



Advancing Xanamem[®] in Alzheimer's Disease

Fully enrolled phase 2b/3 study | Topline data November 2026

Independent DMC recommended study continue unchanged (January 2026)

Corporate Presentation

March 2026

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Corporate summary and investment highlights



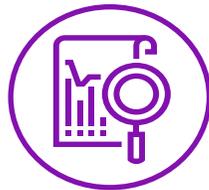
Independent interim validation achieved | Topline phase 2b/3 results November 2026



Validated mechanism with differentiated oral profile

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

NEXT MAJOR VALUE INFLECTION
Phase 2b/3 topline results
November 2026



Biomarker-enriched pivotal trial with independent validation

- Phase 2b/3 XanaMIA study (n=247) fully enrolled; topline results expected November 2026
- January 2026 independent Data Monitoring Committee recommended the study continue unchanged following unblinded interim review



Regulatory pathway to NDA submission

- Current phase 2b/3 study expected to form part of registrational package
- FDA agreement on streamlined pathway to NDA approval with only one additional pivotal trial and standard 1500-person safety database – EMA scientific advice pending



Strong capital position

- Company funded beyond November 2026 topline readout
- Resources focused on execution of the Phase 2b/3 XanaMIA trial and preparation for 2027

Experienced Leadership

Proven experience in clinical development, manufacturing, regulatory & commercialization

Board of Directors



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MBBS; MBA



Dr. Steven Gourlay
CEO & Managing Director
MBBS; FRACP; PhD; MBA



Mr. Malcolm McComas
Non-Executive Director
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Dr. Nicki Vasquez
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PhD



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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 Comms
B.Ec (Hons), CPA, FFIN



Independent interim review: trial continues unchanged



Interim safety and futility review (January 27, 2026)

Recommendation:

- Continue the XanaMIA trial without modification

Interim review process:

- Independent Data Monitoring Committee chaired by Alzheimer's disease trials expert Dr Hans Moebius
- The Committee was not authorized to recommend early stopping for efficacy in order to preserve the trial's statistical integrity
- The Committee confidentially reviewed treatment group data on:
 - ✓ Safety data from all enrolled participants (n=247)
 - ✓ Interim efficacy data representing approximately 37% of the expected final dataset across scheduled timepoints including 52 participants with Week 36 (end of treatment) data

**Independent interim review delivers a positive continuation decision,
clearing safety and futility criteria ahead of November 2026 topline results**

Xanamem: Well defined path to U.S. approval

FDA alignment confirms streamlined late-stage development pathway



Current study

- Phase 2b/3 XanaMIA study (n=247) expected to form part of registrational package

Remaining clinical requirements

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

Regulatory engagement

- FDA alignment achieved September 2025
- Clear guidance on clinical, manufacturing and ancillary studies
- EMA scientific advice scheduled Q2 2026

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

Strong physician interest and demand for Xanamem



Global Alzheimer's therapeutic market expected to exceed \$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

Leading role in management

- 92%** anticipate leading role
- 30% expect top-two agent
 - 0% indicate no role

Oral profile and safety drive enthusiasm

Xanamem positioning in Alzheimer's disease

Oral profile and safety address key limitations of existing therapies

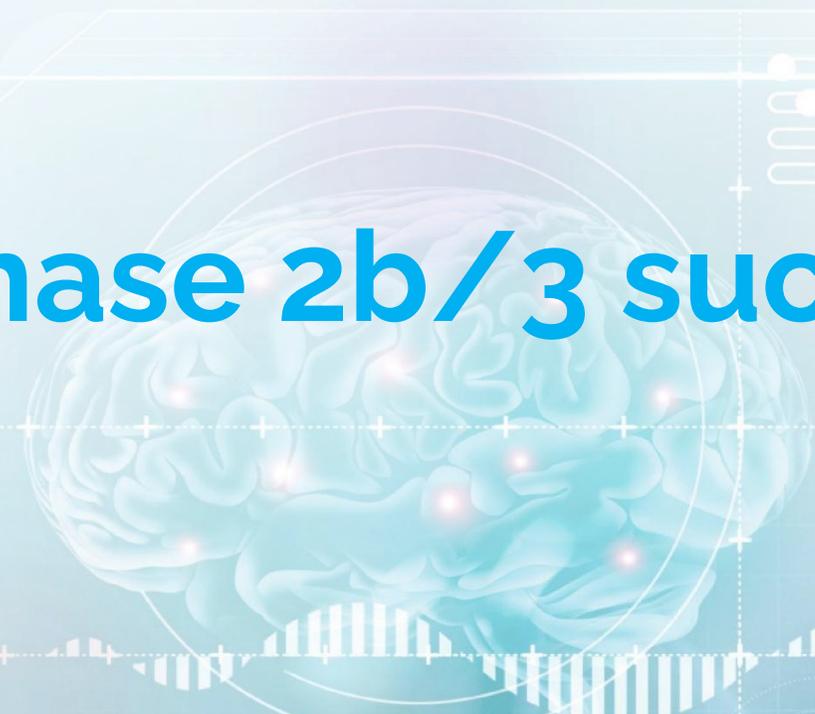
Current therapy limitations

- Anti-amyloid injectables require infusions and extensive MRI monitoring
- ARIA (brain swelling) risk concerns
- Focus on very early AD/MCI
- Administration complexity constrains uptake
- Existing oral therapies offer limited efficacy

Xanamem differentiation

- Once-daily oral therapy
- No ARIA risk observed to date. No MRI monitoring
- Broad eligibility across mild to moderate AD
- Combination-friendly with other treatments
- Viewed as potential first-line therapy

Positioned for phase 2b/3 success



Targeting elevated brain cortisol in Alzheimer's disease



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

Elevated brain cortisol is associated with cognitive decline and neurodegeneration

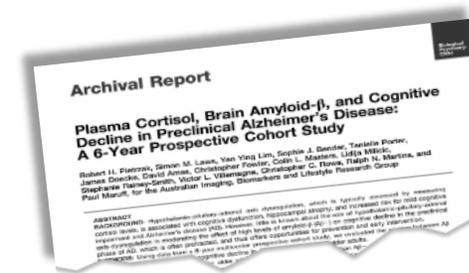


[Watch MOA animation](#)

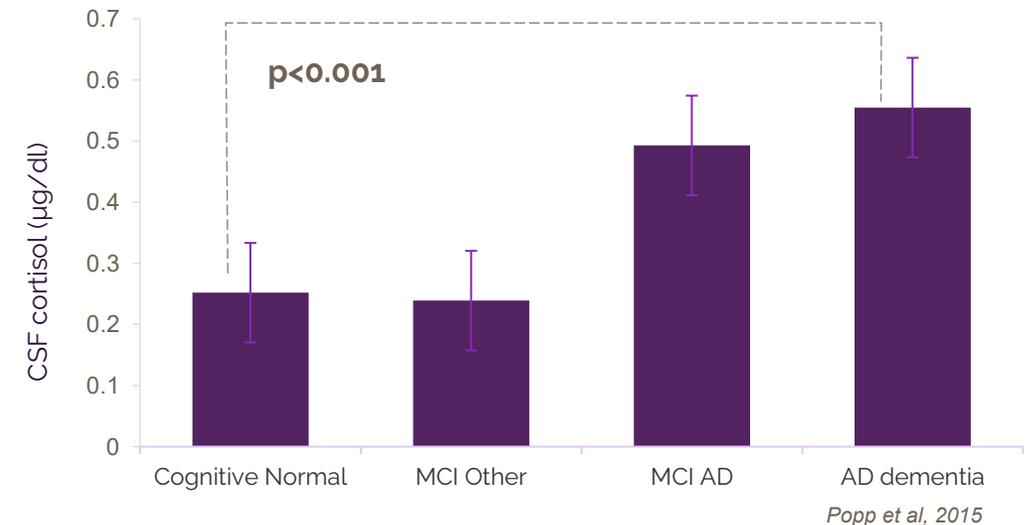
Elevated brain cortisol and Alzheimer's progression

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

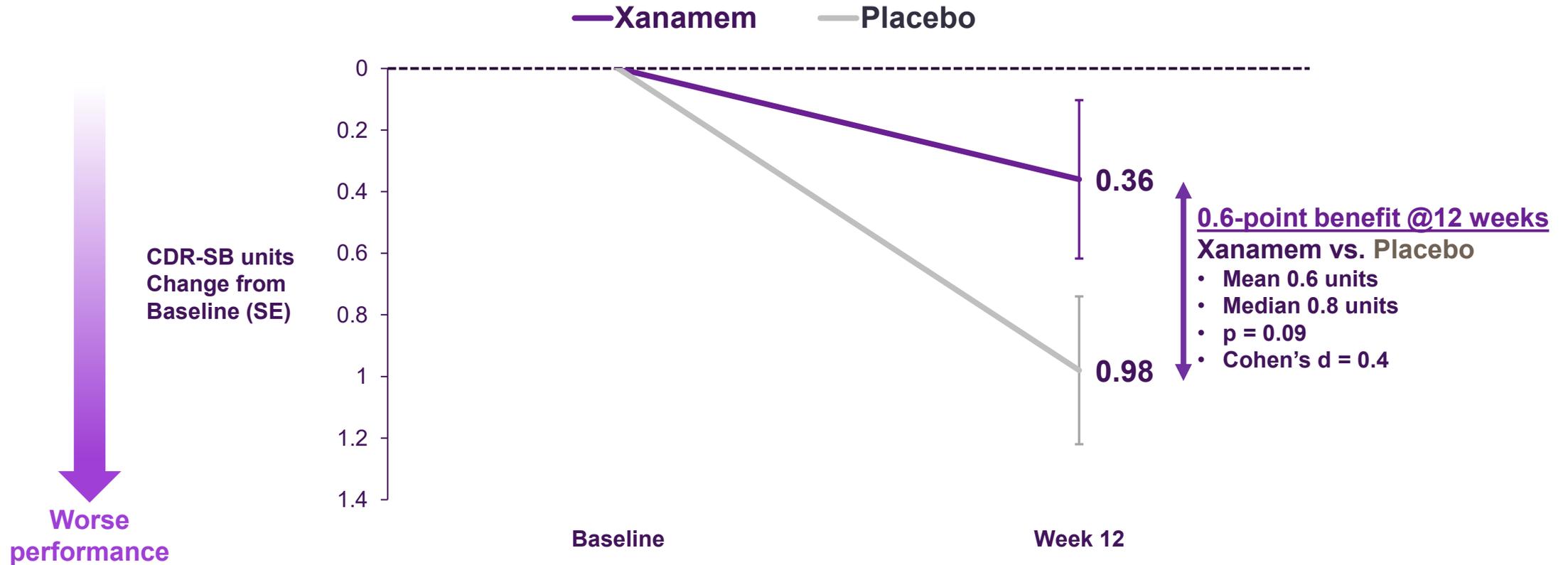


MEAN CSF CORTISOL LEVELS



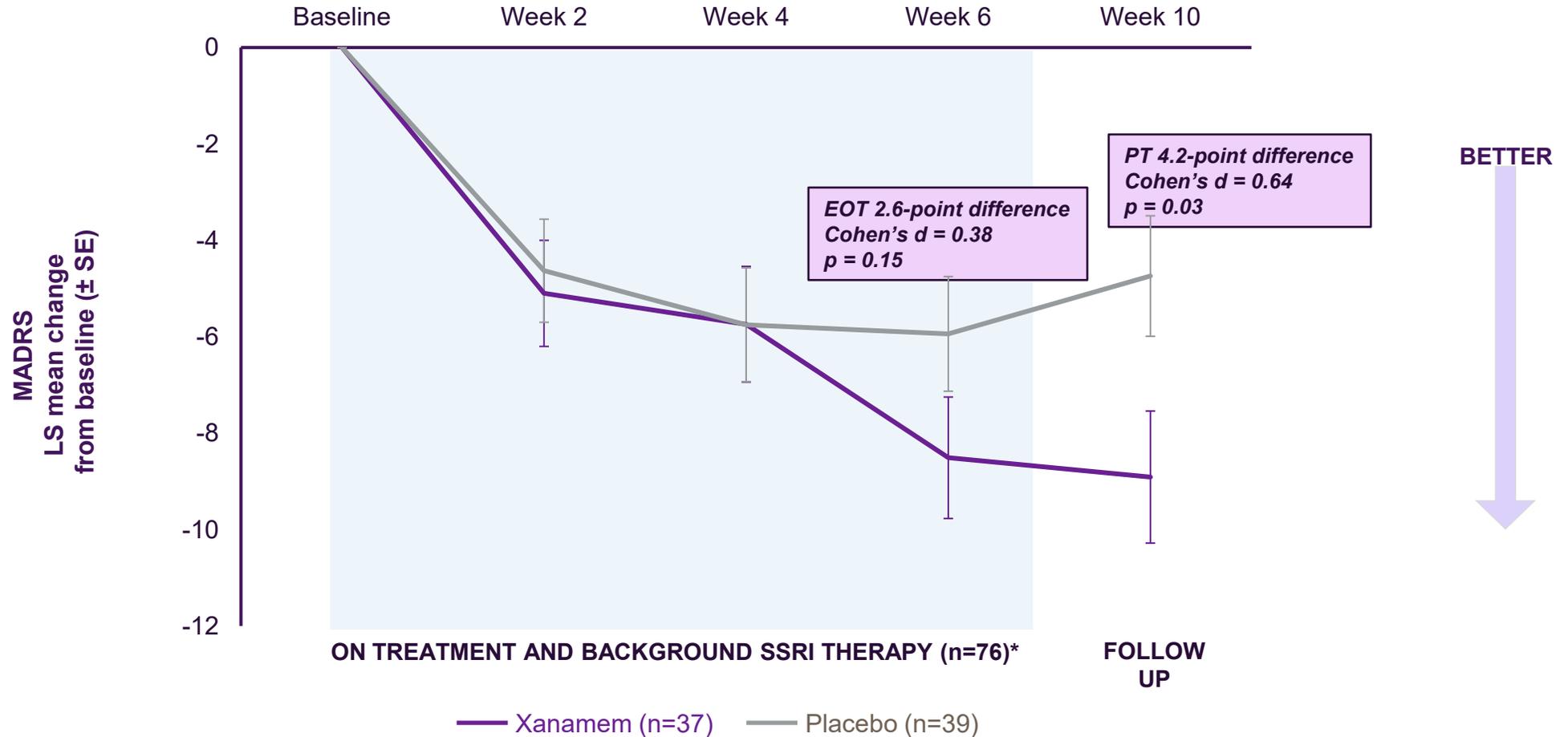
Xanamem: CDR-SB slowed in pTau-positive Alzheimer's

Phase 2a study showed slowing of decline over 12 weeks (n=34)



Durable activity in phase 2 depression study

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

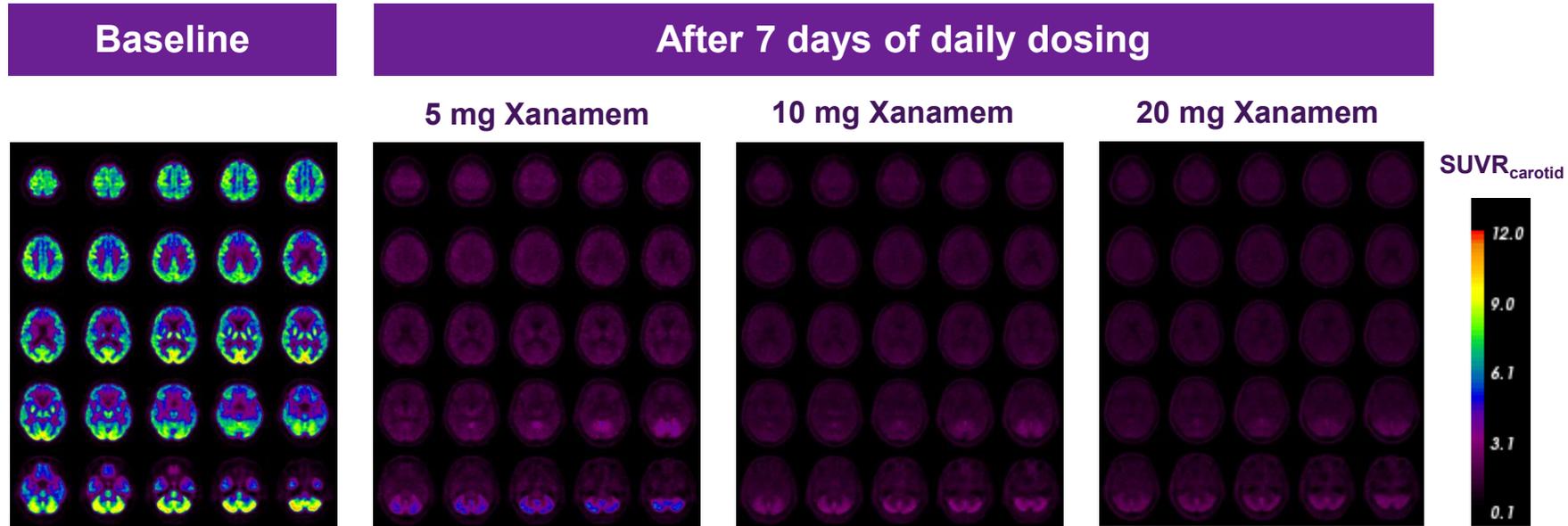


Abbreviations: SSRI, selective serotonin reuptake inhibitor.

*Planned phase 3 population

Xanamem achieves high brain target occupancy

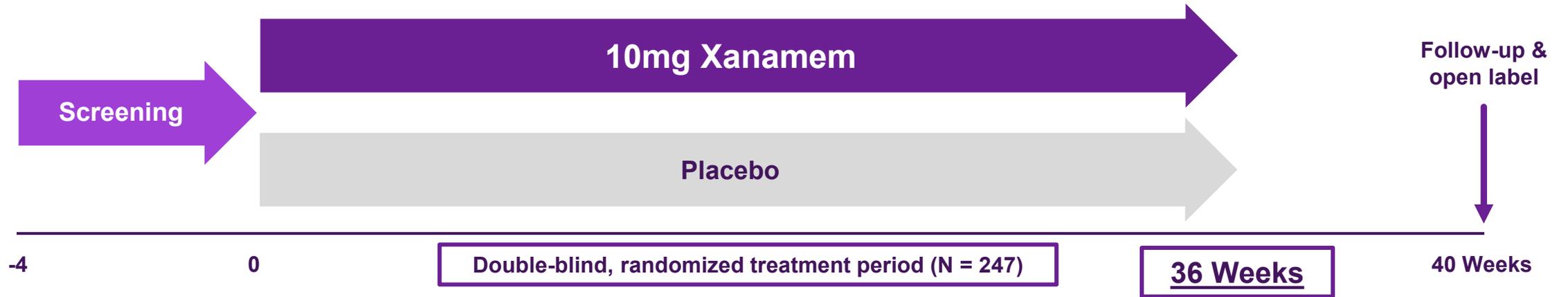
Human PET imaging confirms brain 11 β -HSD1 engagement



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

Rigorous phase 2b/3 trial positioned for success

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



Population	Primary Endpoint	Key Secondary Endpoints	Execution
<ul style="list-style-type: none"> Blood pTau biomarker positive Mild-moderate AD (NIA-AA criteria) 	<ul style="list-style-type: none"> CDR-SB at 36 weeks (functional and cognitive measure) 	<ul style="list-style-type: none"> Cognitive Test Battery Amsterdam Activity of Daily Living 	<ul style="list-style-type: none"> Fully enrolled (n=247) Independent DMC interim review recommended trial continuation Topline results November 2026

Open-label extension enhances long-term dataset

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 Q1 2026

Data contribution

- ≥ 12 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

Summary: positioned for phase 2b/3 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 study

Rigorous, Fully Enrolled Phase 2b/3 Trial

247 patients; interim continuation; November 2026 readout

Strategic implications for commercialization and partnering



AD treatment landscape: meaningful limitations persist

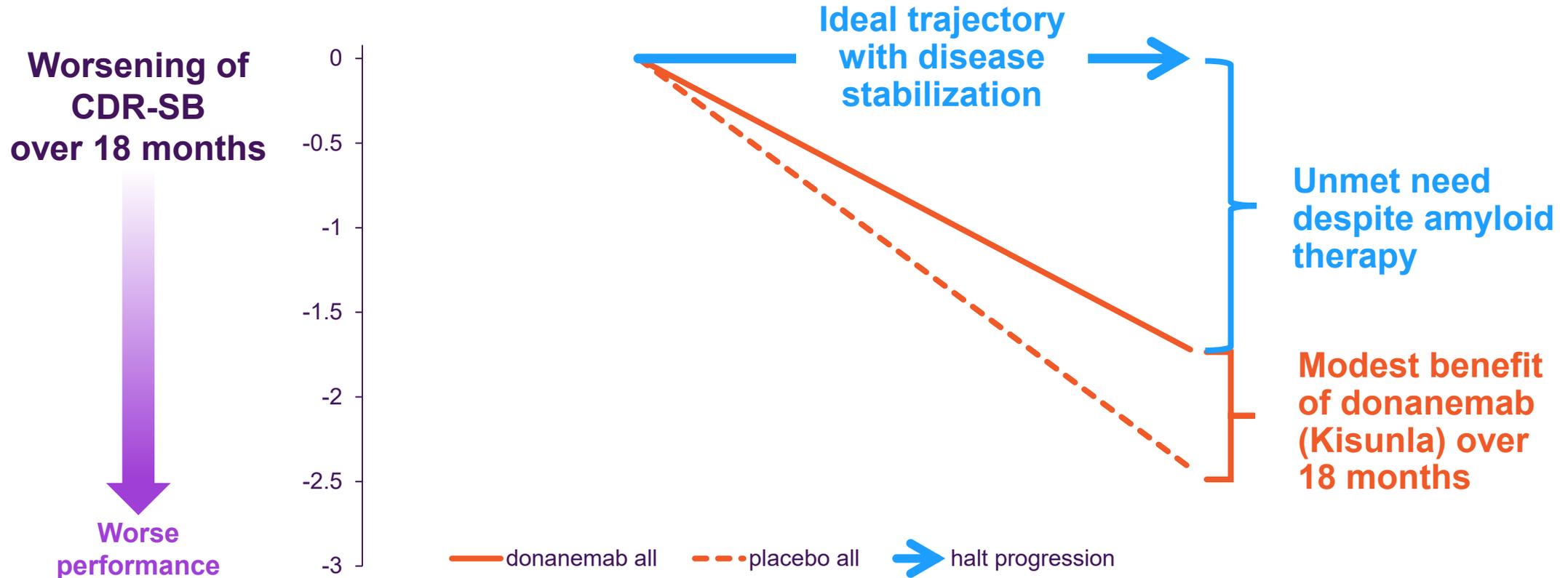


Recent advances have not eliminated meaningful clinical and practical barriers

Mechanistic	Admin	Comments
Older drugs - boosting acetylcholine or glutamate	Oral	<ul style="list-style-type: none"> • Symptomatic benefit only • Gastrointestinal tolerability limitations
Anti-amyloid protein immunotherapies	IV/SubQ	<ul style="list-style-type: none"> • Modest slowing of decline • ARIA risk and MRI monitoring; variable reimbursement
Second-gen anti-amyloid with “brain shuttle”	IV/SubQ	<ul style="list-style-type: none"> • Late-stage trials aimed at improved vascular safety
Xanomem (emestedastat) control of elevated brain cortisol	Oral	<ul style="list-style-type: none"> • Phase 2b/3 pivotal trial (n=247) • Oral, once-daily; no ARIA observed • Combination-compatible
Blarcamesine SIGMAR1 antagonist to block autophagy	Oral	<ul style="list-style-type: none"> • Phase 2b/3 trial; EMA rejection • CNS tolerability concerns reported
Anti-amyloid formation or toxicity	Oral	<ul style="list-style-type: none"> • High historic attrition • Subgroup strategies under evaluation
Anti-tau protein immunotherapy	IV/SubQ	<ul style="list-style-type: none"> • Multiple trial failures to date • Development ongoing

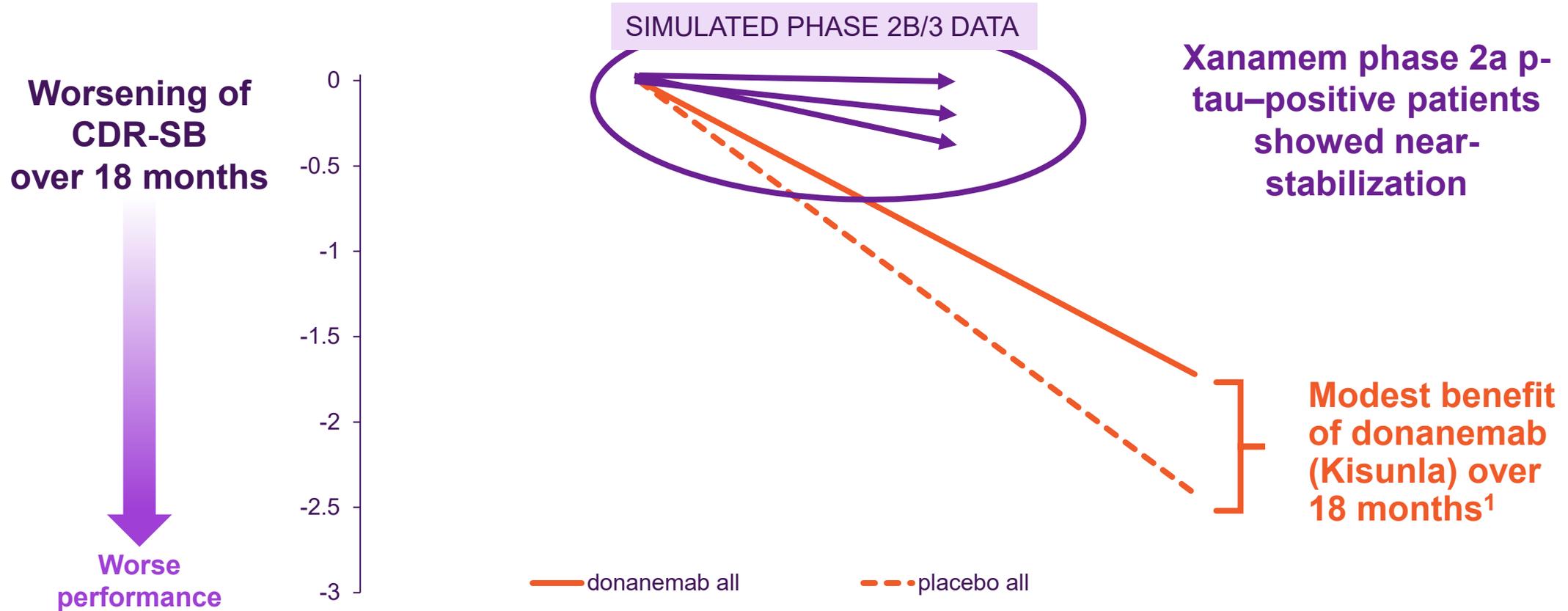
Anti-amyloid therapies modestly slow decline

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

Well-established safety and consistent benefit across key secondary measures



Safety

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

Key secondary endpoints

- Cognition (validated cognitive measures)
- Activities of daily living (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® \(emestedastat/\)](#))

XanaMIA as a near-term catalyst for commercial and partnering acceleration



Commercial opportunity drivers include:

- U.S. neurologists demonstrate strong interest and demand for a safe, effective oral option
- Anti-amyloid injectables face adoption constraints related to administration and monitoring
- Oral profile and safety enable broad patient eligibility
- Combination potential expands first-line and adjunct positioning flexibility

Strategic execution priorities include:

- Advancing selective regional partnerships where terms are favorable
- Phase 2b/3 data positioned to drive global partnering discussions
- Proactive engagement with regulators regarding potential expedited pathways

Summary: commercial and partnering implications



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

Summary



XanaMIA positioned as a registration catalyst

Operational execution and regulatory alignment ahead of pivotal Alzheimer's data



- **On-track with XanaMIA pivotal trial in patients with mild-to-moderate AD**
 - ✓ Full enrolment of 247 participants achieved
 - ✓ Positive interim analysis (Jan 2026); topline results expected Nov 2026
 - ✓ Structured as a registrational study aligned with FDA guidance
- **Executing on streamlined development path for Alzheimer's disease**
 - ✓ Open-label extension XanaMIA trial phase opens in March 2026
 - ✓ Next pivotal trial in planning - to commence in 2027
 - ✓ EMA scientific guidance due in Q2 to align with FDA guidance
 - ✓ Manufacturing and pre-commercialization activities on-track
 - ✓ Ancillary clinical pharmacology trials 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 2036 in most markets¹**
 - ✓ Additional patents extend protection into the 2040s
 - ✓ Regulatory data exclusivity of at least 5 years from marketing approval dates support protection from generic competition in most countries
- **Increasing strategic partnering engagement**
- **Funded beyond November 2026 topline readout**

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

Near-Term Catalysts Through XanaMIA Readout



Milestone	Likely Timing
Positive interim analysis XanaMIA AD trial of all available data (weeks 12, 24 & 36)	Completed
XanaCIDD MDD peer-reviewed journal publication	Q1/2 2026
XanaMIA AD open-label extension (OLE) commences	Q1 2026
ADPD AD conference in Copenhagen	Q1 2026
EMA Scientific Advice meeting for AD	Q2 2026
Clinical Trials Science Forum – streamlined regulatory pathways	Q2 2026
BIO conference in San Diego	Q2 2026
AAIC AD conference in London	Q3 2026
Last patient completes 36-week treatment, 4-week follow-up	Oct 2026
Final topline results, XanaMIA AD trial	Nov 2026
Topline results presentation at major AD scientific meeting	TBD

Contacts

Will Souter

CFO & Investor Relations

M: +61 402 035 716

E. will.souter@actinogen.com.au

Steven Gourlay

CEO & Managing Director

P: +61 2 8964 7401

E. steven.gourlay@actinogen.com.au

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