



**Phase 2-stage clinical company with near-term trial results
mid 2024 and Q2 2025**

De-risked oral therapy for dementia and depression

Corporate Presentation March 2024

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Experienced Leadership and Management

Extensive drug development and commercial experience



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

Company Highlights



Positioned to leverage the wider biotech market tailwinds

1	Clinical-stage	Xanamem® lowers brain cortisol and is in Phase 2 trials to treat patients with cognitive impairment associated with depression and Alzheimer's disease
2	Strong biological rationale & clinical data	Elevated brain 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 Interim results Phase 2b Alzheimer's H1 CY25
6	Protected	Composition of matter protection to 2036 in most markets, multiple patent families including manufacturing and use patents extend market exclusivity
7	Experience	Highly experienced Board and Management with a proven track record, Dr Gourlay's last exit US\$3.7 billion M&A at Principia/Sanofi

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

Attractive product profiles in Depression and Alzheimer's

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



Xanamem
\$2 billion¹

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



Xanamem
\$5 billion¹

1. Peak sales 2034 <https://www.edisongroup.com/research/pressing-forward-with-xanamem>

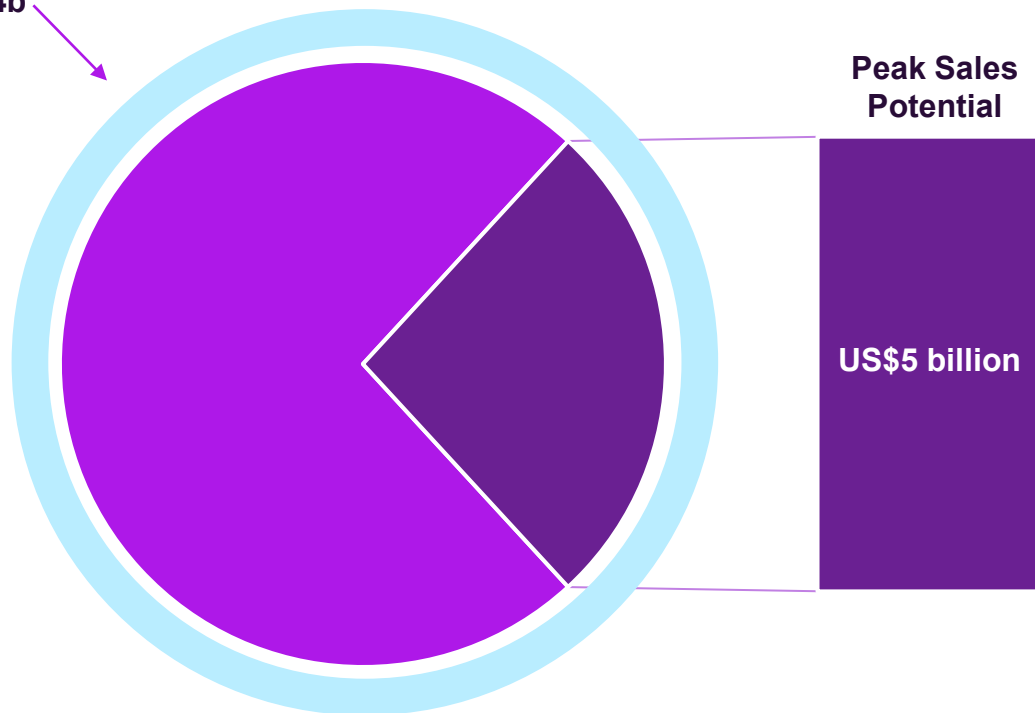
Opportunity across two key markets

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

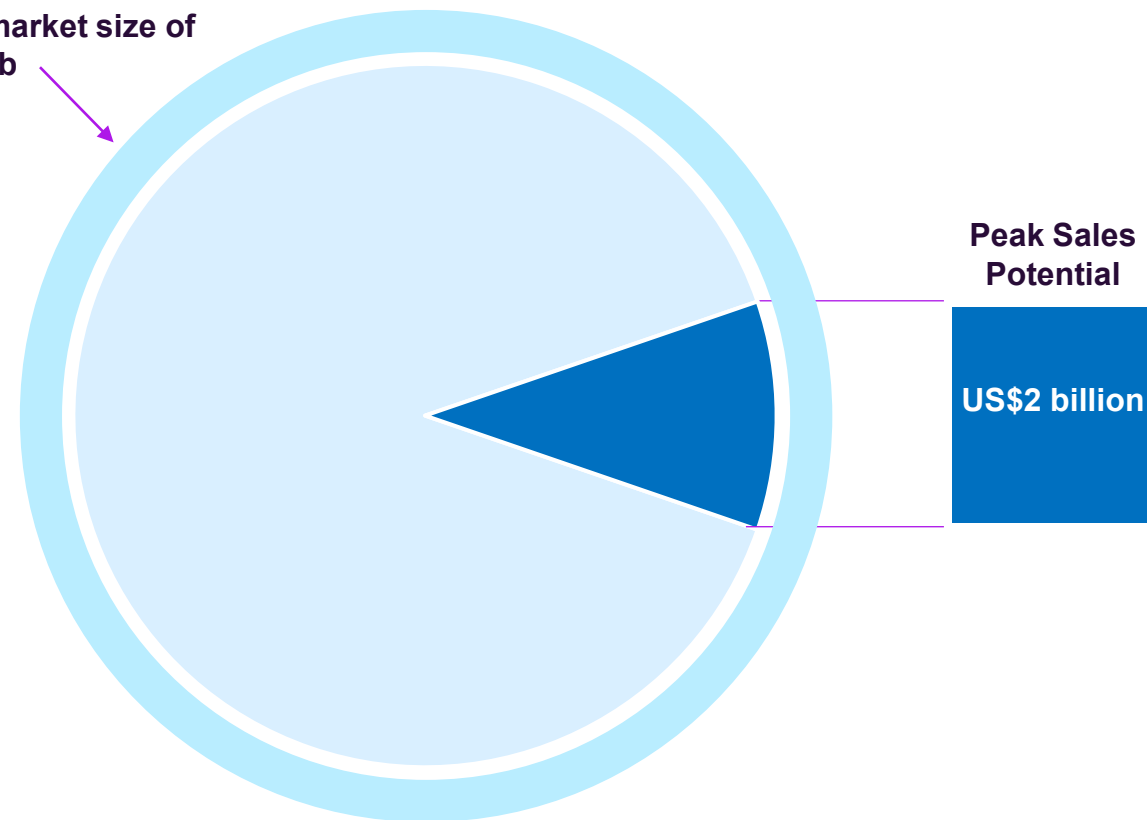
Total market size of
US\$14b



Depression Market

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

Total market size of
US\$17b



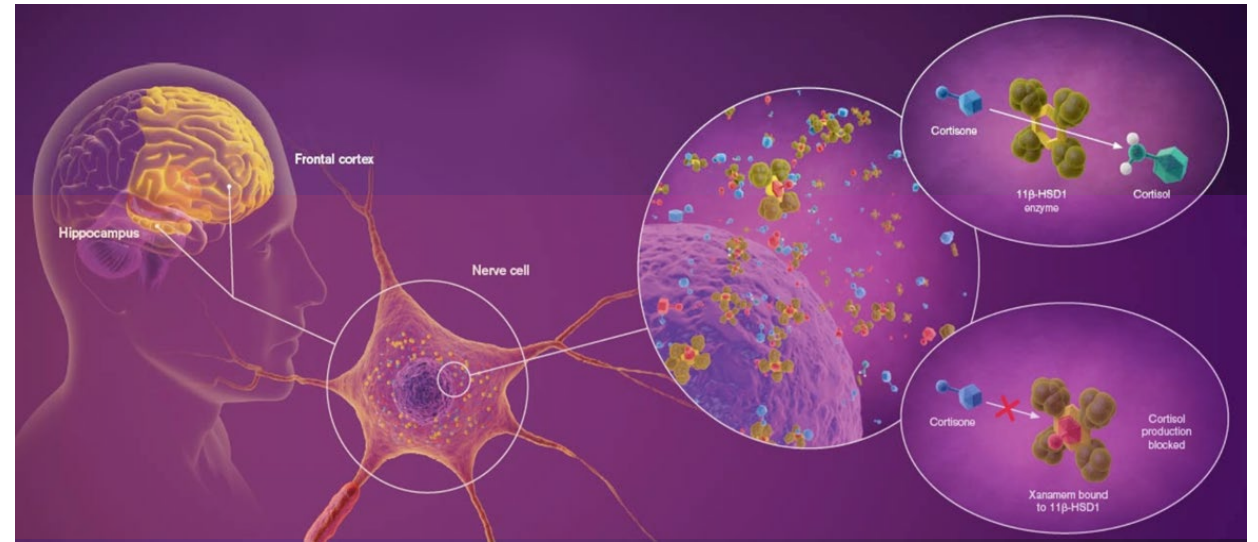
1. <https://www.futuremarketinsights.com/reports/depression-treatment-market>
 2. <https://www.futuremarketinsights.com/reports/alzheimers-diagnostics-and-therapeutics-market>
 3. Peak sales 2034 <https://www.edisongroup.com/research/pressing-forward-with-xanamen>

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

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

Potential to be:

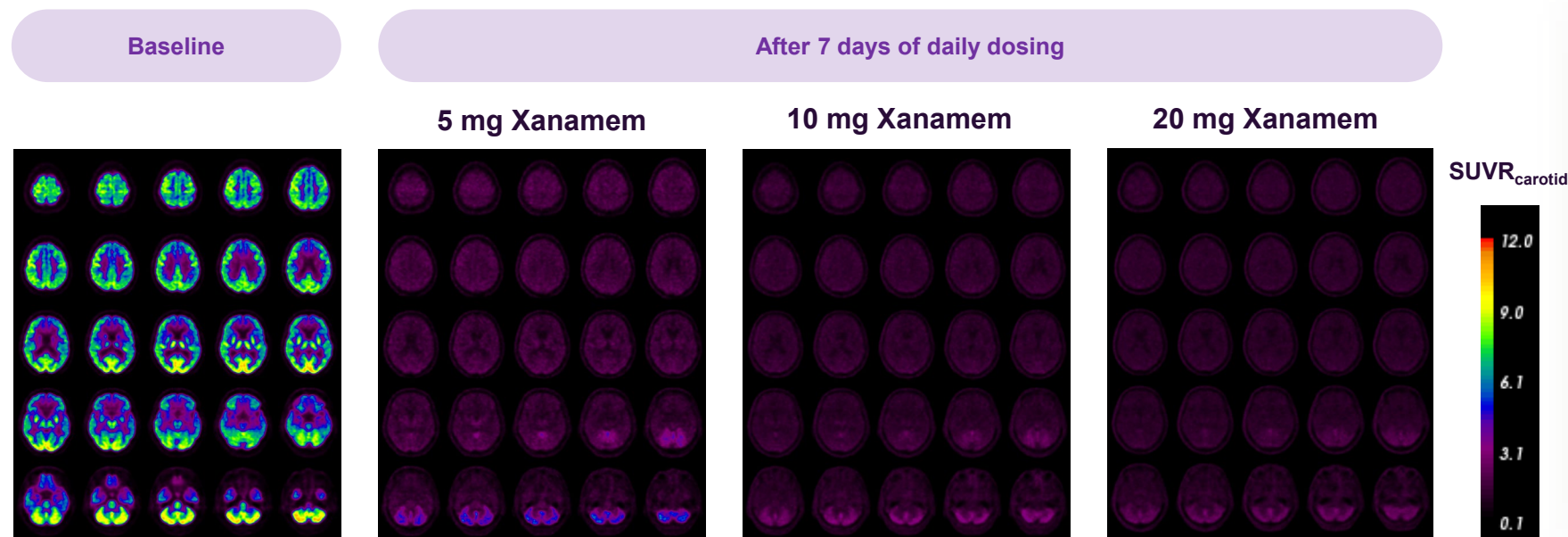
- Rapidly **cognitive enhancing**
- **Disease-modifying** (slowing progression)^{1,3}
- **Anti-depressant effects**



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.

Market Exclusivity

Strong IP portfolio



Strong patent position with over 12 years patent protection for composition of matter in all major markets, broad international cover

Other patents extend potential patent life protection including "methods of use" patents and manufacturing patents

Rare pediatric disease designation gives the option of a tradable "voucher" worth ~US\$100 million from the US FDA if Xanamem is first registered for Fragile X Syndrome - plus extended market exclusivity

Actinogen Xanamem Phase 2 trials underway

De-risked by extensive existing clinical data from four previous trials of Xanamem 10mg

Phase 2a proof-of-concept trial in patients with Depression & Cognitive Impairment (n=160)

**Results
mid 2024**

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

**Interim results
H1 2025
n~100**

Targeting brain cortisol with Xanamem is a promising strategy in 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**

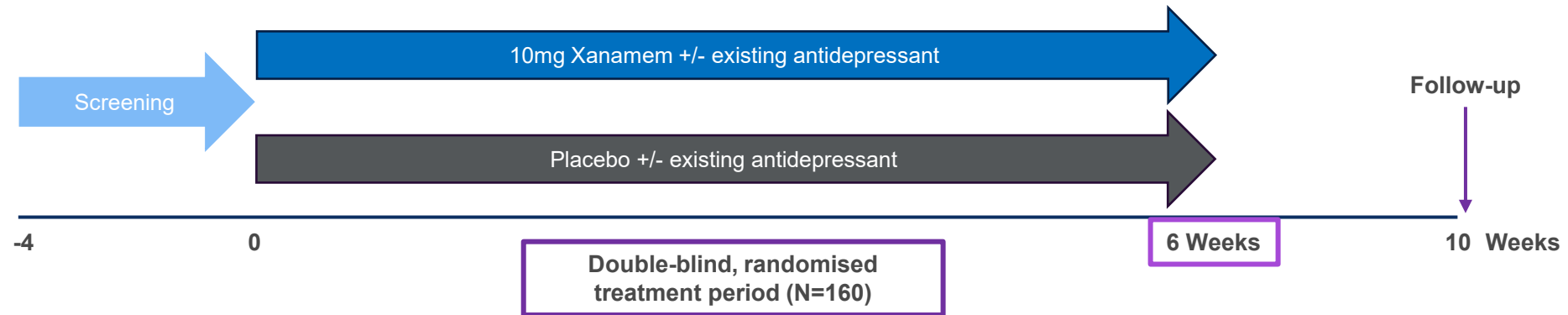
1. 3-year prospective study and review, Conradi et al. 2011
2. Quantitative summary of four decades of research, Stetler & Miller 2011
3. Depression literature review, Malhi & Mann 2018; HPA axis in major depression, Keller et al. 2016
4. GR, **glucocorticoid receptor**; Combined analysis of mifepristone 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 Depression and Cognitive Impairment



Final results mid 2024, primary endpoint validated in prior trials of Xanamem



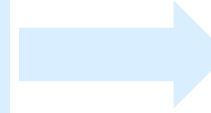
Primary Endpoint	Key Secondary Endpoints
• Cogstate Cognitive Test Battery Attentional Composite (attention and working memory)*	• Montgomery-Åsberg Depression Rating Scale (MADRS) • Executive Function Cognitive Composite • Memory Function Cognitive Composite

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

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Results
mid 2024

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Interim results
H1 2025
n~100



The answers to Alzheimer's Disease are starting to emerge in the clinic...

Alzheimer's proteins amyloid and tau are the pathology – not the cause...

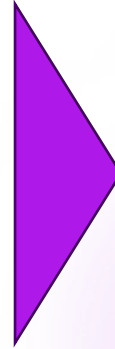
Clearing amyloid produces a very modest benefit

Other causal processes are involved like inflammation, lipids and glucose handling...

Quotes: Dr Howard Fillit

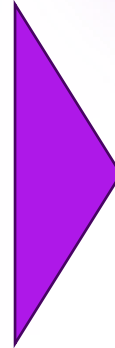
Founder & CSO Alzheimer's Drug Discovery Foundation¹

“Seventy-eight percent of all drugs in clinical development are non-amyloid, non-tau drugs”



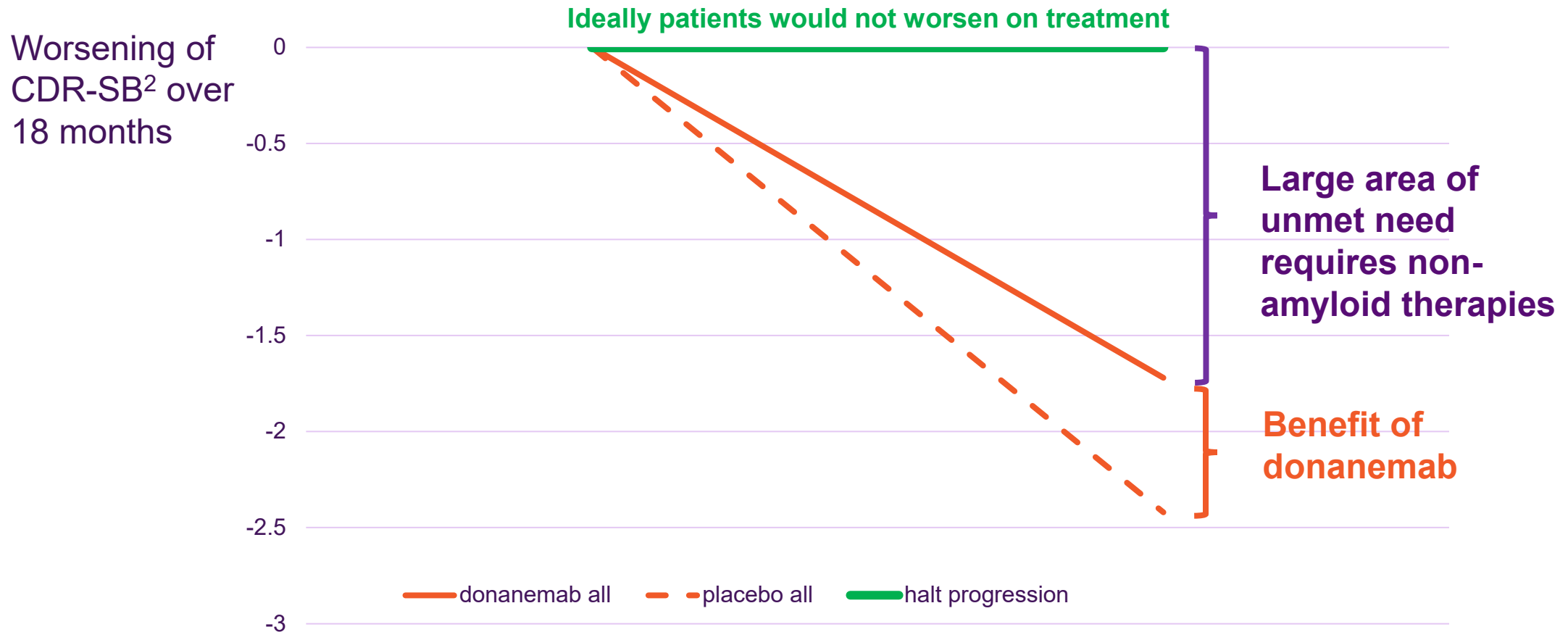
Xanamem is an easy-to-use, oral, non-amyloid, non-tau tablet

“Multiple targets are being addressed now, which is great for the field because I think the way we're going to have to go is combination therapy, addressing all the multiple pathways that are involved in Alzheimer's.”



Xanamem has no concerning drug-drug interactions so can be combined with other drugs

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



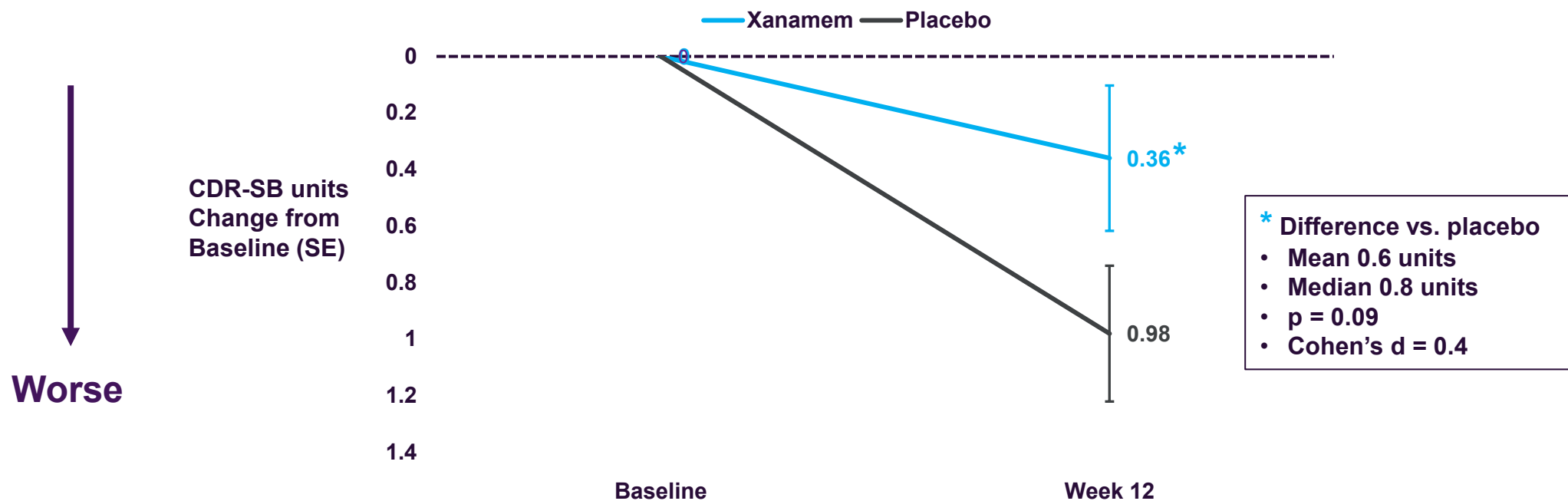
Drugs targeting other mechanisms like Xanemem are needed

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)

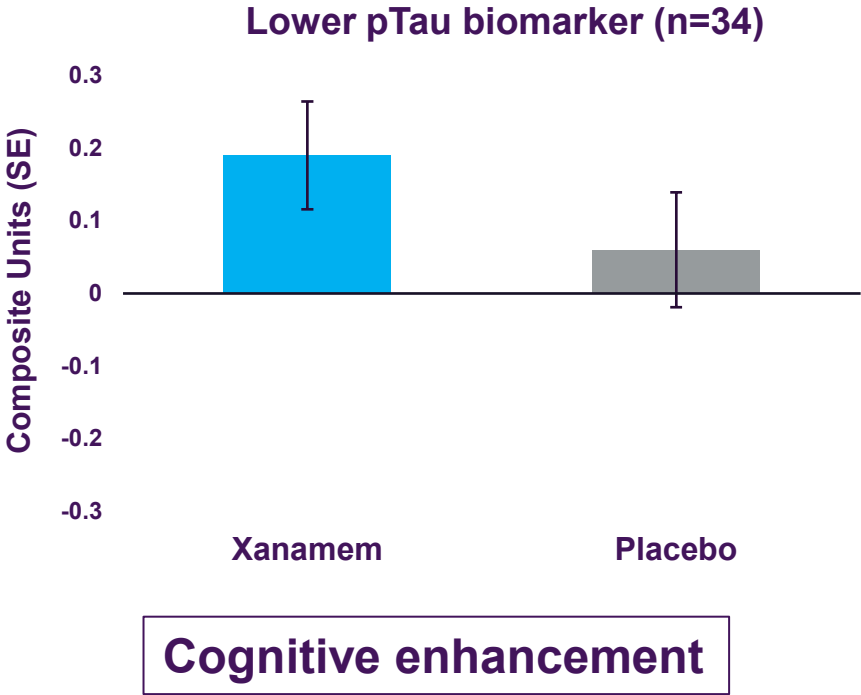
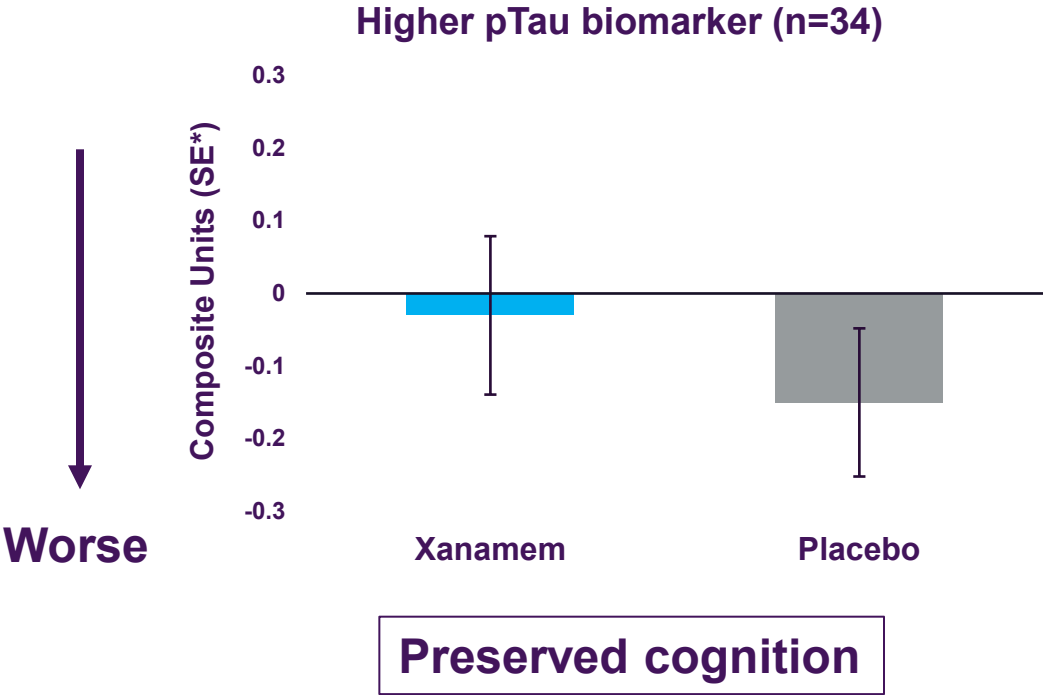


Xanamem benefits extrapolated to 18 months would be ~8x anti-amyloid drugs

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



Positive trends in both high and low plasma pTau biomarker groups

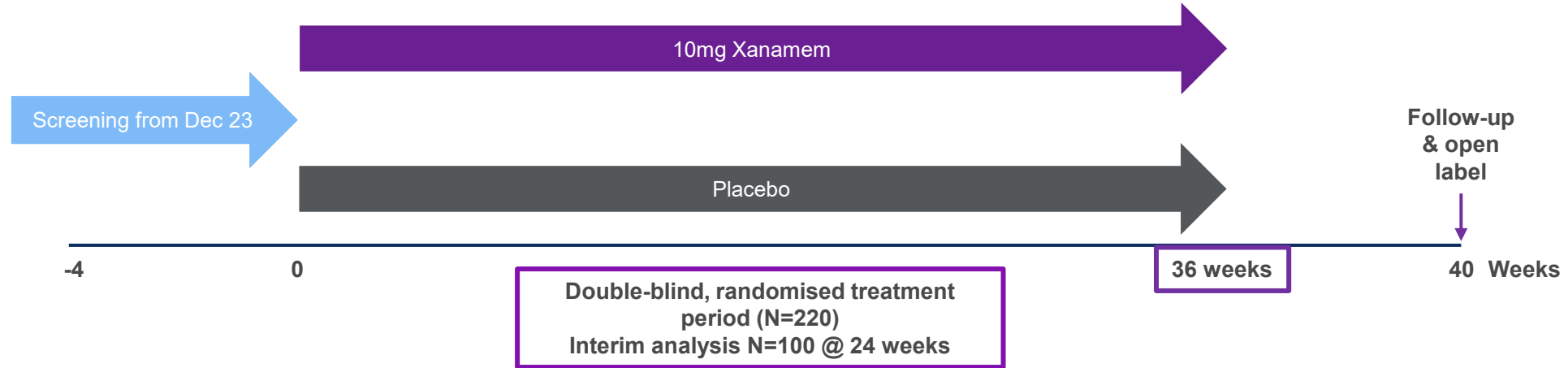


Consistent with Xanamem activity as a cognitive enhancer & disease-modifier

* 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 H1 2025, final results H2 2025



Key inclusion criteria	Primary Endpoint	Key Secondary Endpoints
• 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)

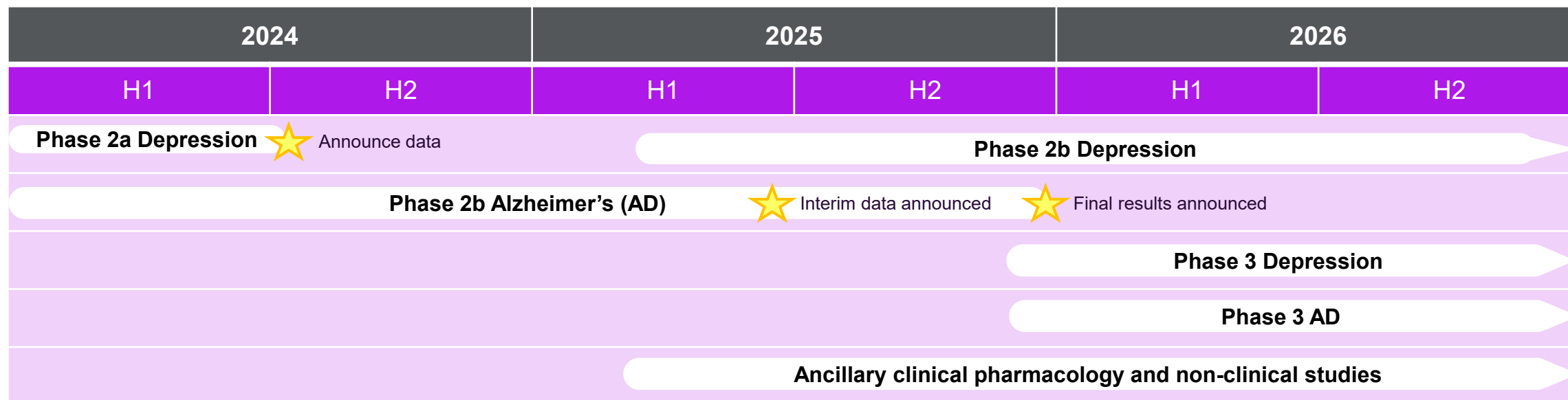
Strong M&A and licensing activity in the CNS sector

Target/Partner	 KARUNA THERAPEUTICS Bristol Myers Squibb	 cerevel abbvie	 tetra SHIONOGI Group Company 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

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 depression Phase 2b
✓ Q1 2024	Phase 2b Alzheimer's trial first patient screened	■ H1 2025	Interim analysis Alzheimer's Phase 2b
■ Q2 2024	Phase 2a depression enrollment complete	■ H2 2025	Final results Alzheimer's Phase 2b
■ Q3 2024	Phase 2a depression trial results	■ H1 2026	Start Alzheimer's Phase 3

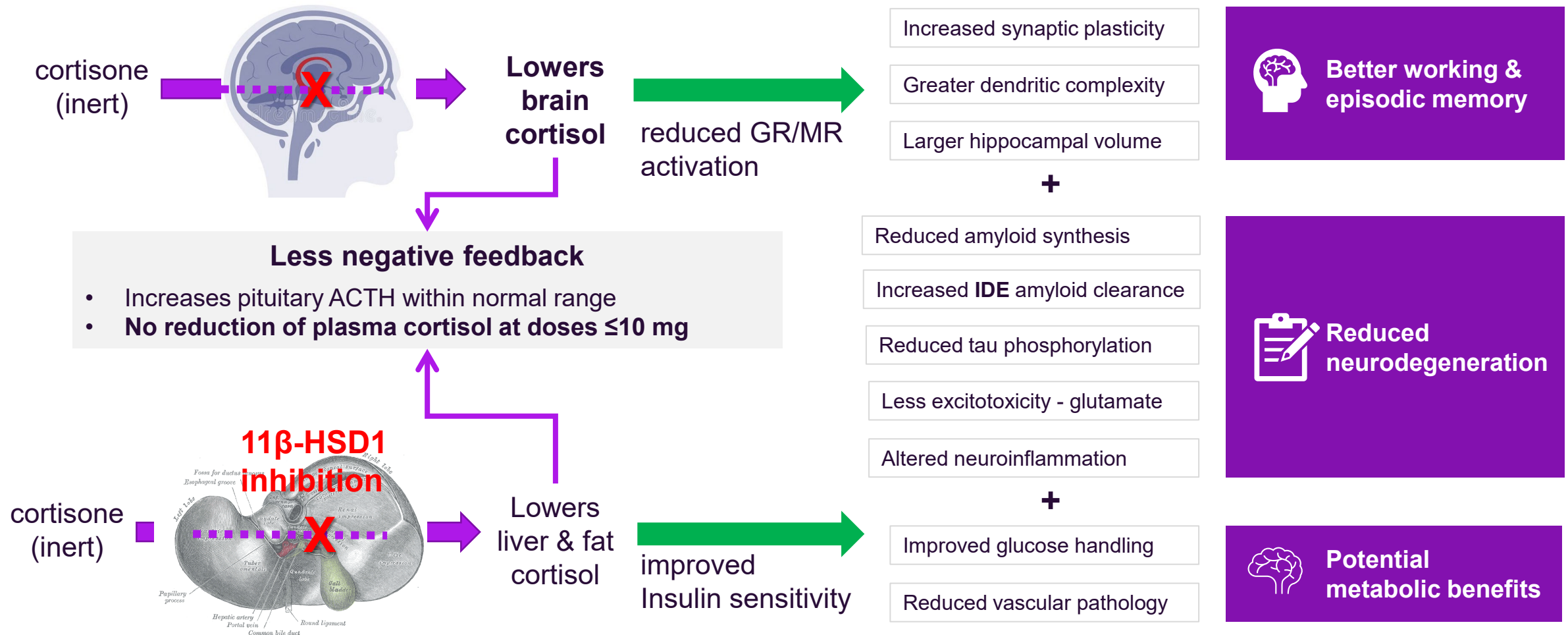


Appendix



11 β -HSD1 inhibition and attenuated cognitive decline

Xanamem has pleiotropic mechanisms of action to reduce or halt cognitive decline



Rationale: Why targeting brain cortisol with Xanamem is a promising strategy in Alzheimer's disease



Multiple streams of data support the hypothesis

Epidemiology, cortisol and animal experiments

- ✓ Cortisol levels are elevated in brain fluid in early Alzheimer's^{1,2}
- ✓ Chronic corticosteroid treatment leads to hippocampal atrophy and cognitive impairment³
- ✓ Elevated cortisol levels are associated with clinical progression⁴⁻⁷
- ✓ Animal models of 11 β -HSD1 inhibition show neuroprotection independent of amyloid

Clinical trials of Xanamem

- ✓ Inhibits brain 11 β -HSD1 target to a high degree in PET study at well tolerated doses⁸
- ✓ Improves attention & working memory (2 trials)⁹
- ✓ Slows progression in CDR-SB and cognition in biomarker-positive patients with mild AD (1 trial)¹⁰
- ✓ Safety demonstrated in >350 people (5 trials)

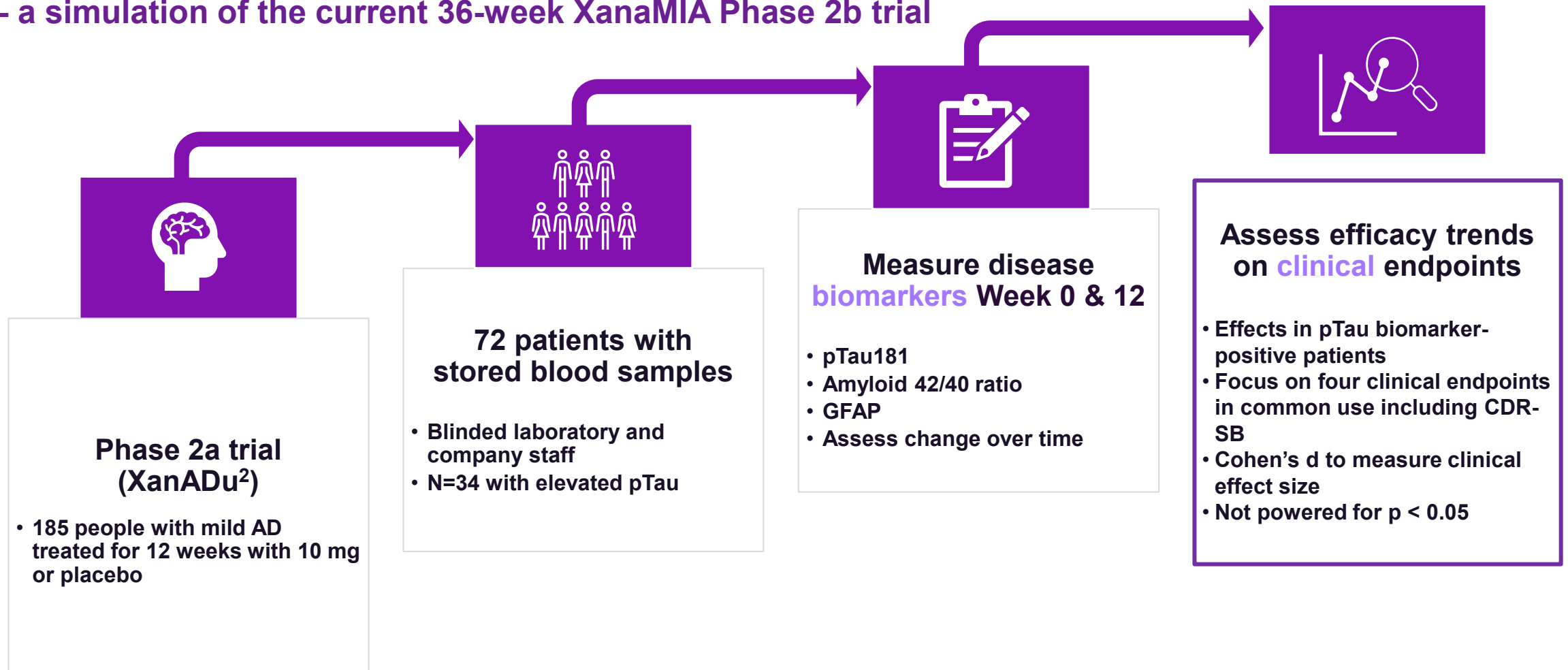
All major Xanamem development risks mitigated

Highly attractive, mid phase 2 profile in dementia and major depression

Preclinical	Animal tox studies	▶	Completed long-term toxicology studies needed for FDA approval	✓
	Alzheimer's mouse model	▶	Neuroprotection in rodent models of Alzheimer's with chemically related enzyme inhibitor	✓
Quality / Manufacturing	Optimization of Manufacturing	▶	Drug substance manufacturing process optimized, low cost of goods	✓
	Stability	▶	Excellent product stability at room temp., shelf-life expected > 4 years	✓
Clinical	Safety profile	▶	Excellent profile, treated over 350 people	✓
	Combinability	▶	Very low drug-drug interaction potential	✓
	Target engagement	▶	Dose range confirmed by brain PET imaging, PK and cognitive tests	✓
	Biomarker	▶	Elevated plasma pTau181 is simple method to identify trial subjects	✓
	New randomized phase 2a & b trial data	▶	Data in early Q3 2024 and H1 2025	■

Methods for double-blind, prospective assessment of biomarker-positive mild AD patients in Phase 2a¹

Re-examining the 12-week XanADu Phase 2a trial with biomarkers
- a simulation of the current 36-week XanaMIA Phase 2b trial



1. Used a pre-specified protocol and statistical analysis plan, blinded laboratory and company personnel
2. Prior phase 2a trial completed in 2019 included participants with a clinical diagnosis but no PET or biomarker confirmation
<https://clinicaltrials.gov/ct2/show/results/NCT02727699?term=actinogen&draw=2&rank=3>

International Cognition Clinical Advisory Board

Preeminent global thought-leaders in clinical trials for assessment of cognition



Prof. John Harrison

Metis Cognition Ltd

- Expert psychologist with a special interest in cognition
- Chartered psychologist with two PhDs and author/co-author of more than 80 books and scientific articles
- Principal Consultant at Metis Cognition, which advises on selection and integration of cognitive testing into therapeutic development programs



Dr Dana C. Hilt (CMO)



- 25+ years of drug development experience, primarily of Central Nervous System (CNS) drugs
- Deep experience in Phases 1 to 4 drug development
- CMO at Frequency Therapeutics and has held senior management positions as Chief Medical Officer at various pharmaceutical companies



Dr Christina Kurre Olsen



- 20+ years research expertise in neuroscience, neuropsychopharmacology, CNS therapeutics and monoclonal antibody immunotherapy
- Strong hands-on knowledge across drug development value chain and a passion for cognition
- Medical Director at Orphazyme A/S



Prof. Paul Maruff



- Chief Innovation Officer at Cogstate Ltd
- Professor in Neuroscience at the Florey Institute of Neuroscience and in Psychology Monash University, Melbourne Australia
- Senior management committee of the Australian Imaging, Biomarkers and Lifestyle (AIBL) study of Alzheimer's Disease
- Involved in the development and approval of 13 new drugs that affect cognition including most recently esketamine for treatment resistant depression



A/Prof Christopher Chen



- Senior Clinician-Scientist, Associate Professor at the Departments of Pharmacology and Psychological Medicine, Yong Loo Lin School of Medicine, National University of Singapore, and Director of the Memory Aging and Cognition Centre, National University Healthcare System.
- Major research and clinical interests are in neuroimaging, molecular biology and treatment of stroke and dementia.
- President of the Asian Society Against Dementia, Secretary-Treasurer of the Asian & Oceanian Association of Neurology.

International Scientific Advisory Boards

Preeminent thought-leader academics involved in the development of Xanamem



Alzheimer's Disease Clinical Advisory Board



Prof. Craig Ritchie
Chair



- World-leading authority on dementia; senior investigator on 30+ drug trials
- Chair of the Scottish Dementia Research Consortium; Professor of the Psychiatry of Ageing' Director of the Centre for Dementia Prevention (University of Edinburgh)



Prof. Colin Masters
AO



- 35+ years research on Alzheimer's Disease and other neurodegenerative diseases
- Laureate Professor of Dementia Research and Head, Neurodegeneration Division at The Florey Institute (UniMelb)



Prof. Jeffrey Cummings



- World-renowned Alzheimer's researcher and leader of clinical trials
- MD, ScD; Founding Director of the Cleveland Clinic Lou Ruvo Center for Brain Health
- Recognised for his work through various awards



Prof. Jonathan Seckl



- Undertaken extensive research in endocrinology
- Senior VP at the university of Edinburgh; Chaired Panels for MRC, Innovate UK and Wellcome Trust
- MBBS UCL, PhD (London)



Prof. Brian Walker



- 20+ years research in the area of disease
- Extensive experience advising for pharmaceutical R&D
- Pro Vice Chancellor for Research Strategy & Resources at Newcastle University, UK



Prof. Scott Webster



- Chair of Medicines at the Centre of Cardiovascular Science, University of Edinburgh
- Former positions across both biotech and academia
- Founder and Chief Scientific Officer at Kynos Therapeutics

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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