ASX ANNOUNCEMENT

Actinogen CEO presents in 'Drug Developers - Finding the Next Neuren Part 2' session at the 2023 Bioshares Biotech Summit, Hobart

Sydney, 25 July 2023. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that its Chief Executive Officer and Managing Director, Dr Steven Gourlay, will present at the **2023 Annual Bioshares Biotech Summit** in Hobart, Australia today.

Dr Gourlay's presentation is titled ***First-in-class/best-in-class Phase 2 oral drug candidate for Alzheimer's Disease & Depression.*** It provides an overview of Actinogen, the Xanamem® therapeutic rationale, validation of the program from the positive results of four clinical trials, and upcoming catalyst points in the Company's clinical development program.

The presentation slides are attached to this announcement.

ENDS

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Announcement authorised by the Board of Directors of Actinogen Medical

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.

About Xanamem

Xanamem's novel mechanism of action is to block the production of cortisol inside cells through the inhibition of the 11β-HSD1 enzyme in the brain. Xanamem is designed to get into the brain after it is absorbed in the intestines upon swallowing.

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease and excess cortisol is known to be toxic to brain cells. Cognitive impairment is also a feature in Depression and many other diseases. Cortisol itself is also associated with depressive symptoms and when targeted via other mechanisms has shown some promise in prior clinical trials.

The Company has studied 11β-HSD1 inhibition by Xanamem in more than 300 volunteers and patients, so far finding a statistically significant improvement in working memory and attention, compared with placebo, in healthy, older volunteers in two consecutive trials and clinically significant improvements in functional and cognitive ability in patients with biomarker-positive mild AD. Previously, 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. A series of Phase 2 studies in multiple diseases is being conducted to further confirm and characterize Xanamem's therapeutic potential.

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.

® Xanamem is a registered trademark of Actinogen Medical Limited

Actinogen

First-in-class/best-in-class Phase 2 oral drug candidate for Alzheimer's Disease & Depression

Four trials validate Xanamem® as a novel, differentiated, safe and efficacious candidate

Corporate Presentation July, 2023

Presented at the Bioshares Biotech Summit July 25, 2023

Non-confidential

Dr Steven G Gourlay, CEO

Disclaimer

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The answers to Alzheimer's Disease are starting to emerge….

Actinogen (ACW.AX) & Xanamem Summary

- Xanamem is an oral treatment with rapid onset of clinical activity
- Cortisol target validation in animal models and by cognitive benefit shown in multiple controlled trials of Xanamem
- Excellent safety profile, low drug interaction potential
- Commercial tablet formulation developed
- Intellectual property protection including composition of matter
- Experienced team based in Australia, US and UK

Actinogen (ACW.AX) Trials Underway

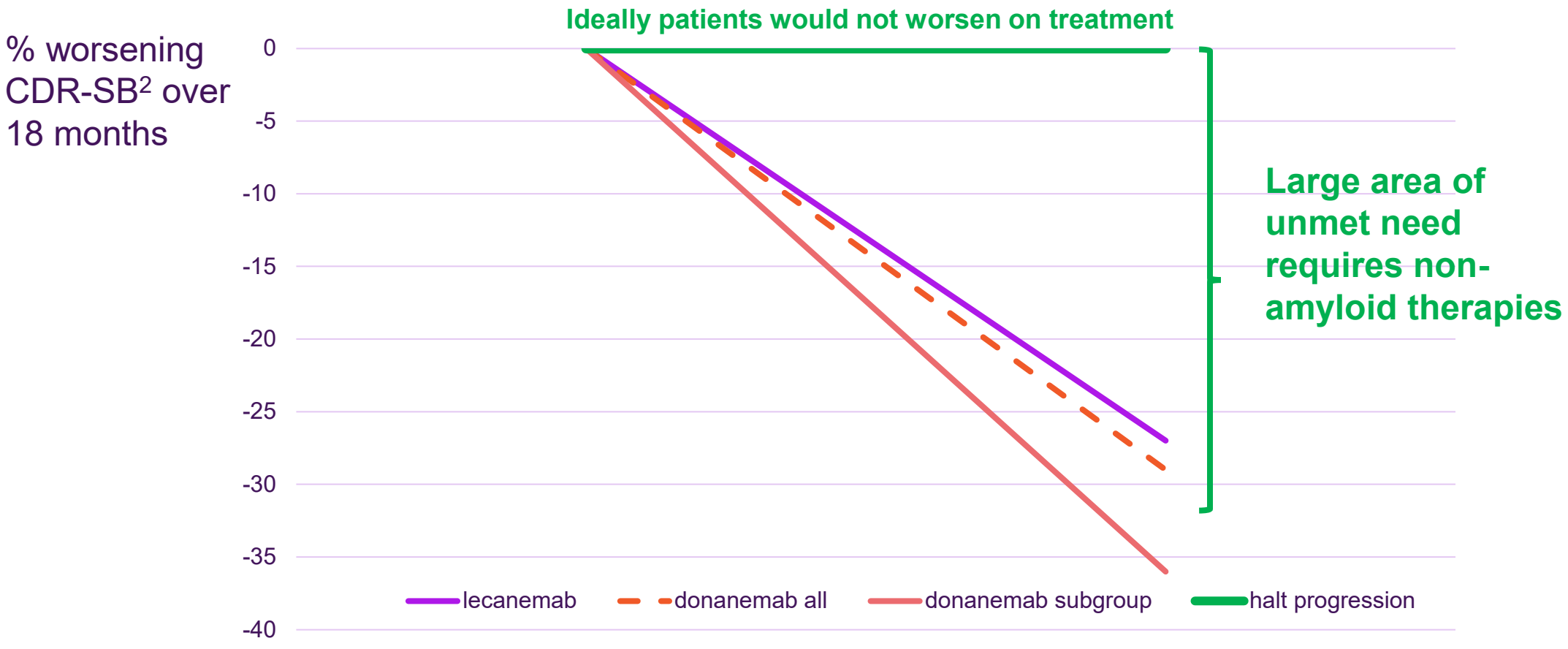
Phase 2a proof-of-concept trial in Depression/Cognitive Impairment

n=160, results H1 2024

Phase 2b confirmatory trial in mild-moderate AD

n=330, results H2 2025 (interim analysis early 2025)

Newer anti-amyloid antibodies shown to slow but not halt progression of AD[1]



Drugs targeting other mechanisms like Xanamem are needed

1. Lecanemab and donamemab are anti-amyloid antibodies given as an intravenous infusion every 2 or 4 weeks (van Dyck et al. 2022; DOI: 10.1056/NEJMoa2212948 n=1795 and Sims JR at al. *JAMA*. Published online July 17, 2023. doi:10.1001/jama.2023.13239
2. CDR-SB is an 18-point scale measuring functional status and was the primary endpoint for lecanemab and a secondary endpoint for donanemab

Newer amyloid antibodies and oral Xanamem have multiple, positive cognitive trials data[1]

Actinogen Oral Xanamem	• Safely targets **brain tissue cortisol** • 2 trials: improved attention & working memory • 1 trial: trends to reduce AD progression, improve cognition • Low drug interaction potential – good combination candidate
Eisai-Biogen i.v. infusion of lecanemab every 2 weeks	• Approved on ability to reduce **brain amyloid** • Potential to cause brain swelling and bleeding • 2 trials reduced progression modestly • Will need to be combined with other therapies
Lilly i.v. infusion of donanemab every 4 weeks until amyloid cleared	• Full approval expected ~8 months, reduces **brain amyloid** • Higher rates of brain swelling and bleeding, 3 deaths reported • 2 trials reduced progression modestly • Will need to be combined with other therapies

[1] Companies claiming efficacy based on uncontrolled data, biomarkers or imaging not included in this comparison

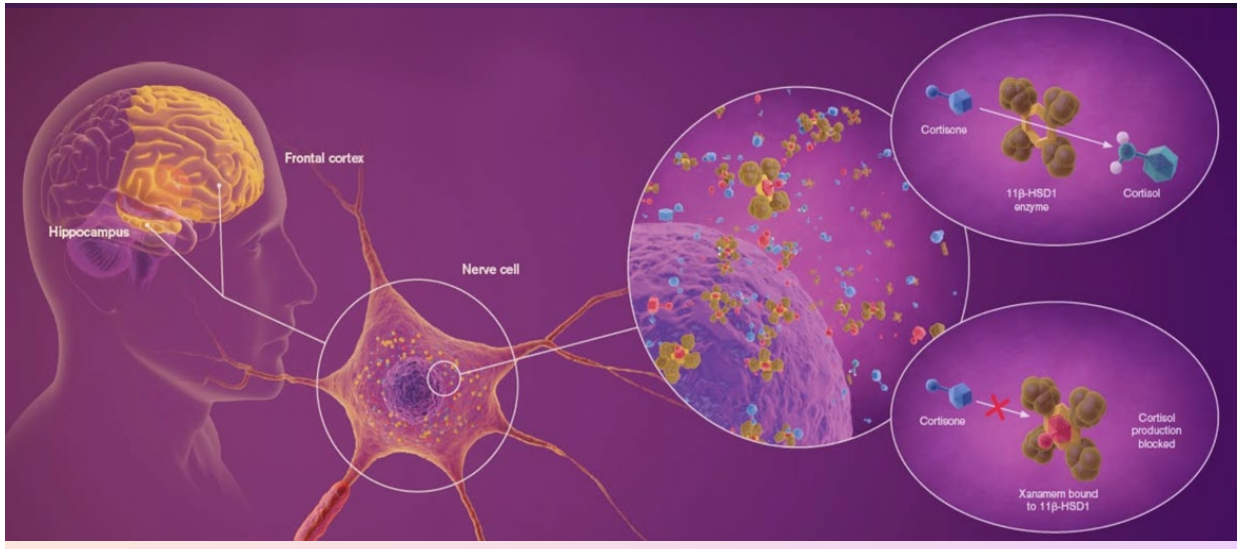
Xanamem: oral, low-dose, once-a-day treatment with a unique, non-amyloid/tau mechanism

Mouse experimental studies & clinical trials validate cortisol target for treatment of AD[1-4]

Brain penetrant 11β-HSD1 small molecule enzyme inhibitor **reduces cortisol inside brain** cells[3,4] - modulating signalling pathways and underlying disease processes

Potential to be:

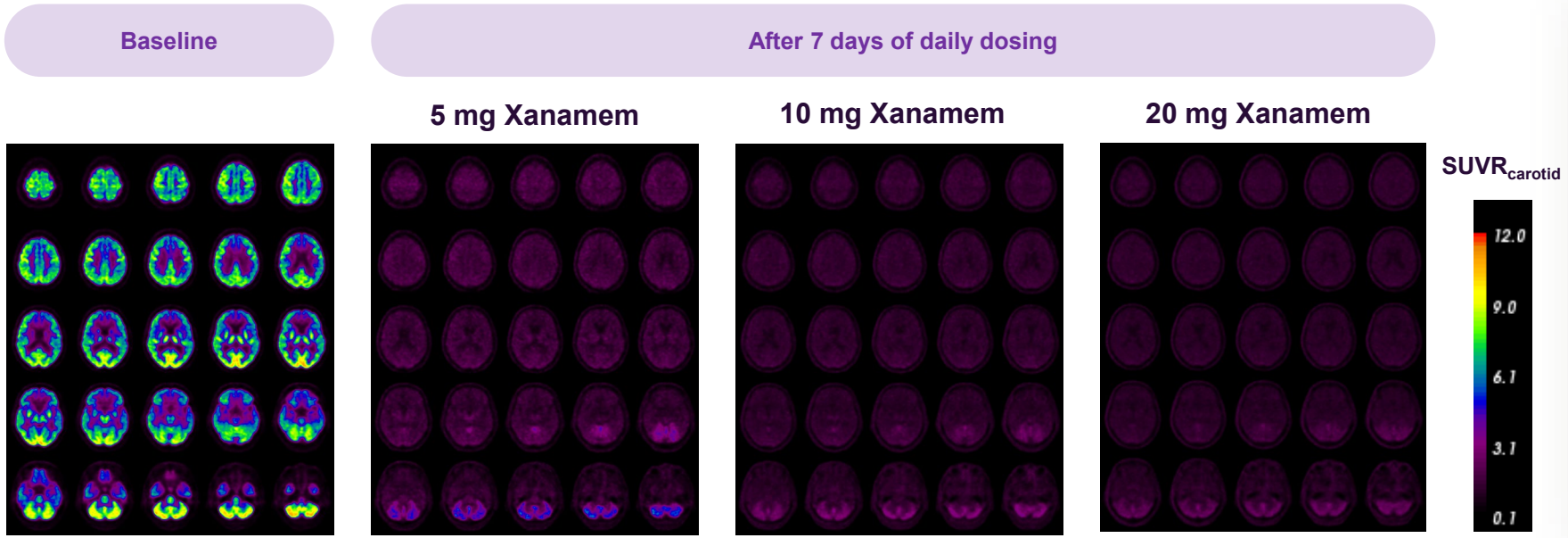
- Rapidly **cognitive enhancing**
- **Disease-modifying** (slow or halt progression) in AD[1,3]
- **Anti-depressant**



1. Sooy et al. 2015 showing effects on amyloid plaque reduction in an aged mouse model after 28 days associated with increases in insulin degrading enzyme – at 13 month cognitive protection was independent of continued amyloid deposition; 2. Popoli et al. 2011 microglial cell modulation in rats, effects on glutamate, cannabinoid and other signalling pathways; 3. Hilt, D. Oral symposium AD/PD International Conference 2023; Actinogen website: Actinogen – News; 4. based on human PET scan evidence (data on file), Webster et al. 2017 Selection and early clinical evaluation of the brain-penetrant 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) inhibitor UE2343 (Xanamem™)

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

Previous enzyme inhibitors[1] have not achieved adequate brain concentrations



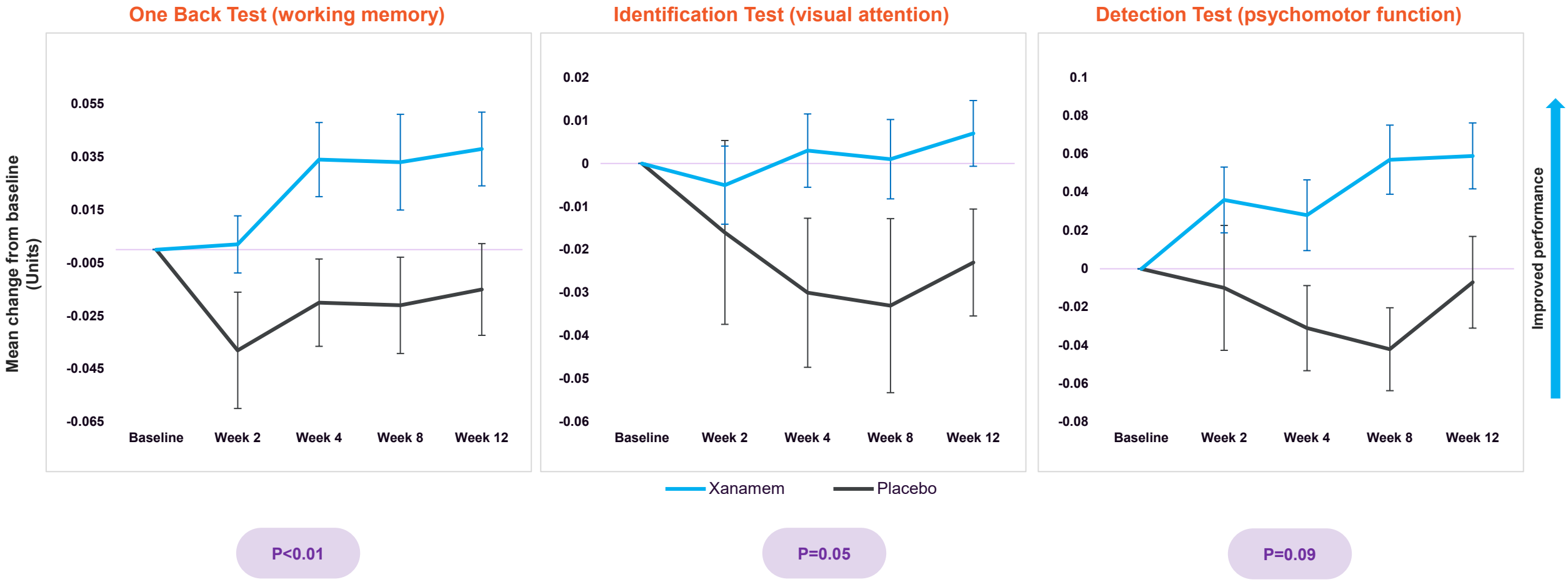
PET data[2] demonstrates that Xanamem extensively binds to the 11β-HSD1 enzyme throughout the brain, with high post-treatment effects (absence of colour) after 7 days at all doses, slightly less at a 5 mg dose.

This is consistent with full hormonal pharmacodynamic activity seen with 10 mg in clinical trials. 5 and 10 mg show excellent clinical tolerability and safety.

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.

Attention/Working Memory improved by 4 weeks*

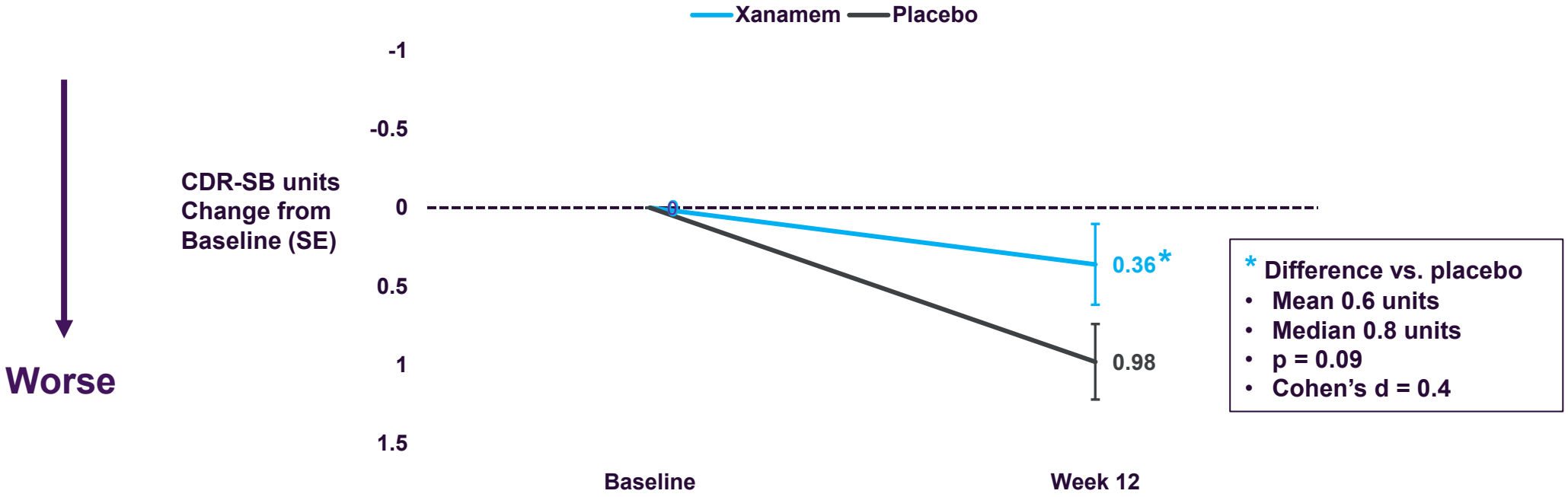
Cogstate computerized testing in cognitively normal older, 20 mg daily vs. placebo



* XanaHES trial, n = 30 Xanamem 20mg vs n = 12 Placebo; no treatment effects on three other tests of episodic memory (Actinogen data on file)

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

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

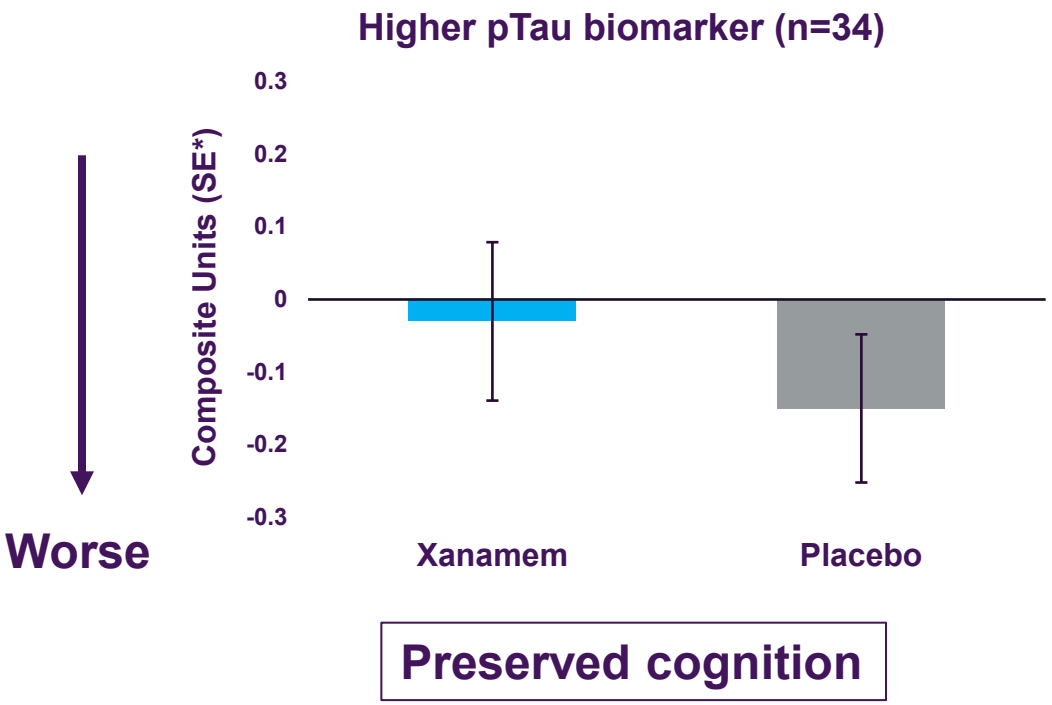


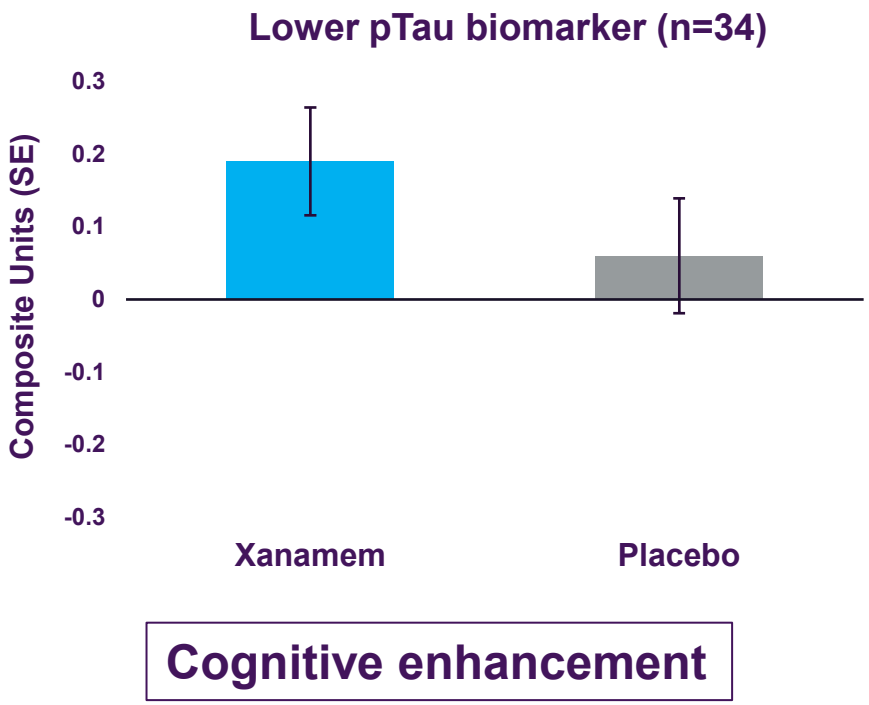
Extrapolated to 18 months effect size would be more than 3 points

* 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; 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

Cognitive composite scores suggest potential clinical benefit across dementia patient sub-types*

Positive trends in both high and low plasma pTau biomarker groups





Preserved cognition

Cognitive enhancement

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

Well-demonstrated, excellent safety profile

No emerging safety signals

TEAE term ACW0002*	Xanamem (n=91)	Placebo (n=94)	Total (n=185)
Headache	5 (5.5%)	2 (2.1%)	7 (3.8%)
Dizziness	4 (4.4%)	3 (3.2%)	7 (3.8%)
Diarrhea	1 (1.1%)	4 (4.3%)	5 (2.7%)
Fatigue	3 (3.3%)	1 (1.1%)	4 (2.2%)
Nerve conduction abnormal	1 (1.1%)	3 (3.2%)	4 (2.2%)
Somnolence	1 (1.1%)	3 (3.2%)	4 (2.2%)
Decreased appetite	2 (2.2%)	0 (0.0%)	2 (1.1%)

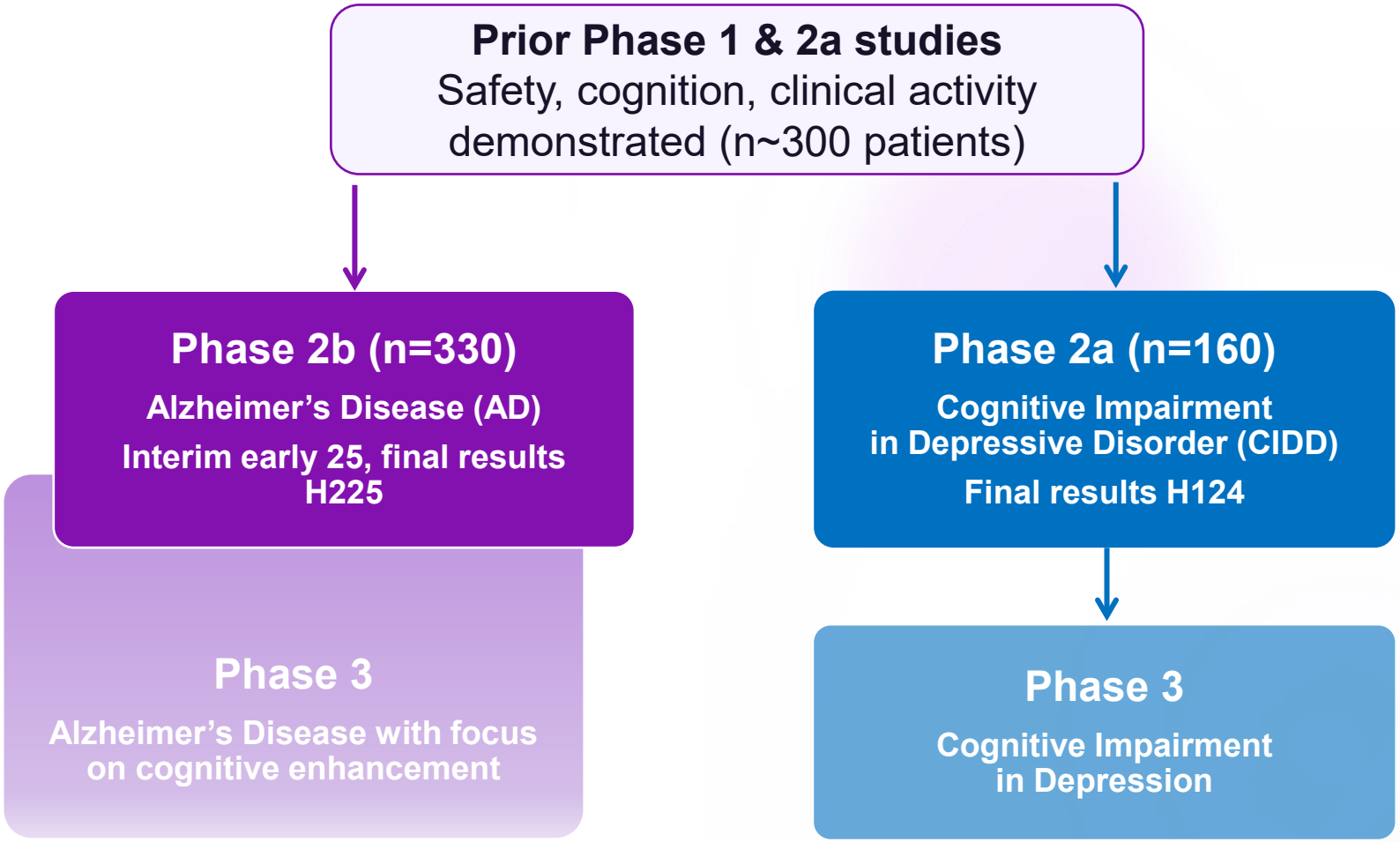
* TEAEs reported by more than one patient in any group in the largest clinical study to date

✓ No treatment-related Serious Adverse Events in clinical program

https://clinicaltrials.gov/ct2/show/results/NCT02727699?term=actinogen&draw=2&rank=3

Xanamem AD & Depression programs

Building on three independent Phase 1 and 2 studies showing safety and procognitive activity



Upcoming catalysts

2023

- **Phase 2b trial in AD to commence**
- **Results of FDA End-of-Phase 2, EMA, UK regulatory interactions**
- **Peer-reviewed publications**
- **CTAD (AD) and other presentations**

2024

- **Depression Phase 2a trial results H1**
- **Phase 2b AD interim analysis late H2 / early 2025**

2025

- **Commence Depression Phase 3**
- **Phase 2b AD results H2**

Timetable for trial results for oral AD therapies

Year	Drug or company	Target	Steve's probability of success
2023	deferiprone	Iron	Low
	TauRx	Tau*	Low
	NE3107	ERK1/2	Low
	simufilam	Filamen A*	Low-Medium
2023	**varoglutamstat**	**pglu-Aβ/QC***	**Medium**
	CT1812	Sigma-2*	Low
2024	Valiltramprosate	Amyloid form.*	Low-Medium
	LY337268	OGA*	Low
2025	**Xanamem**	**cortisol**	**Medium-High**
2026	**semaglutide**	**GLP-1**	**Medium**

* Amyloid or tau protein-related mechanisms

Xanamem is one of just a few credible oral drug candidates in development

Actinogen summary

Actinogen Medical (ASX:ACW) is developing a novel oral treatment with rapid onset of clinical activity to improve cognition, function and quality of life

Attractive disease indications and rationale

- ✓ **Strong cortisol rationale for treatment of multiple diseases**: early stages of Alzheimer's disease & other dementias, depression & related cognitive impairment; cognitive impairment in schizophrenia; many others

Favourable pharmaceutical properties

- ✓ Demonstrated target engagement in brain and HPA axis[1] in human trials
- ✓ **Low dose and cost of goods, ≤10mg**
- ✓ **Low drug-drug interaction potential** suitable for combination therapy

Substantial clinical data

- ✓ **>300 subjects or patients safely treated**
- ✓ Cognitive enhancement **activity in three placebo-controlled trials**
- ✓ Positive Phase 2a data - **clinical benefit** in biomarker-positive AD patients

Protected and funded

- ✓ Molecule in-licensed from U Edinburgh in 2014 to ASX-listed shell co. (ACW.AX)
- ✓ Key patents in place[2] ~A$100m funding for Xanamem program to date
- ✓ **Cash ~A$12.2M (Mar 23), mkt cap. ~A$70m, seeking development partners**

High functioning semi-virtual company model

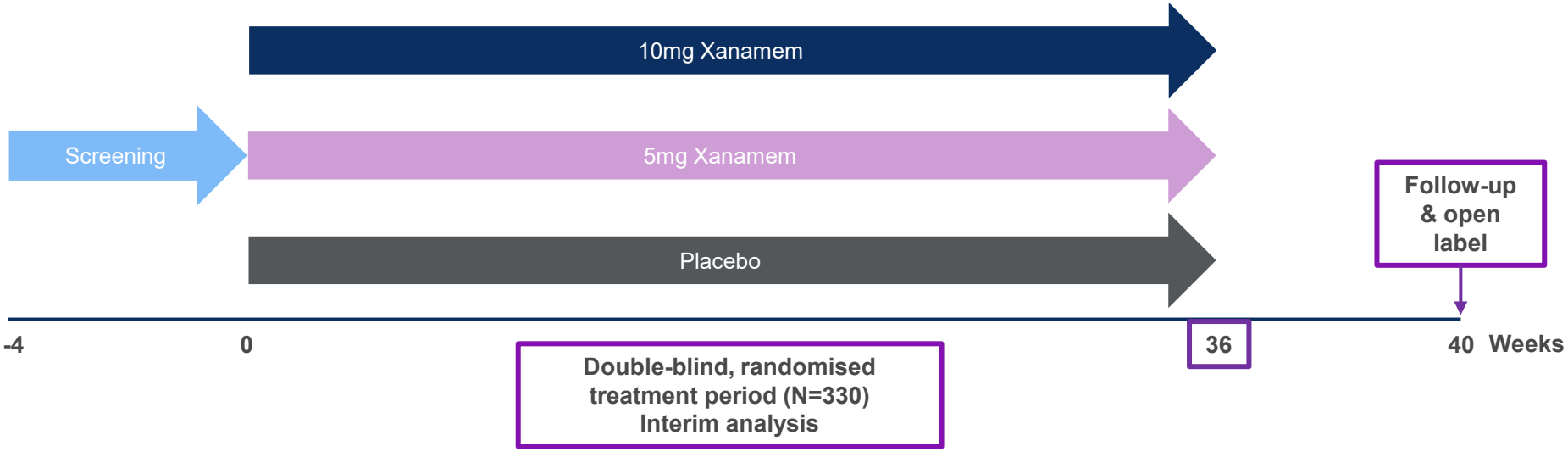
- ✓ Core team of 15 highly skilled employees based in Australia & US
- ✓ Leveraging senior consultants in various fields in Australia, Asia, UK and USA
- ✓ **Australian-based projects gain 48% as R&D cash rebate**

1. Hypothalamic-Pituitary-Adrenal axis (body's system to regulate blood levels of cortisol)
2. Composition of matter to 2031 plus 5-year extension in most countries, new patents published and in process including use and manufacturing

Appendix

XanaMIA Phase 2b trial in Alzheimer's Disease

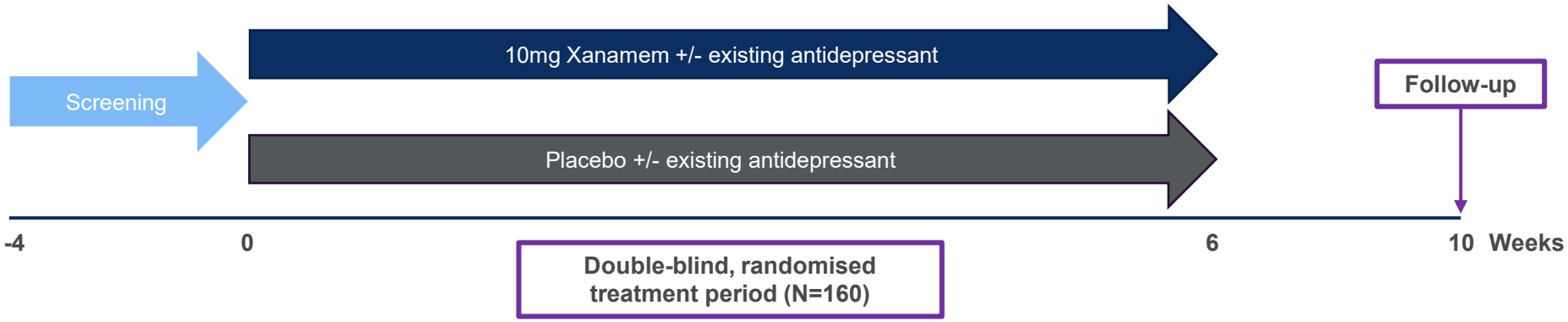
Matching patients and endpoints used in the positive Ph 2a analysis



Key inclusion/exclusion criteria	Primary Endpoints	Key Secondary Endpoints	Key Implementation Features
• Clinical diagnosis of **mild to moderate dementia** due to AD (NIA-AA, MMSE 18-26) • Blood **p-tau181** to confirm progressive AD diagnosis • Cognitive impairment test	• **Cognitive Test Battery (cognitive measures)**	• **CDR-SB (functional measure)** • **Amsterdam Activity of Daily Living** scale • Executive Function & Episodic Memory Function Composites • Care Giver questionnaire / Patient Global Improvement	• **Global** trial sites including US, AU, Asia, EU and other • **Actinogen "hands-on" operational model** • **FPI H2 CY23** • **Interim analysis late CY24/25** • **Final results CY25**

NIA-AA=National Institute of Aging - Alzheimer's Association; CDR-SB Clinical Dementia Rating Scale – Sum of Boxes

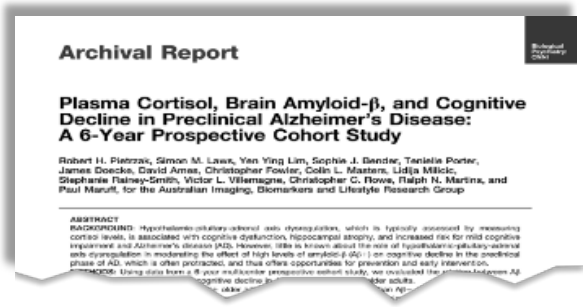
XanaCIDD proof-of-concept trial in Depression



Key inclusion/exclusion criteria	Primary Endpoints	Key Secondary Endpoints	Key Implementation Features
• Primary diagnosis of **MDD** • **Persistent depressive symptoms despite existing therapy** • **Cognitive impairment** relative to demographic norms	• **Cogstate Cognitive Test Battery Attentional Composite** (attention and working memory)	• Montgomery-Åsberg Depression Rating Scale (**MADRS**) • Executive Function Cognitive Composite • Memory Function Cognitive Composite	• **Australia & UK** trial sites • **Actinogen "hands-on" operational model** • First patient treated Dec 22 • **Final Results H1 CY24**

Many studies support the association between elevated cortisol and AD development and progression[1-9]

- Higher cortisol levels in human aging are associated with hippocampal atrophy[1,2]
- Chronic corticosteroid medication is associated with hippocampal and amygdalar atrophy and cognitive impairment[3]
- Higher plasma cortisol leads to a much greater risk of developing AD[4,5] and accelerated effect of Aβ+ on decline in global cognition, episodic memory, and attention[6,7]
- Higher CSF cortisol levels in AD patients are associated with more rapid clinical worsening and cognitive impairment[3]
- Individuals at high risk of AD due to the APOE-ε4 allele have higher CSF cortisol[9] and lecanemab showed no treatment effect in ε4/ε4 patients[10]

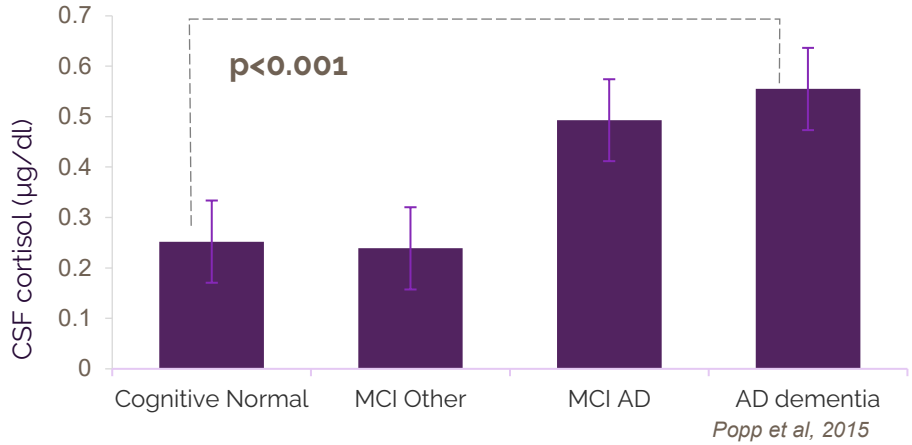

Archival Report

Plasma Cortisol, Brain Amyloid-β, and Cognitive Decline in Preclinical Alzheimer's Disease: A 6-Year Prospective Cohort Study

aibl

The Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing

MEAN CSF CORTISOL LEVELS

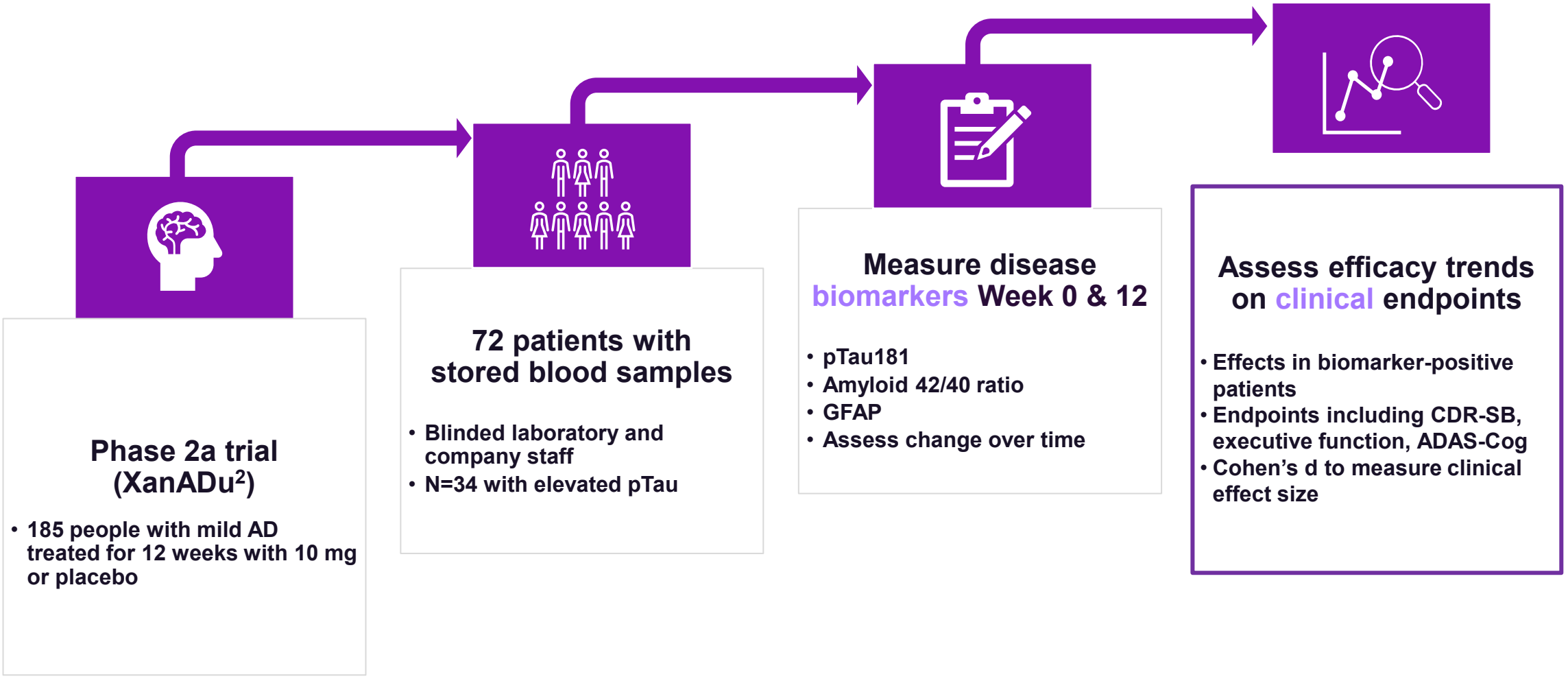


Popp et al, 2015

1. Geerlings et al., 2015, Neurology 85: 1-8; 2. Lupien et al., 1998, Nat Neurosci 1:69–73; 3. Shorey et al. 2023 https://doi.org/10.1016/j.brainres.2022.148157; 4. Lehallier et al., 2016, JAMA Neurology 73(2), 203-212; 5. Ennis et al., 2017, Neurology 88(4):371-378; 6. Pietrzak et al., 2017, Biol Psychiatry: Cognitive Neuroscience and Neuroimagery, 2:45-52; 7. Csernansky et al., 2006, Am J Psychiatry 163:2164-2169; 8. Popp et al., 2015, Neurobiol. Aging 36:601–607; 9. Peskind et.al. 2001 Neurology 56(8):1094-8; 10. van Dyck et al. N Engl J Med 2023; 388:9-2.

Methods for double-blind, prospective assessment of biomarker-positive mild AD patients in Phase 2a[1]

A simulation of the Phase 2b XanaMIA trial



1. Used a pre-specified protocol and statistical analysis plan, blinded laboratory and company personnel
2. Prior phase 2a trial completed in 2019 https://clinicaltrials.gov/ct2/show/results/NCT02727699?term=actinogen&draw=2&rank=3

Experienced Leadership and Management

Extensive drug development and commercial experience, two new key appointments in 2023

Experienced Board of Directors...

Dr. Geoff Brooke

Chairman

MBBS; MBA

- **30+ years experience** in the healthcare investment industry
- Founder and MD of Medvest Inc and GBS Ventures, Chairman of Cynata Therapeutics, Board Member of Acrux

Dr. George Morstyn

Non-Executive Director

MBBS; PhD; FRACP; MAICD

- **25+ years experience** in biotech investment and drug development
- Board member of Cancer Therapeutics and Symbio

Mr. Malcolm McComas

Non-Executive Director

BEc, LLB; FAICD; SF Fin

- **25+ years experience** in the financial services industry
- Chairman of Pharmaxis and Fitzroy River Corporation

Dr. Nicki Vasquez

Non-Executive Director

PhD

- **25+ years experience** in biopharmaceutical discovery research and development
- Chief Portfolio Strategy & Alliance Officer at Sutro Biopharma

…with a talented management team in place

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

Jeff Carter

Chief Financial Officer

B. Fin Admin; M. App. Fin; CA

Tamara Miller

SVP Product Development

M.Med Sci; BSc; MSc; PMP; CPPM

Dana Hilt

Chief Medical Officer

MD

Cheryl Townsend

VP Clinical Operations

RN, M Health Law

Dr Christian Toouli

Head of Business Development

PhD; GAICD

See full team and bios at:
https://actinogen.com.au/about-us/

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)

FREQUENCY THERAPEUTICS

- 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

ORPHAZYME

- 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

Cogstate

- 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

NUS National University of Singapore

- 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

THE UNIVERSITY of EDINBURGH

- 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

THE FLOREY · THE UNIVERSITY OF MELBOURNE · The Royal Melbourne Hospital

- 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

Cleveland Clinic

- 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

Scientific Advisory Board

Prof. Jonathan Seckl

THE UNIVERSITY of EDINBURGH

- 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

Newcastle University

- 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

THE UNIVERSITY of EDINBURGH

- 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