



**Phase 2-stage clinical company with near-term trial results
mid 2024 and 2025**

Easy-to-use oral therapy for dementia and depression
\$8.9 million placement and rights issue information

Corporate Presentation

6 May 2024

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Company Highlights



Positioned to achieve two major phase 2 milestones in next 15 months

1	Clinical-stage, advanced manufacturing	Xanamem® lowers brain cortisol and is in Phase 2 trials to treat patients with cognitive impairment associated with depression and Alzheimer's disease; to-be-marketed pill formulation completed, stable at room temperature
2	Strong biological rationale & clinical data	Elevated brain fluid cortisol is strongly associated with Alzheimer's and depression Positive clinical efficacy data from three placebo-controlled trials
3	Safe, oral, easy to use	Safely treated > 350 people to date, low oral once-daily dose, very low drug interaction potential good for combination therapy
4	Large global market opportunity	Depression: Market \$17 billion ¹ Alzheimer's: Market \$14 billion ²
5	Near-term milestone	Phase 2a depression results Q3 CY24 Peer reviewed manuscripts Q2-4 CY24 Phase 2b Alzheimer's interim results mid CY25
6	Protected	Composition of matter protection to 2036 in most markets, multiple patent families including manufacturing and use patents extend market exclusivity further
7	Experienced team	Highly experienced Board and Management with a proven track record, Dr Gourlay's last exit US\$3.7 billion M&A at Principia/Sanofi
8	Funded	Cash \$6.3 million (no debt), fundraising targeting \$8.9 million, plus R&D rebate expected >\$4.8 million (Q4) provides cash runway to late 2025

1. <https://www.futuremarketinsights.com/reports/depression-treatment-market>
2. <https://www.futuremarketinsights.com/reports/alzheimers-diagnostics-and-therapeutics-market>

\$8.9m¹ May 2024 Capital Raising Overview

Company summary

- ~\$80m market cap
- 2,326m ordinary shares on issue
- 194m unlisted options 3.75 cents, expiry Sept 2026
- Current cash (pre-raise) \$6.3m² with no debt
- Anticipated higher R&D rebate this year in Q4 CY24 (FY23 rebate: \$4.8 million)

Offer structure

- \$8.9m via Placement and Rights Issue
- \$5.0m Placement to institutional and sophisticated investors of 200m shares
- Rights Issue of up to 155m new shares to raise up to \$3.9m from existing shareholders on the same terms, remaining “Shortfall” below \$3.9m may be placed
- 1 for 2 unlisted options exercisable at 5 cents with 36-month expiry (31 May 2027)

Offer pricing

- 2.5 cents, representing a 21% discount to the 30-day VWAP of 3.2 cents

Rights issue and “top up offer”

- Right for eligible shareholders to subscribe for new shares on a 1:15 basis, on the same terms, with the opportunity to apply to top up for any amount³
- Directors pre-committed to take up their rights⁴
- Record date for holdings 7pm Friday 10 May

Use of funds

- Progress XanaMIA phase 2b Alzheimer’s trial through interim results in mid-2025 (n=100) and working capital, cash runway to late 2025

1 Unless stated otherwise, all financial data is in Australian dollars

2 As at 31 March 2024

3 Subject to availability under the maximum shares to be issued in the Rights Issue of 155m, and at the Company's discretion

4 Total commitment of \$187,834

Market Exclusivity

Strong IP portfolio



Strong patent position with up to 12 years market exclusivity based on “composition of matter” patents and extensions in all major markets

Other patents extend potential patent life protection including “methods of use” patents, patient selection with biomarkers, manufacturing and formulation patents

Latest international patent publication teaches the use of the blood biomarker pTau for the selection of patients for Xanamem[®] treatment

Strong M&A and licensing activity in the CNS sector

Target/Partner	 KARUNA THERAPEUTICS Bristol Myers Squibb	 cerevel abbvie	 tetra SHIONOGI	 prothena Bristol Myers Squibb	 SOSEI NEUROCRINE BIOSCIENCES	 Sumitomo Pharma Otsuka	 alector gsk GlaxoSmithKline	 Sage Therapeutics Biogen	 ucb Pharma Roche
Drug	KarXT	Emraclidine	BPN-14770	PRX-005	NBI-1117567	ulotaront, SEP-378614 and others	AL-001	BIIB-124	Bepranemab
Phase	Phase 3	Phase 2	Phase 2	Phase 1	Phase 2	Phase 3	Phase 3	Phase 3	Phase 1
Indication	Schizophrenia	Schizophrenia/ Other	Fragile X Syndrome/ Alzheimer's	Alzheimer's (tau antibody)	Schizophrenia	Schizophrenia/ Depression	Dementias (progranulin target)	Depression	Alzheimer's Disease (tau antibody)
Deal Type	Acquisition	Acquisition	Acquisition*	Licensing*	Licensing	Licensing	Licensing	Licensing	Licensing
Upfront Consideration	US\$14.0b	US\$8.7b	US\$0.04b	US\$0.1b	US\$0.1b	US\$0.3b	US\$0.7b	US\$1.5b	US\$0.1b
Earnout	n/a	US\$460	US\$0.46b	US\$2.1	US\$2.6b	US\$0.6b	US\$1.5b	US\$UNK	US\$2.0b
Total Consideration	US\$14.0b	US\$8.7b	US\$0.5b	US\$2.2b	US\$2.7b	US\$0.9b	US\$2.2b	>US\$1.5b	US\$2.1b
Date	Dec-23	Dec-23	May-20	Jun-21/Oct-23	Nov-21	Sep-21	Jul-21	Nov-20	Jun-20

* By exercise of previously negotiated option during earlier development

 Neuropsychiatry
acquisitions

 Alzheimer's disease phase 1 & 3 licensing

Experienced Leadership and Management

Extensive clinical and commercial experience guides Xanamem development



Talented management team...

...with an experienced Board



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



30+ years' experience in development of novel therapeutics
Former founding CMO at US-based Principia Biopharma Inc



Dana Hilt
Chief Medical Officer
MD



25+ years of drug development experience, primarily CNS drugs
Chief Medical Officer at various pharmaceutical companies



Will Souter
Chief Financial Officer
BComm, LLB



Extensive experience in advisory, executive and non-executive roles in private and public markets
Particular experience in IPOs, capital markets and transactions



Cheryl Townsend
VP Clinical Operations
RN, M Health Law



30 years experience in Clinical Operations and Medical Affairs
10 years as Regional Head Asiapac in rare diseases



Fujun Li
Head of Manufacturing
PhD



30+ years experience in drug development and manufacturing
Held multiple executive level roles in CMC and technical operations



Michael Roberts
Head of IR and Comms
B.Ec (Hons), CPA, FIN



30 years in finance & communications
ASX Top 50 investor relations at Brambles, Lion and Foster's Group



Dr. Geoff Brooke
Chairman
MBBS; MBA



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



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



Dr. Nicki Vasquez
Non-Executive Director
PhD

Attractive product profiles in Depression and Alzheimer's

Rapidly acting oral therapy with dual action on cognitive impairment / depression

Cognitively enhancing and disease modifying oral therapy for all stages of Alzheimer's disease

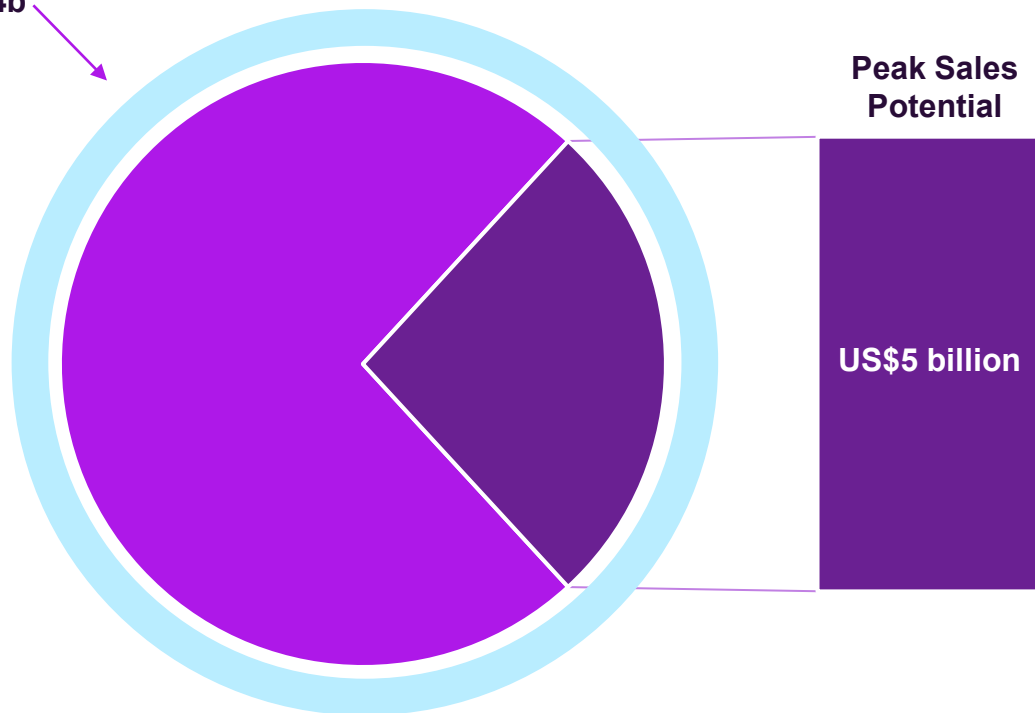
Opportunity across two key markets

Significant market opportunity across both Alzheimer's disease (AD) and Depression

Alzheimer's Disease Market

US\$14 billion market¹ with peak sales potential of US\$5 billion³

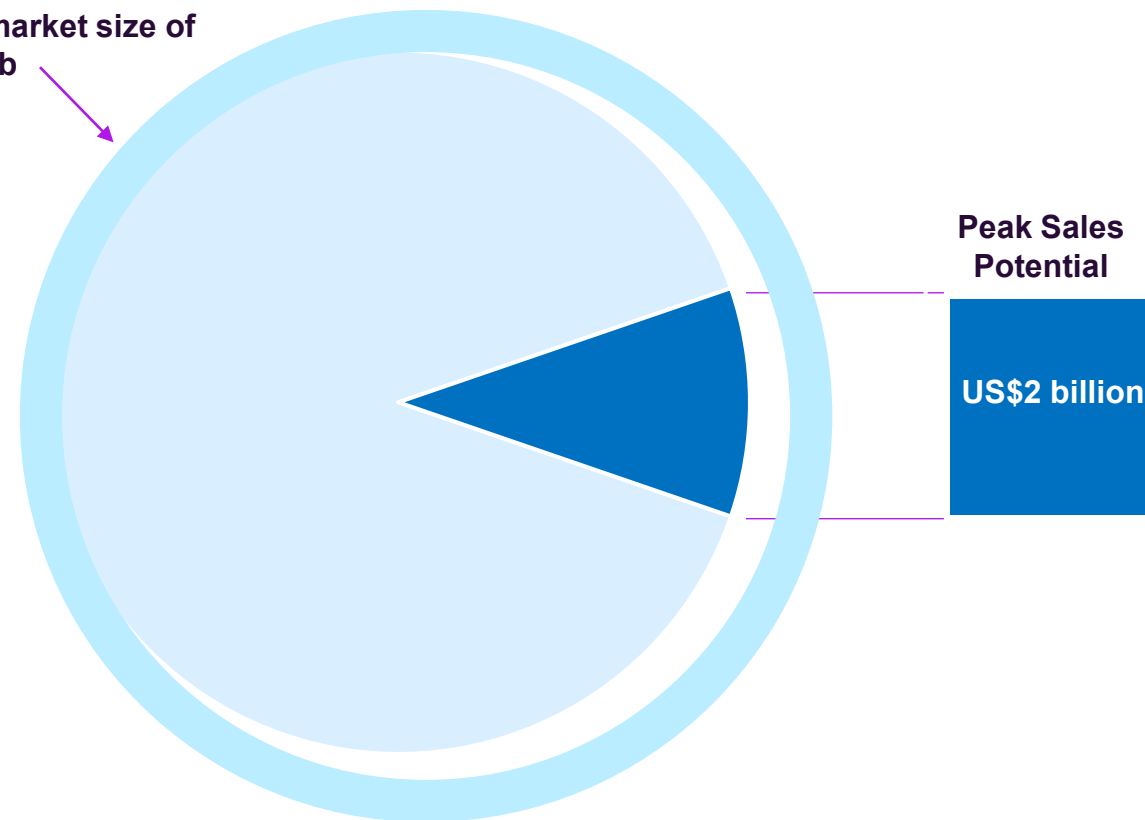
Total market size of
US\$14b



Depression Market

US\$17 billion market² with peak sales potential of US\$2 billion³

Total market size of
US\$17b



1. <https://www.futuremarketinsights.com/reports/depression-treatment-market>
 2. <https://www.futuremarketinsights.com/reports/alzheimers-diagnostics-and-therapeutics-market>
 3. Peak sales 2034 <https://www.edisongroup.com/research/pressing-forward-with-xanamen>

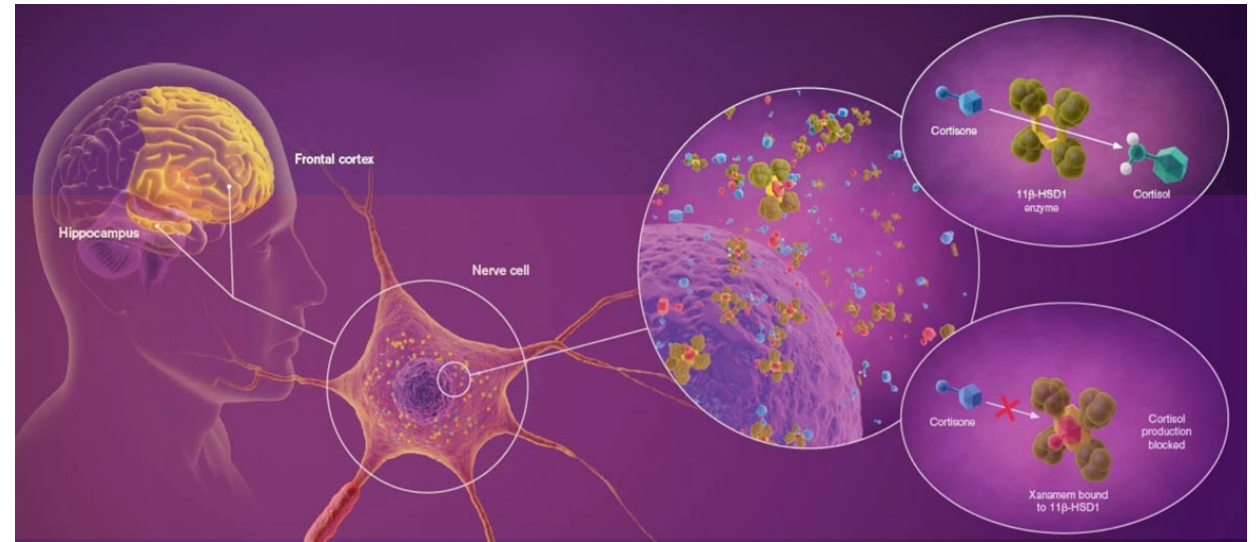
The science and the trials

Xanamem: Oral, once-a-day treatment with a unique mechanism

Xanamem is a brain penetrant 11β -HSD1 small molecule enzyme inhibitor which **reduces brain tissue cortisol**^{3,4}

Potential to be:

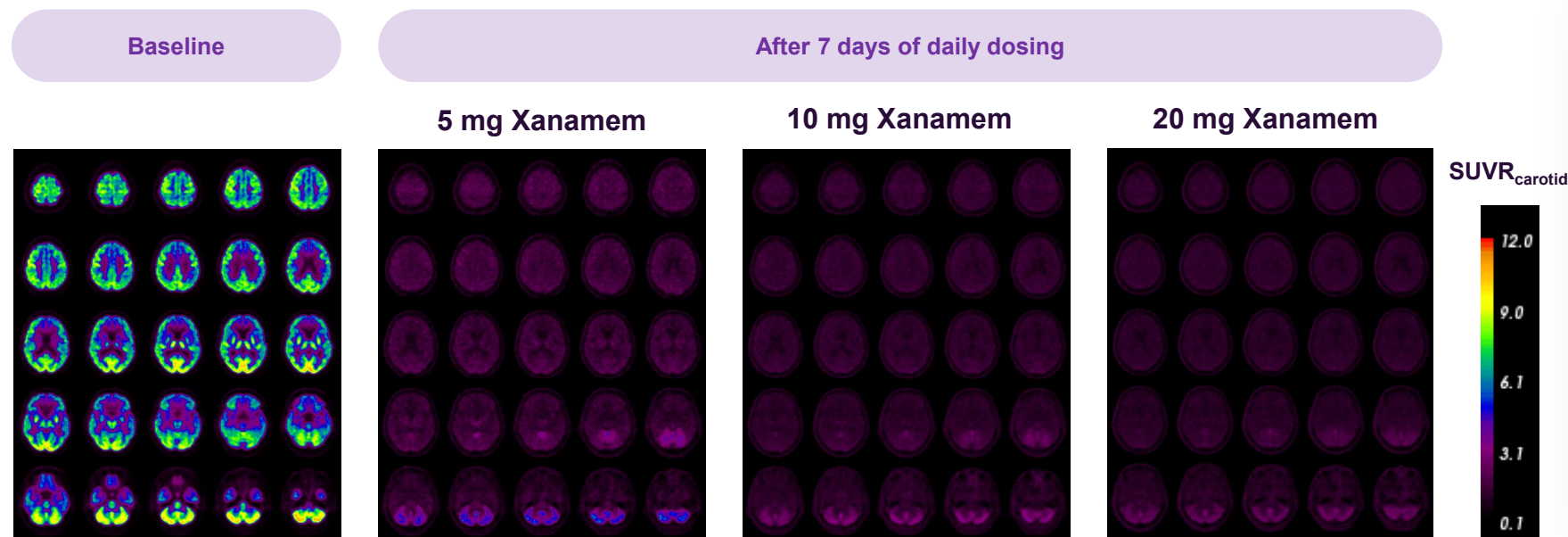
- Rapidly **cognitive enhancing**
- **Disease-modifying** (slowing progression)^{1,3}
- **Anti-depressant effects**



Mouse experimental studies, brain cortisol levels & human clinical trials validate cortisol as a target for the treatment of AD¹⁻⁵

PET data shows full target engagement in the brain at low doses

Previous enzyme inhibitors¹ have not achieved adequate brain concentrations



PET data² demonstrates that Xanamem extensively binds to the 11 β -HSD1 enzyme throughout the brain, with high post-treatment effects (absence of colour) 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.

Validates 10mg dose in efficacy trials

1. ABT-384 was claimed to have brain penetrant ability based on likely hepatic effects on deuterated cortisol (Katz et al. 2013), negative 12-week AD trial (Marek et al. 2014)

2. Study population consisted of ~50% healthy older subjects who were cognitively normal and ~50% with Alzheimer's disease. Subjects dosed for seven days.

Baseline: Mean of baseline scans of patients in that dose group; After dose: Mean of post-dosing (7 days) scans in that dose group.

Actinogen Xanamem Phase 2 trials underway

Supported by extensive existing clinical data from four previous trials of Xanamem 10mg

Phase 2a proof-of-concept trial in patients with Cognitive Impairment & Depression (n=167)

**Results
Q3 2024**

Phase 2b confirmatory trial in patients with mild-moderate Alzheimer's disease (n=220)

**Interim results
Mid 2025
N=100**

Targeting brain tissue cortisol with Xanamem is a promising strategy in cognitive impairment & depression

- ✓ Elevated cortisol associated with severe, melancholic depression²
- ✓ Cortisol levels associated with treatment outcomes, relapse, & cognition³
- ✓ 80-90% of MDD patients report neurocognitive symptoms¹
- ✓ Cognitive symptoms often persist during remission¹
- ✓ Positive effects with GR receptor antagonism with mifepristone⁴
- ✓ Meta-analysis of clinical cortisol approaches⁵

✓ **Xanamem has improved human cognition in 2 trials with same cognitive endpoint to be used⁶**

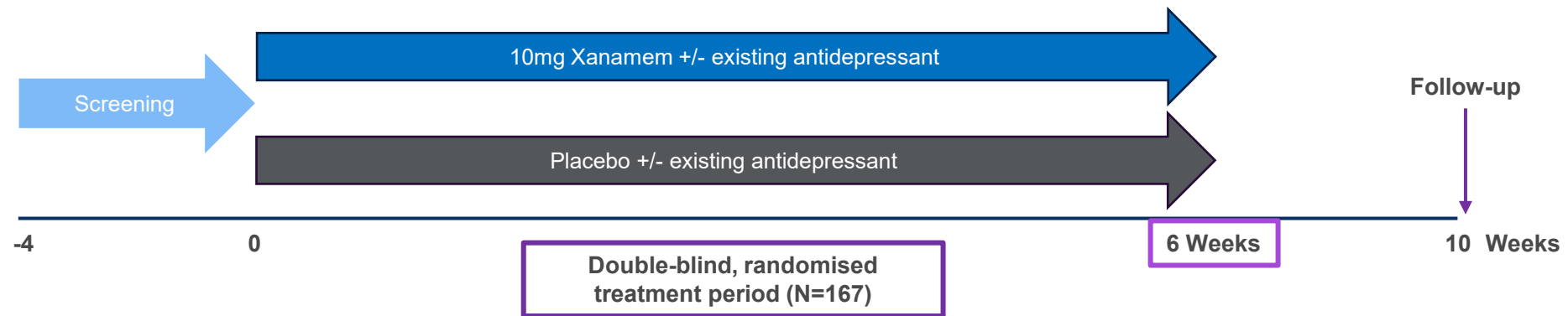
1. 3-year prospective study and review, Conradi et al. 2011
2. Quantitative summary of four decades of research, Stetler & Miller 2011
3. Depression literature review, Malhi & Mann 2018; HPA axis in major depression, Keller et al. 2016
4. GR, **glucocorticoid receptor**; Combined analysis of mifepristone for psychotic depression, Block et al. 2018; mifepristone effects on depression in bipolar disorder, Young et al. 2004; Evidence from clinical studies with CRH₁ receptor antagonists, Holsboer & Ising 2008
5. Meta-analysis of prior trials aimed at reducing cortisol, Ding et. al 2021
6. Two Xanamem placebo-controlled trials showing improved working memory & attention (Actinogen data on file)



XanaCIDD proof-of-concept Phase 2a trial in Cognitive Impairment & Depression



Results early Q3 2024, primary endpoint validated in prior trials of Xanamem



Primary Endpoint	Key Secondary Endpoints
• Cogstate Cognitive Test Battery Attentional Composite (attention and working memory)*	• Montgomery-Åsberg Depression Rating Scale (MADRS) • Executive Function Cognitive Composite • Memory Function Cognitive Composite

* Same attention and working memory tests shown to demonstrate Xanamem effect in the XanaHES and XanaMIA Part A trials (see Slide 7)

XanaCIDD trial blinded data review: methods

- Blinded analysis to ensure data quality just prior to end of trial enrolment
- Analysis used all available data from up to 148 participants*
- Trial data is pooled, meaning that treatment assignment was not unblinded (decoded)
 - Company and trial personnel will not know who received active vs. placebo treatment until the end of the trial
 - No Xanamem effect can be directly evaluated from pooled data
- Primary endpoint is the “Attention Composite” made up of three computerized, reaction time tests
- Secondary endpoints include the Montgomery-Asberg Depression Rating Scale (MADRS), other cognitive composites and responder analyses

* Sensitivity analyses using completing participants showed similar results, data are preliminary and not final

Trial is progressing well with pooled data trending in the right direction, results due in early Q3 2024



OBSERVATIONS

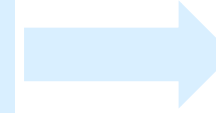
- Assessment of data quality found no concerning trends by country or clinical site
- Clinical safety profile remains excellent, with no serious adverse events related to Xanamem
- Improvement seen in **all three computerized tests** that make up the primary endpoint “Attention Composite”
 - Improvements greater than in prior trial placebo groups^{1,2,3}
 - Improvements of $\geq 30\%$ of a baseline standard deviation are potentially clinically significant in the field of cognition⁴
- 32% change-from-baseline improvement of MADRS scores is in the range reported for active & placebo groups in prior trials⁵

1. Detection test no change in depressed patients over 12 weeks: LaMonica et al 2018 [doi: 10.1371/journal.pone.0203343](https://doi.org/10.1371/journal.pone.0203343)
2. Stability over 12 weeks in older cognitively normal people and those with Alzheimer's: Lim 2013 et al. Archives of Clinical Neuropsychology 28 (2013) 320–330
3. Cognitively normal older volunteer data - Actinogen data on file
4. Acetylcholinesterase inhibitor Cohen's d (change as a % of baseline standard deviation) range 0.2 to 0.3 (20 to 30%): Rockwood 2004
5. Placebo group depression trial response rate reviews: Stone et al. 2022 [BMJ 2022;378:e067606](https://doi.org/10.1093/bmj/378.e067606) Jones et al. 2021 [doi:10.1001/jamanetworkopen.2021.25531](https://doi.org/10.1001/jamanetworkopen.2021.25531)

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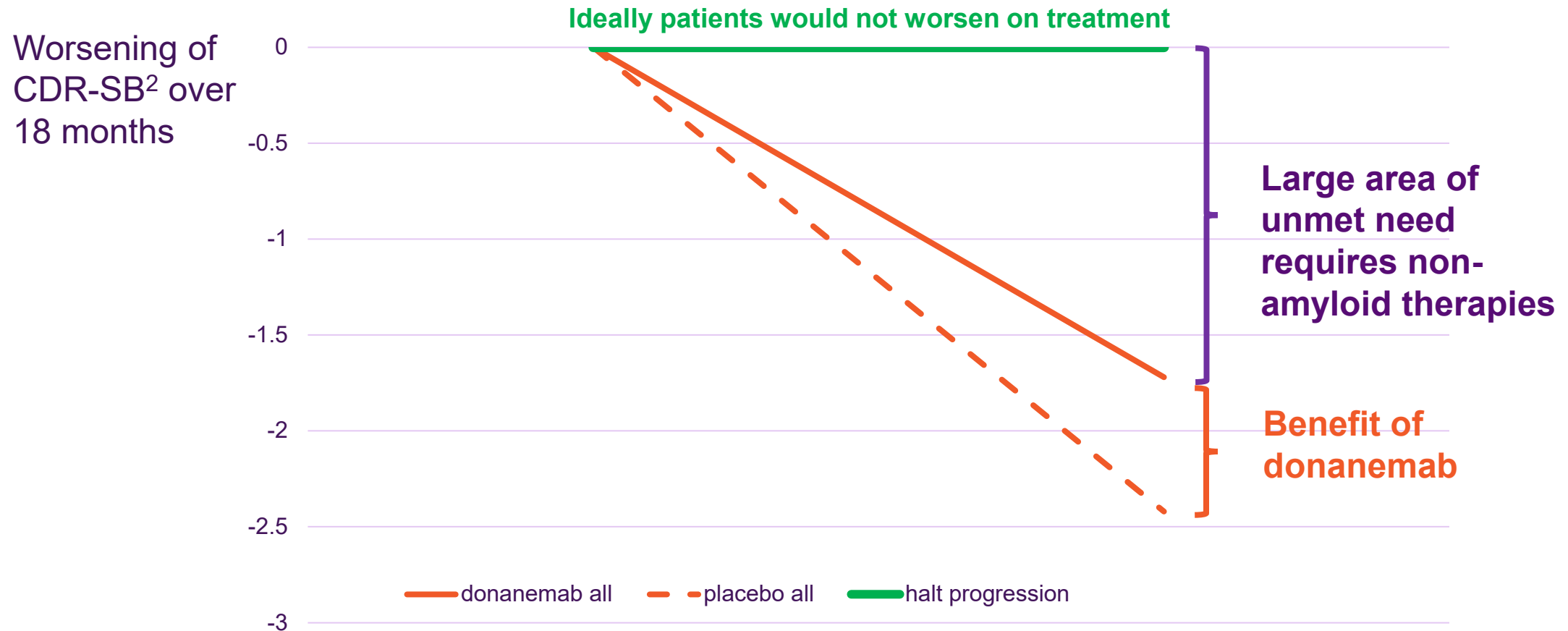
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Interim results
Mid 2025
N=100

Newer anti-amyloid “immunotherapy” antibodies shown to slow but not halt progression of AD¹



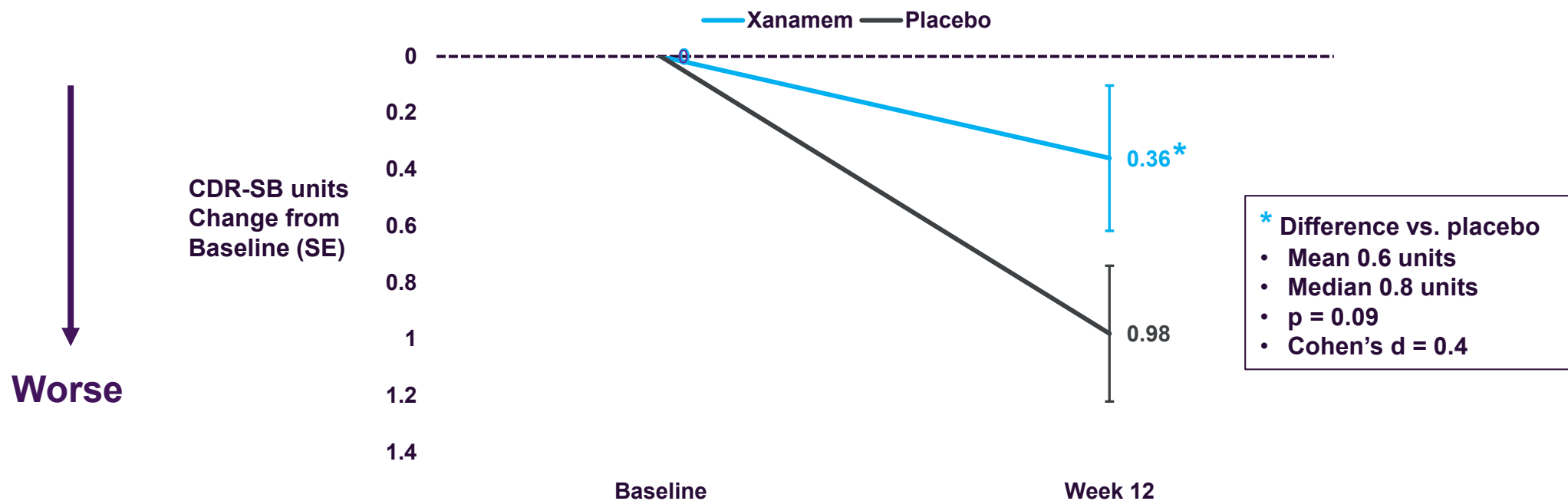
Drugs targeting other mechanisms like Xanemem are needed

1. Donanemab is an anti-amyloid antibody given as an intravenous infusion every 4 weeks until amyloid clearance (Sims JR at al. *JAMA*. Published online July 17, 2023. doi:10.1001/jama.2023.13239 Data shown are for whole population studied with absolute difference to placebo of 0.7 points, intermediate tau population difference also 0.7 points

2. CDR-SB is an 18-point scale measuring functional and cognitive status, patients in the donanemab trial had an average baseline score of 4 ± 2 points

Xanamem significantly slows the rate of functional decline (CDR-SB) in patients with mild AD*

Patients with elevated plasma pTau181 indicating progressive, amyloid-positive disease (n=34)



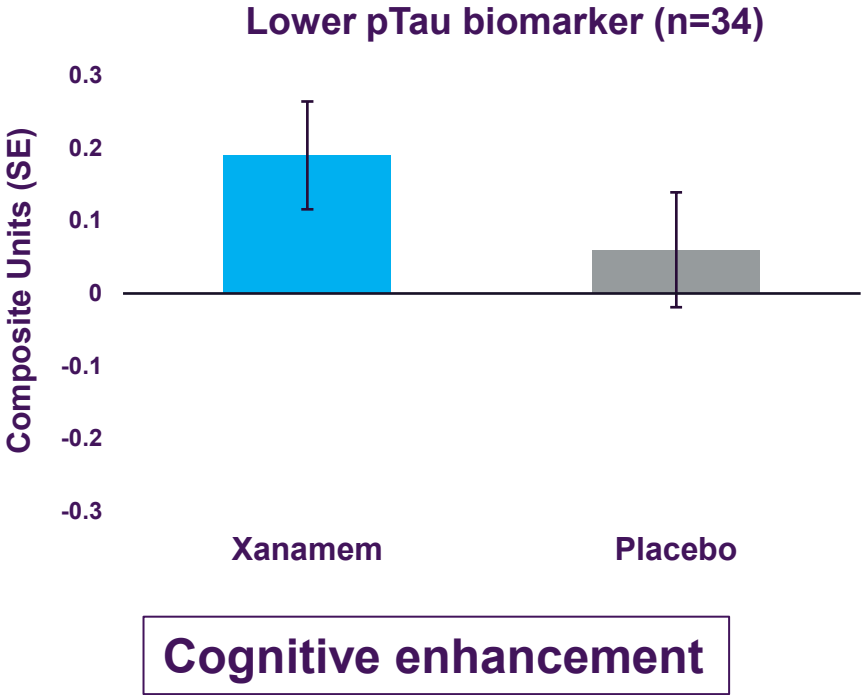
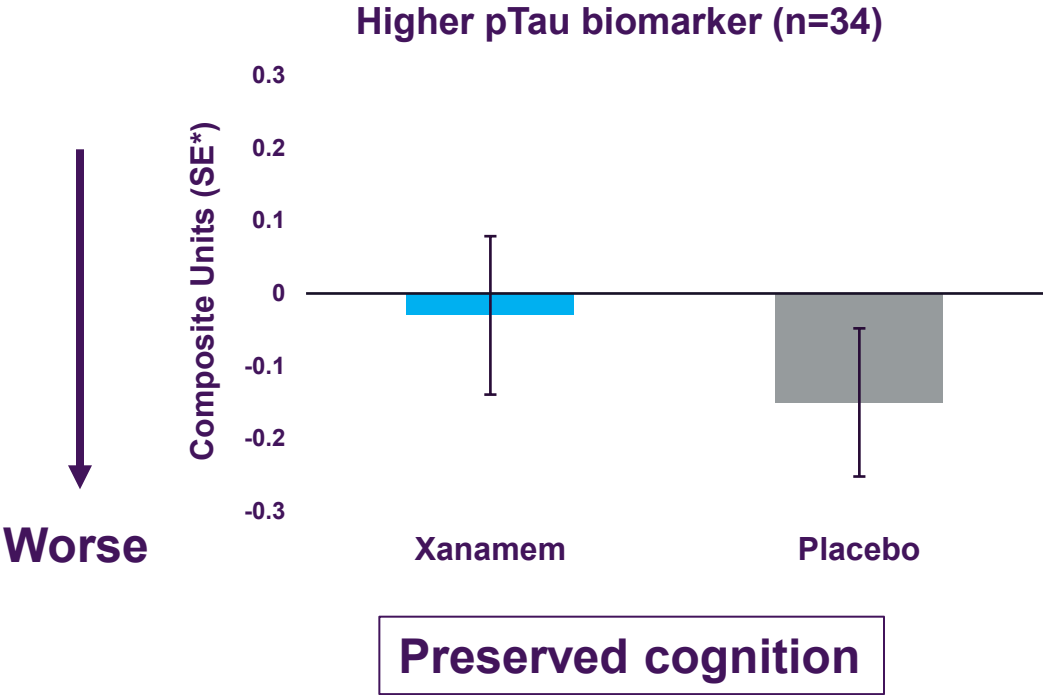
Xanamem benefits extrapolated to 18 months would be ~8x anti-amyloid drugs

* CDR-SB Clinical Dementia Rating Scale – Sum of Boxes is a measure of patient function and is an endpoint used by the FDA; Patients with a pre-treatment plasma pTau181 level greater than the pre-specified median of 6.74 pg/mL to indicate AD pathology and likelihood of progressive disease; similar effect size for pTau >10.2 pg/mL cutoff; extrapolated effect size 8-10 times greater than 0.4-0.45 reported for lecanemab (USPI Leqembi 2023 & van Dyck et al. 2022; DOI: 10.1056/NEJMoa2212948) if extrapolated to 18 months; no treatment effect detected in ADASCog-14 or ADCOMS

Cognitive improvements suggest potential clinical benefits across dementia patient sub-types*



Positive trends in both high and low plasma pTau biomarker groups

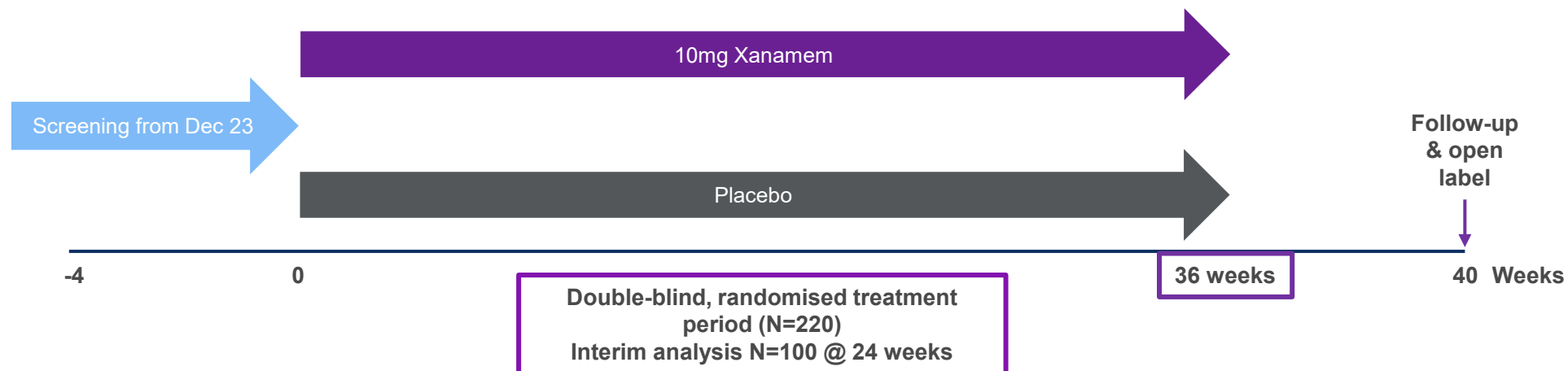


Consistent with Xanamem activity as a cognitive enhancer & disease-modifier

* Post hoc analysis of composite of word recall & recognition, CFT & COWAT tests (p=NS), error bars show Standard Error of the Mean; low pTau patients less likely to have amyloid-positive disease, results consistent with volunteer data shown in Slide 7

XanaMIA Phase 2b trial in Alzheimer's Disease

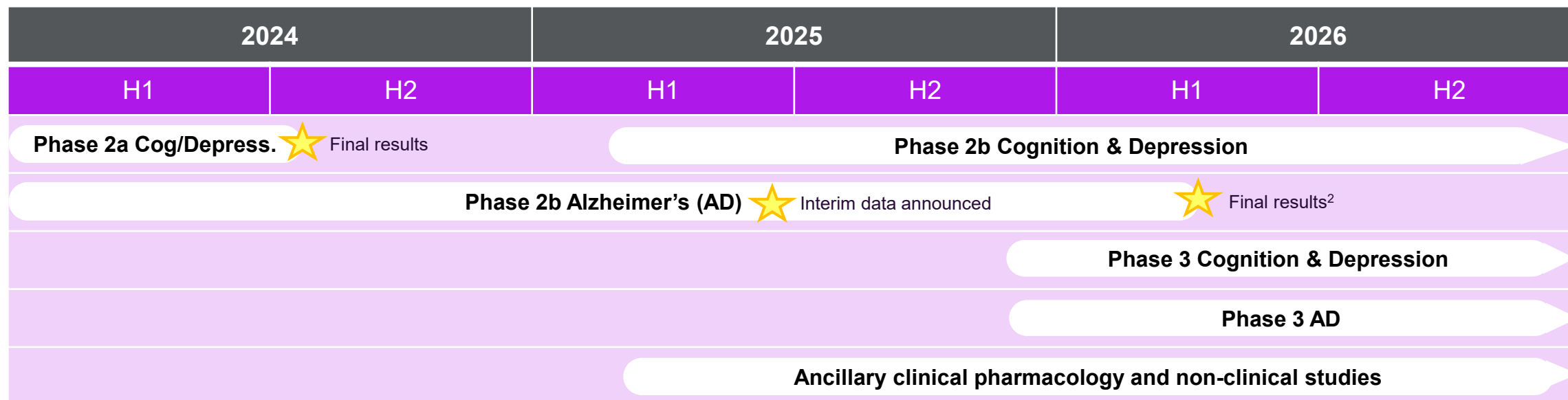
Initial, interim results in mid 2025, final results H1 2026



Key inclusion criteria	Primary Endpoint	Key Secondary Endpoints	Implementation
- Blood pTau biomarker positive - Mild-moderate Alzheimer's by NIA-AA criteria	Cognitive Test Battery (7 cognitive measures)	- CDR-SB (functional and cognitive measure) - Amsterdam Activity of Daily Living (functional measure)	- Commence enrolment at up to 15 Australian sites - Interim analysis when 100 people complete 24 weeks - Add US sites when feasible

Recent Milestones & Upcoming Catalysts¹

✓ Q1 2024	Human PET study peer-review publication	■ Q2-4 2024	Various peer-review publications, abstracts
✓ Q1 2024	UK Innovation Passport granted	■ Q1 2025	Start cognition & depression Phase 2b
✓ Q2 2024	Phase 2b Alzheimer's trial first patient treated	■ Mid 2025	Interim analysis Alzheimer's Phase 2b
✓ Q2 2024	Phase 2a cognition & depression full enrollment	■ H1 2026	Final results Alzheimer's Phase 2b ²
■ Q3 2024	Phase 2a cognition & depression trial results	■ H1 2026	Start Alzheimer's Phase 3



1. Indicative clinical program timelines subject to change, 2. Assumes additional US sites can be added from 2024

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**Strong biological
rationale & clinical data**

Elevated brain fluid cortisol is strongly associated with Alzheimer's and depression
Positive clinical efficacy data from three placebo-controlled trials

3

Safe, oral, easy to use

Safely treated > 350 people to date, low oral once-daily dose, very low drug interaction potential good for combination therapy

4

**Large global market
opportunity**

Depression: Market \$17 billion¹
Alzheimer's: Market \$14 billion²

5

Near-term milestone

Phase 2a depression results Q3 CY24
Peer reviewed manuscripts Q2-4 CY24
Phase 2b Alzheimer's interim results mid CY25

6

Protected

Composition of matter protection to 2036 in most markets, multiple patent families including manufacturing and use patents extend market exclusivity further

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Experienced team

Highly experienced Board and Management with a proven track record, Dr Gourlay's last exit US\$3.7 billion M&A at Principia/Sanofi

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Funded

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Appendix



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

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 Glutaminy-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

Tau – a brain protein

Ttau – total tau levels including both phosphorylated and non-phosphorylated tau

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