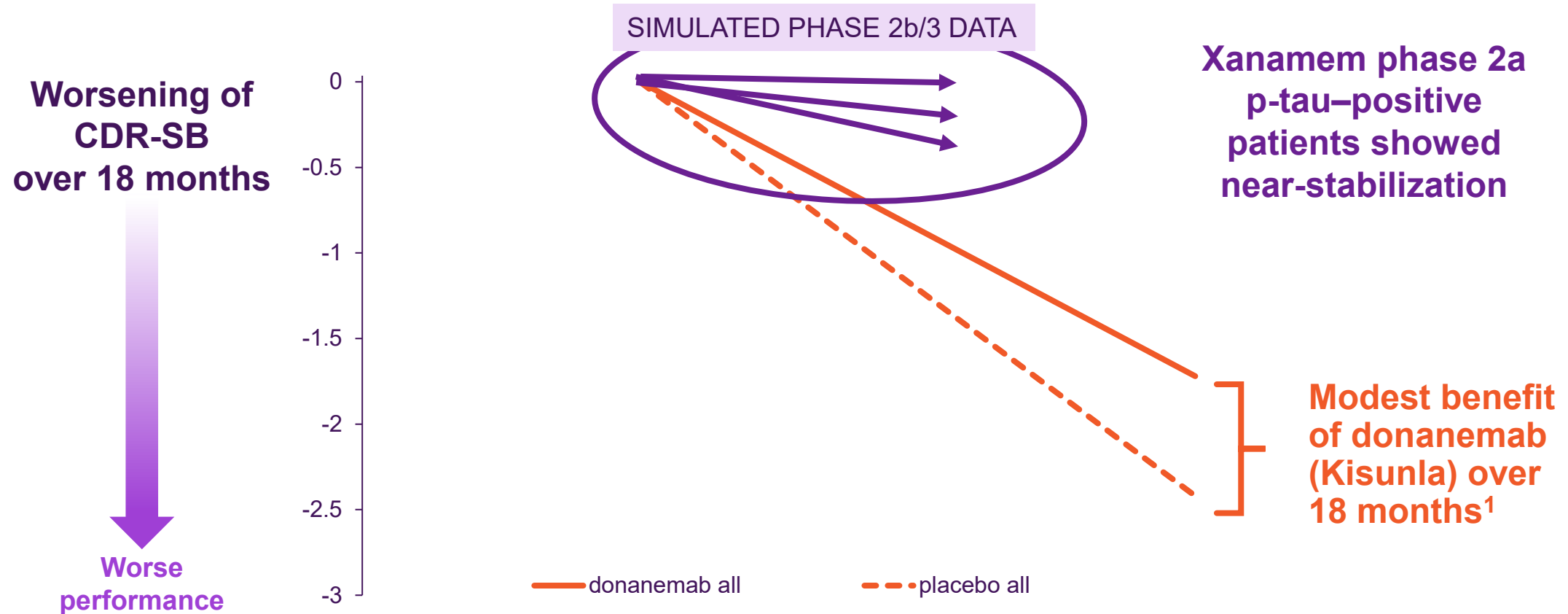
Anti-amyloid therapies only modestly slow decline

Disease stabilization represents an important therapeutic aspiration



Additional therapeutic mechanisms remain an important area of investigation

Potential for greater magnitude of effect on CDR-SB



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

Recent milestones



Positive interim safety, efficacy futility reviews

Independent Data Monitoring Committee chaired by expert Dr Hans Moebius

Recommendation:

- Jan 2026 “non-futile” recommendation to continue the XanaMIA trial without modification
- Jun 2026 positive safety review without futility assessment

Formal interim review process in January:

- The Committee was not authorized to recommend early stopping for efficacy in order to preserve the trial’s statistical integrity and alpha
- The Committee confidentially reviewed treatment group data on:
 - ✓ Safety data from all enrolled participants (n=247)
 - ✓ Approximately 37% of the expected final dataset across scheduled timepoints including 52 participants with Week 36 (end of treatment) data

Independent DMC reviews deliver positive continuation decisions, clearing safety and futility criteria ahead of November 2026 topline results

Open-label extension commenced March 2026

Long-term safety and efficacy durability extension to Phase 2b/3



Design

- All participants offered active Xanamem 10mg after completion of double-blind phase
- Initiated March 2026 with high initial enrolment (>80% continuation from main trial)

Data contribution

- Some data available in November this year
- ≥ 14 months additional safety exposure
- Longitudinal assessment of CDR-SB, cognition, and activities of daily living
- Observational comparison of early vs delayed treatment initiation
- Potential to show durability of benefit

Strategic impact

- Expands cumulative safety database
- Supports regulatory engagement
- Informs durability of clinical effect

Clear regulatory pathway to approval in US and EU

Regulatory guidance from FDA & EMA supports streamlined late-stage development



Current trial

- XanaMIA pivotal trial (n=247) expected to form key part of registrational package
- Open-label phase has commenced with high uptake from main trial participants

Regulatory engagement

- FDA guidance September 2025, EMA May 2026
- Both aligned on clinical, manufacturing and ancillary studies

Remaining clinical requirements

- One additional single-dose phase 3 trial (10 mg vs placebo) required¹
- Open-label safety trials
- Limited number of clinical pharmacology and nonclinical studies

1. FDA and EMA may accept a single pivotal trial plus adequate supportive evidence for approvals under certain circumstances

Commercial and partnering positioning



Structural Limitations of Anti-Amyloid

Infusion burden, ARIA risk, and cost limit broad adoption

Differentiated Oral Profile

Xanamem is positioned with a favorable risk-benefit and ease-of-use profile

Potential for Meaningful Stabilization

Targeting elevated brain cortisol may enable functional impact beyond modest slowing

XanaMIA as a Value Catalyst

Phase 2b/3 readout is positioned to accelerate commercial and strategic partnering activity

Positioned for clinical success

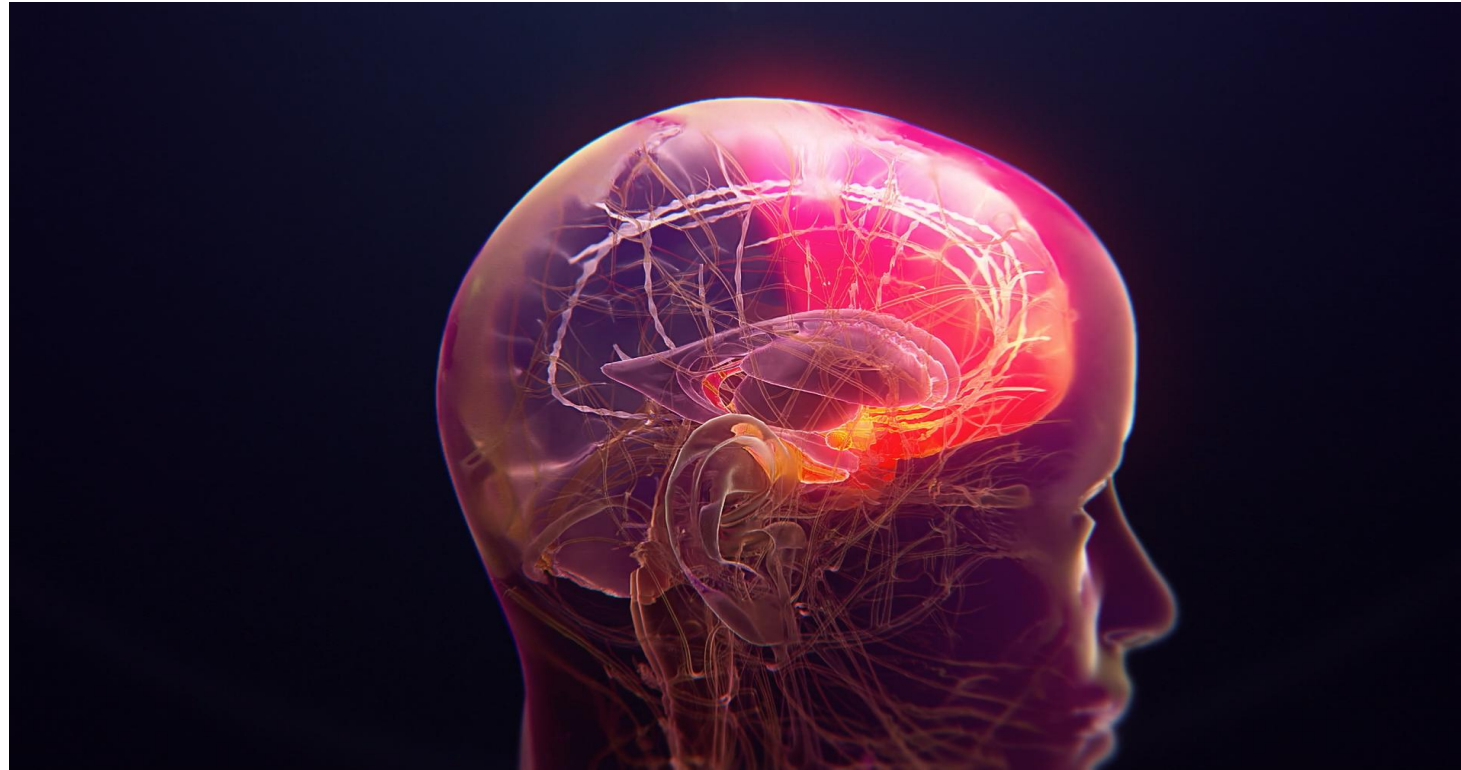


Targeting elevated brain cortisol in Alzheimer's disease



Xanomem selectively inhibits brain 11 β -HSD1 while preserving adrenal cortisol function

Elevated brain cortisol is associated with cognitive decline and neurodegeneration

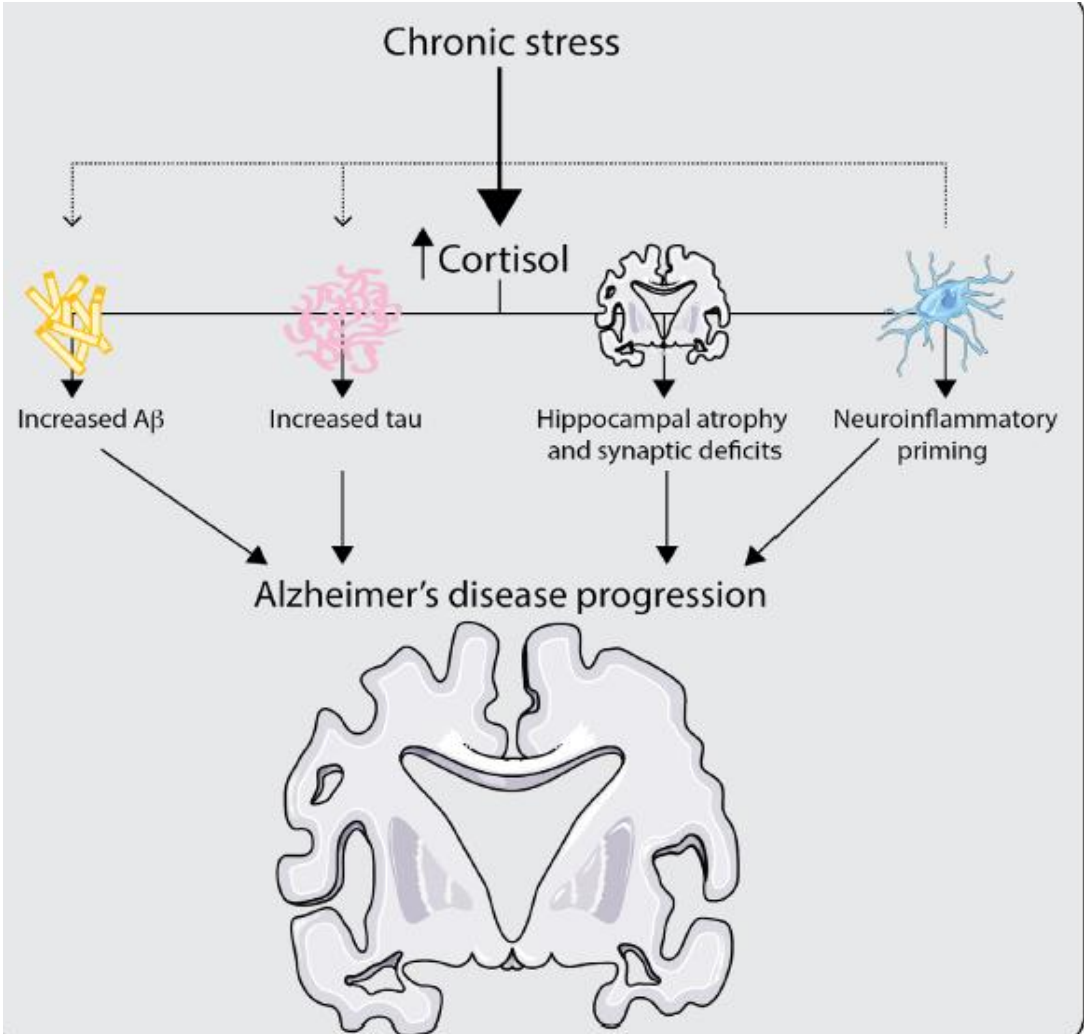
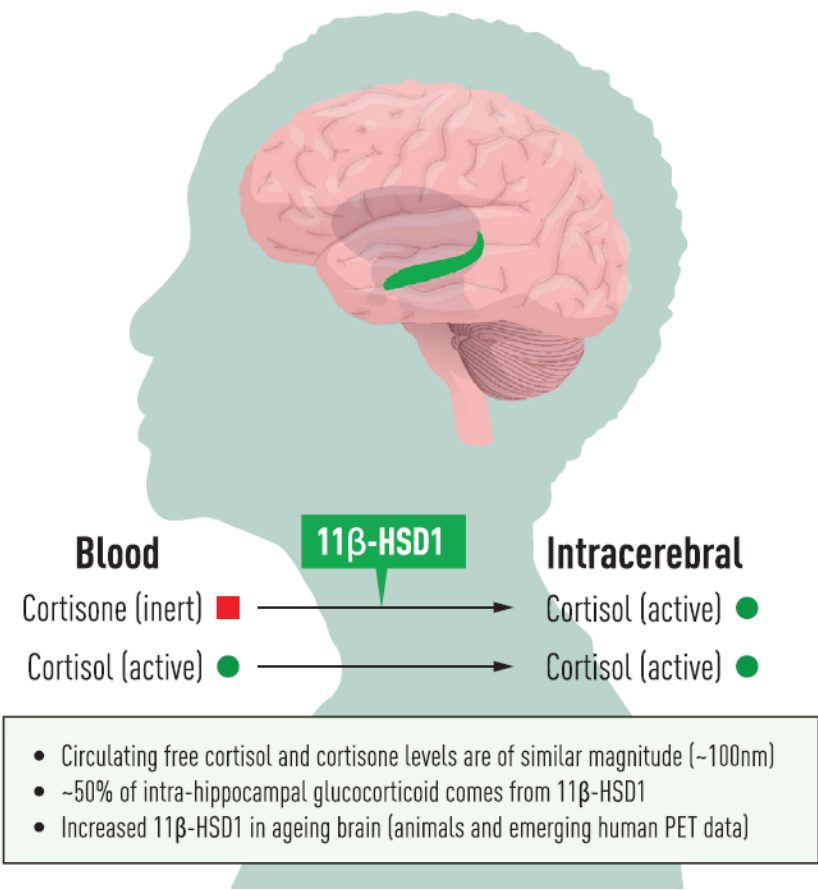


[Watch MOA
animation](#)

Cortisol and the Alzheimer's brain



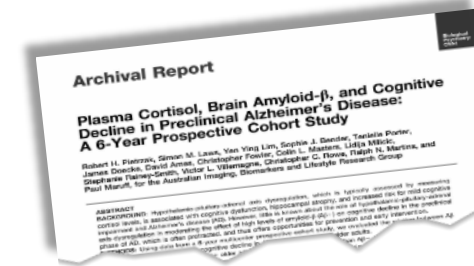
“Stress” and/or genetic factors may drive multiple AD mechanisms via cortisol



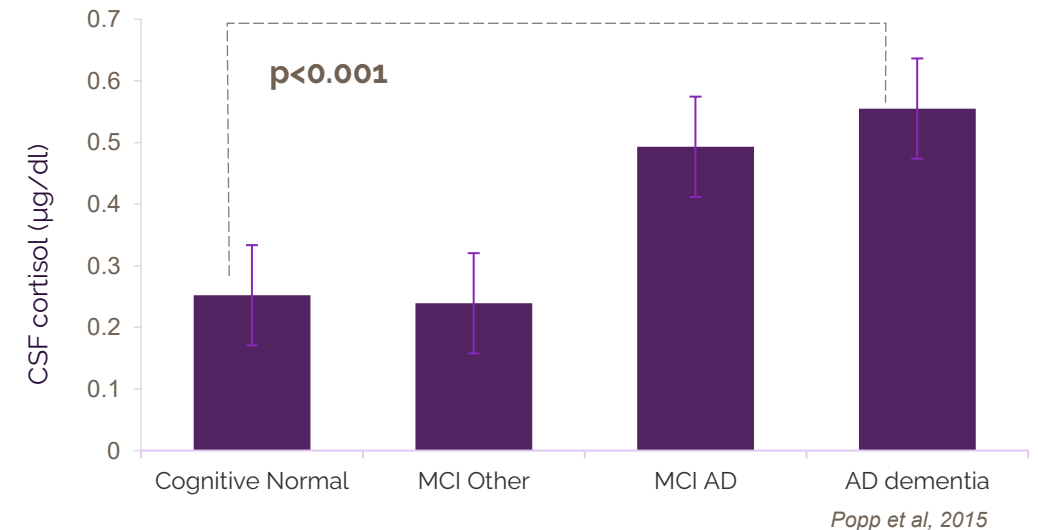
Elevated brain cortisol and Alzheimer's progression

Human observational and biomarker data support cortisol as a disease driver

- Higher plasma cortisol associated with increased AD risk (AIBL study)
- Cortisol accelerates cognitive decline and interacts with A β pathology
- APOE- ϵ 4 carriers exhibit higher CSF cortisol levels
- Elevated CSF cortisol correlates with more rapid clinical worsening

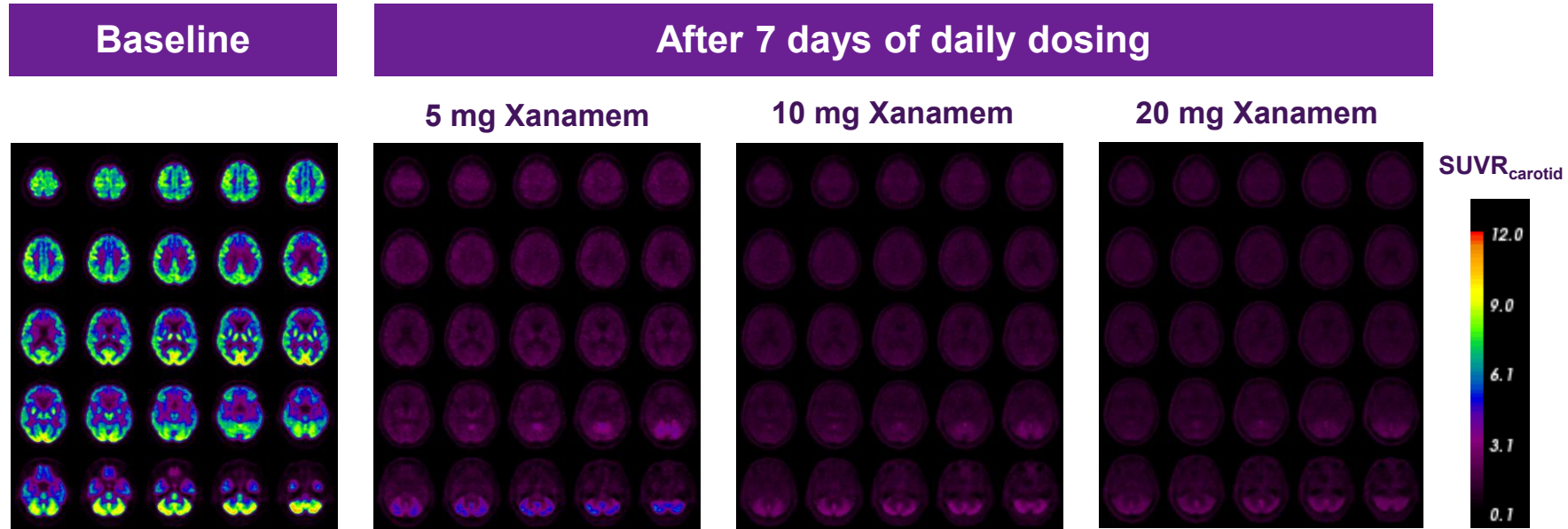


MEAN CSF CORTISOL LEVELS



Xanamem achieves high brain target occupancy

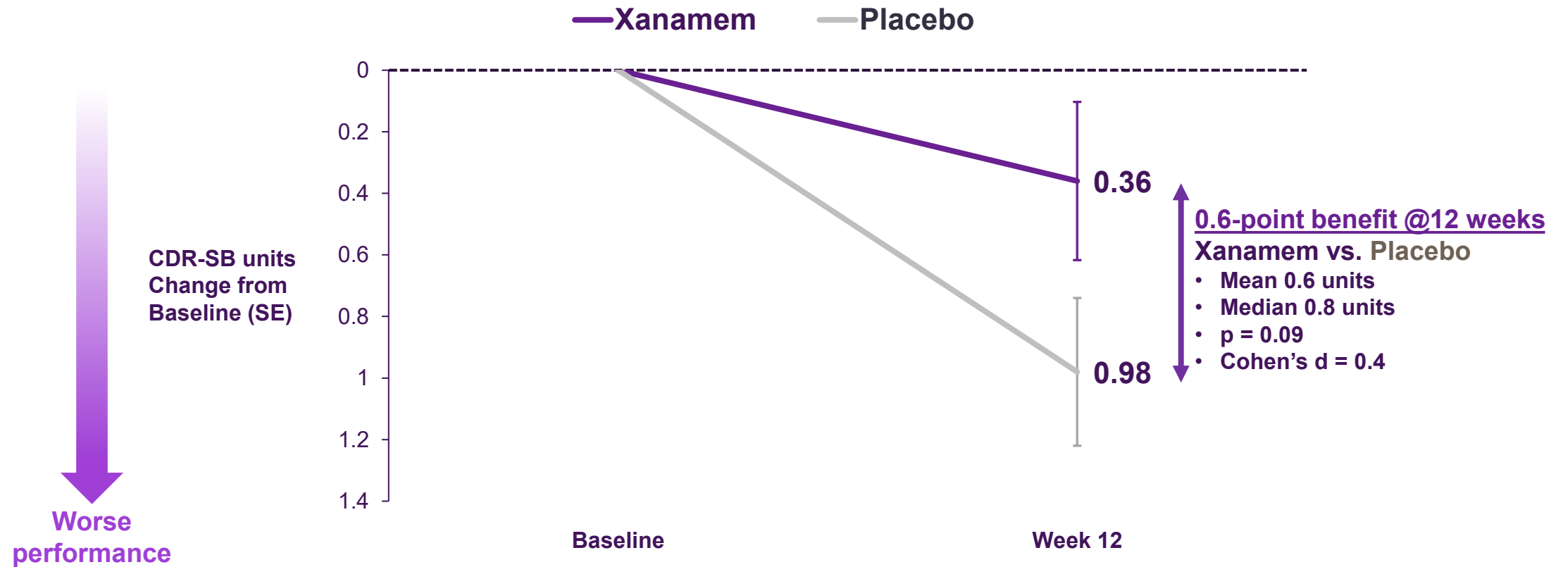
Human PET imaging confirms brain 11 β -HSD1 engagement



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

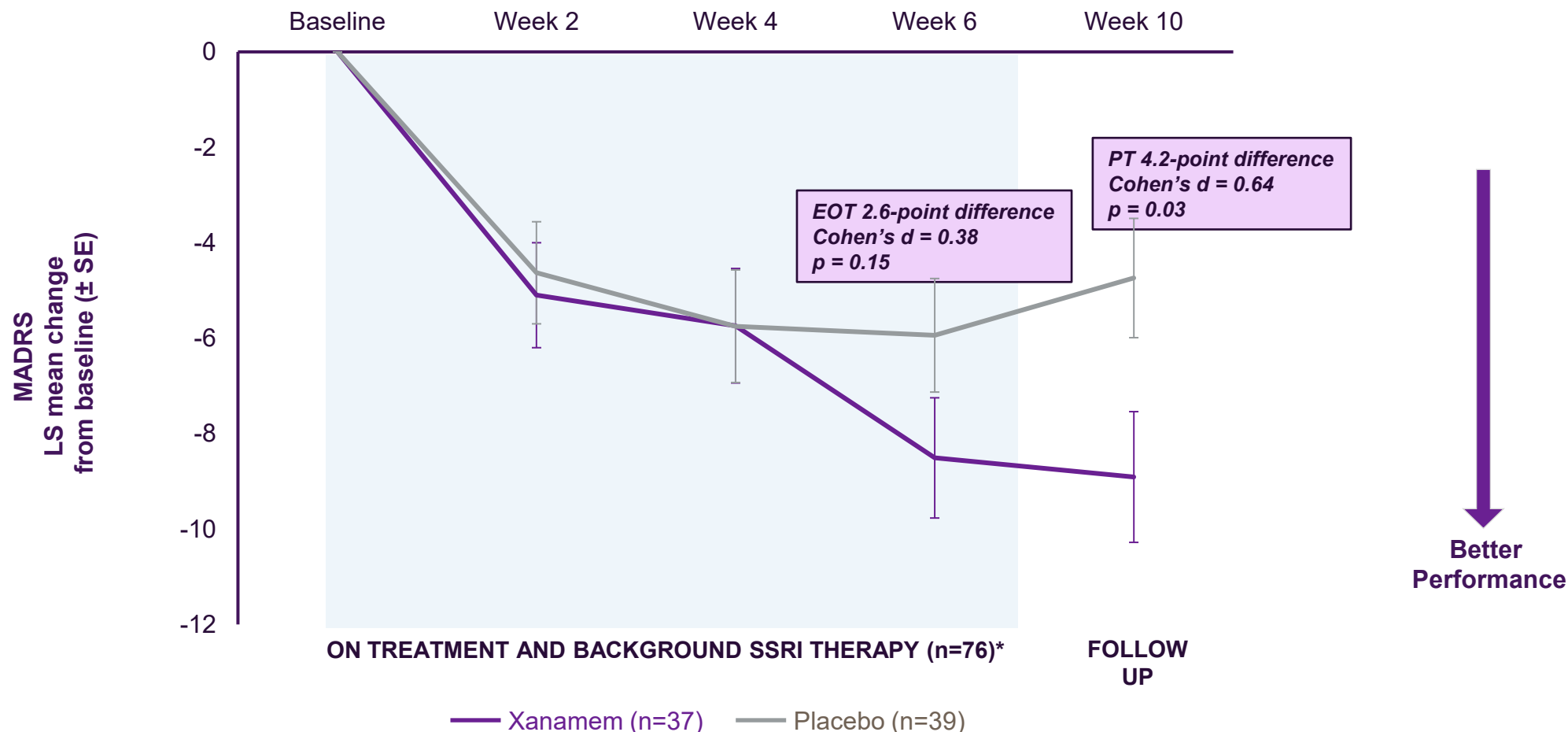
CDR-SB slowed in pTau-positive Alzheimer's

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



Durable activity in phase 2 depression trial

10 mg demonstrated separation from placebo overall and on background SSRI therapy



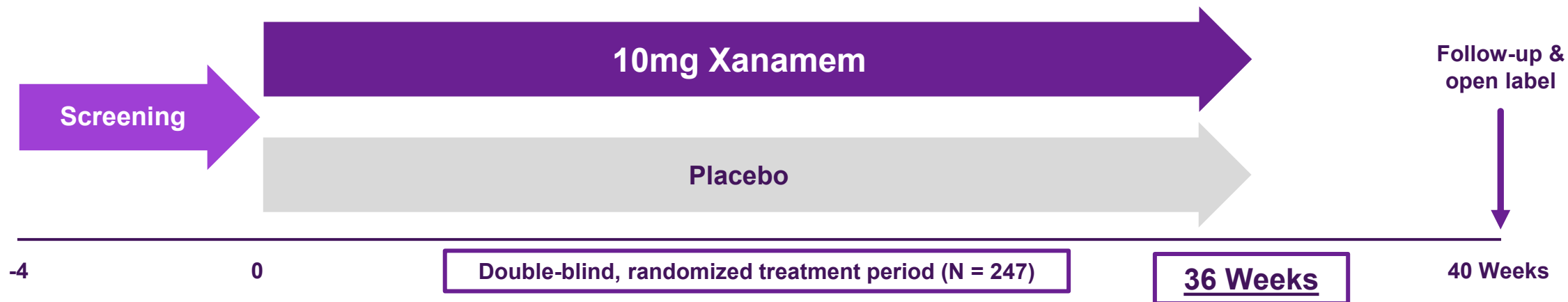
Abbreviations: SSRI, selective serotonin reuptake inhibitor.

*Planned phase 3 population

Taylor et al., 2026, *The British Journal of Psychiatry* doi:10.1192/bjp.2026.10689

Rigorous pivotal trial positioned for success

Fully enrolled (n=247) across U.S. and Australia; topline results November 2026



Population	Primary Endpoint	Key Secondary Endpoints	Execution
- Blood pTau biomarker positive - Mild-moderate AD (NIA-AA criteria)	CDR-SB at 36 weeks (functional and cognitive measure)	- Cognitive Test Battery - Amsterdam Activity of Daily Living	Final participant visit completed (n=247) - Independent DMC interim review recommended trial continuation - Open-label ext. commenced Topline results November 2026

Well-established safety, industry-standard endpoints



Safety

- Well-tolerated across clinical program
- No serious adverse events related to Xanamem reported to date (n ~ 500)¹
- No ARIA adverse events observed

XanaMIA endpoints

- CDR-SB at 36 weeks is primary endpoint
- Cognition (validated cognitive measures)
- “Amsterdam” activities of daily living instrument (functional measures)

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 [Actinogen – Xanamem® \(emestedastat\)/](#))

Phase 2b/3 summary and rationale for success

Clear Biological Rationale

Elevated brain cortisol implicated in cognitive decline and neuronal injury

Demonstrated Brain Target Engagement

High 11β -HSD1 occupancy confirmed by human PET imaging

Clinical Signal in Enriched Alzheimer's Population

CDR-SB slowing in pTau positive patients over 12 weeks

Consistent CNS Activity Across Indications

Durable separation from placebo in Phase 2 depression trial

Rigorous, Fully Enrolled Pivotal Trial

247 patients; interim continuation; November 2026 readout

Summary



XanaMIA trial positioned as a game-changer

Pivotal Alzheimer's data from a well-designed 36-week trial due in November



- **Unique and novel cortisol control mechanism with strong scientific rationale**
- **Biomarker-enriched population with mild-to-moderate AD, CDR-SB primary endpoint**
 - ✓ Final participant visit completed in the 247-participant trial
 - ✓ Positive interim analysis Jan 2026 followed by positive June safety review
 - ✓ Topline results expected Nov 2026
 - ✓ Structured as a registrational trial aligned with FDA & EMA guidance
- **Executing on streamlined development path for Alzheimer's disease**
 - ✓ Open-label extension XanaMIA trial phase opened in March 2026
 - ✓ Next pivotal trial in planning - to commence mid 2027
 - ✓ Manufacturing and pre-commercialization activities on-track
 - ✓ Ancillary clinical pharmacology and nonclinical studies to start in 2027

Commercial and strategic strength ahead of readout



Leadership, market validation, lifecycle protection, and financial readiness



- **Experienced leadership team with proven track records across development, approval, commercialization, and strategic transactions**
- **Strong physician demand across ~100 U.S. Alzheimer's specialists**
 - ✓ ~80% indicate intent to prescribe within first 6 months of launch
- **Composition of matter protection to at least 2036 in most markets¹**
 - ✓ Additional patents extend protection into the 2040s
 - ✓ Regulatory data exclusivity of at least 5 to 6 years from marketing approval dates provided additional protection from generic competition in major markets
- **Increasing strategic interest and engagement as results approach**
- **Funded well beyond November 2026 topline Alzheimer's readout**
- **Anti-depressant activity** a good feature for Alzheimer's prescribing information

1. Patent protection extensions for the initial composition of matter patent (2031) of between 5 and 10 years apply in nearly all countries

Appendix



2026 catalysts leading to November Alzheimer's results

Milestone	Likely Timing
Positive interim analysis XanaMIA AD trial of all available data (weeks 12, 24 & 36)	Completed
XanaMIA AD open-label extension (OLE) commences & reports initial enrolment data	Completed
EMA Scientific Advice meeting for AD	Completed
Third Independent Data Monitoring Committee safety review	Completed
XanaCIDD MDD peer-reviewed journal publication	Completed
AAIC AD conference in London – BD and KOL meetings	Completed
Bioshares conference Queenstown, NZ	Completed
Clinical Trials Science Forum – the future of Alzheimer's treatment	Completed
Last participant assessment visit in XanaMIA pivotal trial	Completed
Final topline results, XanaMIA pivotal AD trial	Nov 2026
Topline results presentation at major AD scientific meeting	TBD

AD treatment landscape: meaningful limitations persist



Recent advances have not eliminated meaningful clinical and practical barriers

Mechanistic	Admin	Comments
Older drugs - boosting acetylcholine or glutamate	Oral	• Symptomatic benefit only • Gastrointestinal tolerability limitations
Anti-amyloid protein immunotherapies	IV/SubQ	• Modest slowing of decline • ARIA risk and MRI monitoring; variable reimbursement
Second-gen anti-amyloid with “brain shuttle”	IV/SubQ	• Late-stage trials aimed to improve ARIA risk
Xanamem (emestedastat) control of elevated brain cortisol	Oral	• Phase 2b/3 pivotal trial (n=247) • Oral, once-daily; no ARIA observed • Combination-compatible
Blarcamesine SIGMAR1 antagonist to block autophagy	Oral	• Phase 2b/3 trial; EMA rejection • CNS tolerability concerns reported
Anti-amyloid formation or toxicity	Oral	• High historic attrition • Subgroup strategies under evaluation
Anti-tau protein immunotherapy	IV/SubQ	• Multiple trial failures to date • Development ongoing
PDE-5 inhibitor (AriBio/Fosun)	Oral	• Failed phase 2, now phase 3 in different population with different endpoints, due to read out Q4 2026

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