ASX ANNOUNCEMENT

Actinogen CEO presents to Spark Plus Biotech conference

Sydney, 24 February 2023. Actinogen Medical ASX: ACW ("ACW" or "the Company") announces that CEO Dr Steven Gourlay will present at the Spark Plus Biotech Conference in Singapore today, 24 March 2023.

The presentation is attached to this announcement and focuses on four main topics:

- Why anti-amyloid antibodies have limited utility in Alzheimer's disease
- Four clinical trials showing Xanamem® activity
- Forward planning to optimise the pathway to regulatory approvals
- Creating value from partnerships.

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 its capsule.

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease, and Xanamem has shown the ability to enhance cognition in healthy, older volunteers. 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 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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ACTINOGEN MEDICAL ENCOURAGES ALL CURRENT INVESTORS TO GO PAPERLESS BY REGISTERING THEIR DETAILS WITH THE DESIGNATED REGISTRY SERVICE PROVIDER, AUTOMIC GROUP.

Actinogen

Four trials validate Xanamem® activity & Alzheimer's Disease program

Positive Phase 2a data with large CDR-SB effect size

Dr. Steven Gourlay MBBS PhD MBA, CEO & MD

Spark Plus Biotech Day

February 24, 2023

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Actinogen and Xanamem snapshot

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

Favourable pharmaceutical properties

- ✓ Demonstrated target engagement in brain and HPA axis[1] in human trials
- ✓ **Low dose, ≤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**
- ✓ Large **CDR-SB effect** in pTau-positive mild AD of 0.6-0.8 points - Phase 2a data

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

Protected and funded

- ✓ Molecule in-licensed from U Edinburgh in 2014 to ASX-listed shell co. (ACW.AX)
- ✓ Comprehensive patents in place[2]
- ✓ **Cash position ~A$14.5M, mkt cap. ~A$180m at 31 Dec 2022**

High functioning semi-virtual company model

- ✓ Core team of 10 fulltime employees based in Australia, 25 in extended team
- ✓ Leveraging senior consultants in various fields in Australia, Asia, UK and USA
- ✓ **Australian-based operations gains 43.5% 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

Actinogen is targeting large markets with significant unmet medical need

Xanamem represents a "pipeline in a pill" as chronically elevated brain cortisol is implicated in a broad range of blockbuster indications

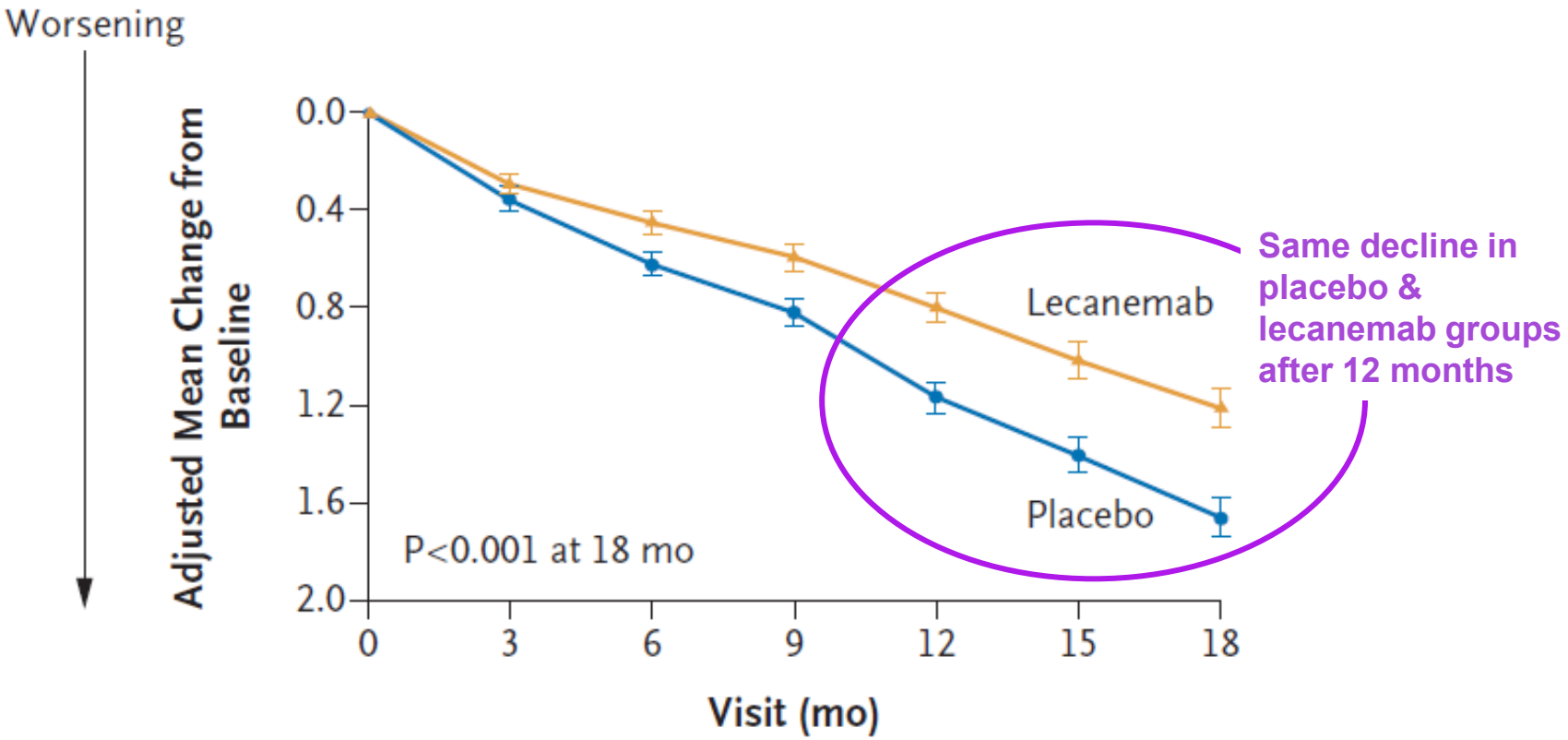
Examples of priority indications	Global Prevalence (millions)	Global Market size (billions)	Growth (CAGR)
Alzheimer's Disease	33[1]	**US$9.8 (2027)[2]**	6.27% (2022-2027)[2]
Major Depressive Disorder	280[3]	**>US$20 (2027)[4]**	7.2% (2021-2027)[4]
Cognitive Impairment Associated with Schizophrenia (CIAS)	24[5]	**>US$13 (2031)[6]**	3.7% (2021-2031)[6]
Cognitive Impairment in Bipolar Disease	46[7]	**US$6.9 (2027)[8]**	3.9% (2020-2027)[8]

Multiple major clinical and commercial opportunities

1 Alzheimer's Disease International (link)
2 IMARC Group Alzheimer's Drug Market (link)
3 World Health Organisation – Depression facts (link)
4 GM Insights Depression Report (link)
5 Research&Markets CIAS Report (link)
6 Reportlinker Schizophrenia Market Report (link)
7 https://www.singlecare.com/blog/news/bipolar-disorder-statistics/
8 Reportlinker Global Bipolar Disorder Therapeutics Report (link)

Why anti-amyloid antibody infusions are not a cure

Lecanemab slows progression <u>slightly</u> during the first 12 months but not beyond*



Same decline in placebo & lecanemab groups after 12 months

No. of Participants							
Lecanemab	859	824	798	779	765	738	714
Placebo	875	849	828	813	779	767	757

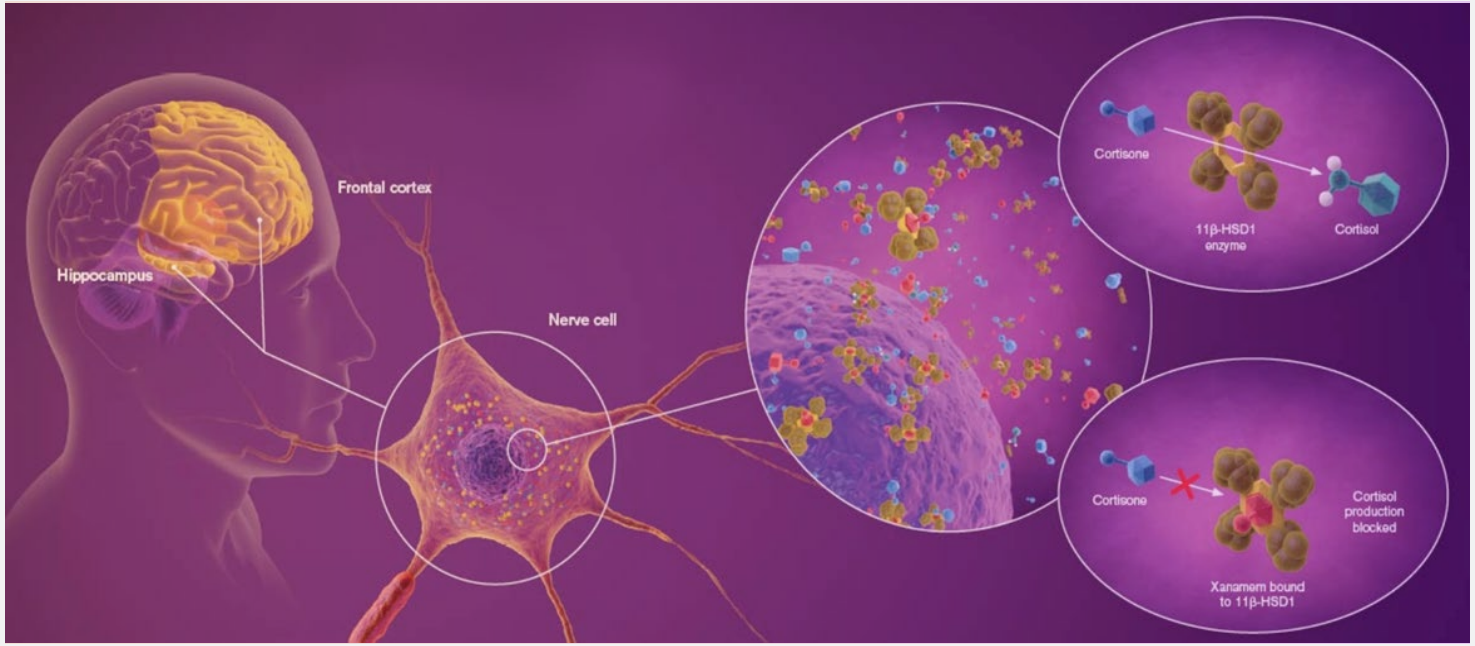
* Amyloid largely cleared by 12 months, CDR-SB effect size = 0.45 points at 18 months, van Dyck et al. 2022; DOI: 10.1056/NEJMoa2212948

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

Only known brain penetrant 11β-HSD1 small molecule enzyme inhibitor reduces cortisol inside brain cells - modulating signaling pathways and underlying disease processes[1,2]

Potential to be:

- Rapidly cognitive enhancing
- Disease-modifying (slow or halt progression) in AD
- Anti-depressant

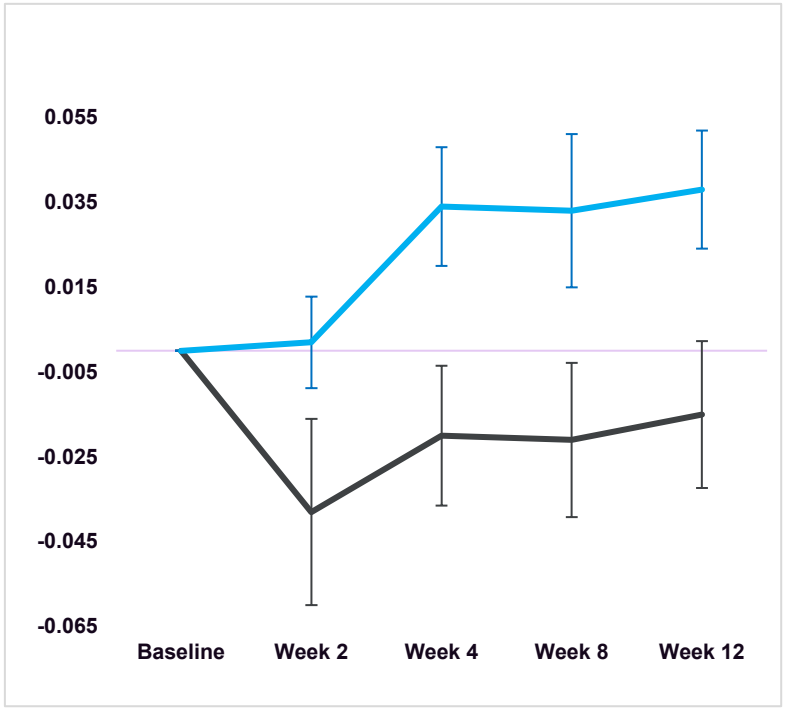


1. Xanamem® is a CNS (Central Nervous System) penetrant small molecule based on human PET scan evidence and cerebrospinal fluid (CSF) measurements
2. Sooy et al. 2015 showing effects on amyloid plaque reduction in an aged mouse model after 28 days associated with increases in insulin degrading enzyme; Popoli et al. 2011 microglial cell modulation in rats, effects on glutamate, cannabinoid and other signalling pathways

2019: Attention/Working Memory improved by 4 weeks*

Computerized cognitive testing using Cogstate system in cognitively normal older people

One Back Test (working memory)



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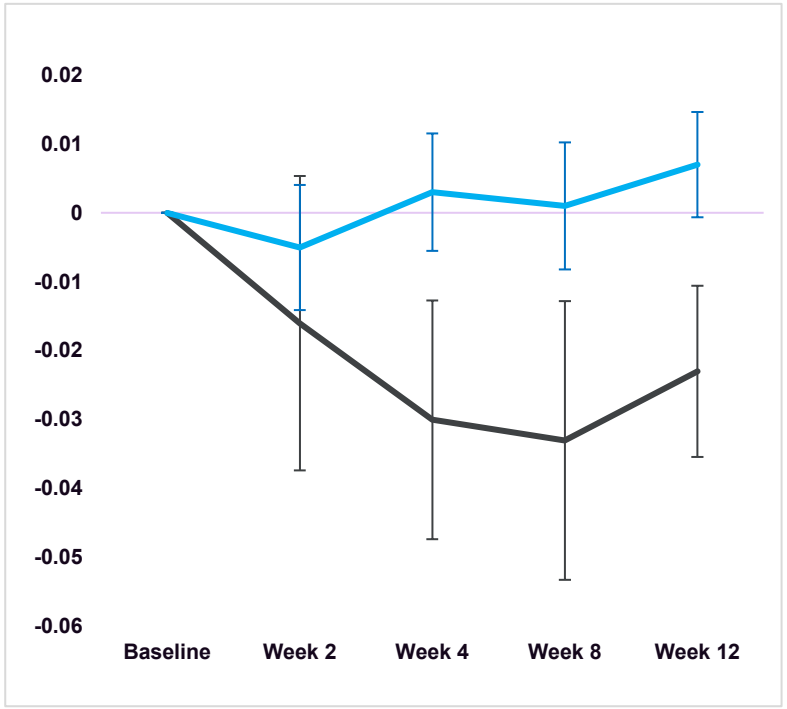
Identification Test (visual attention)



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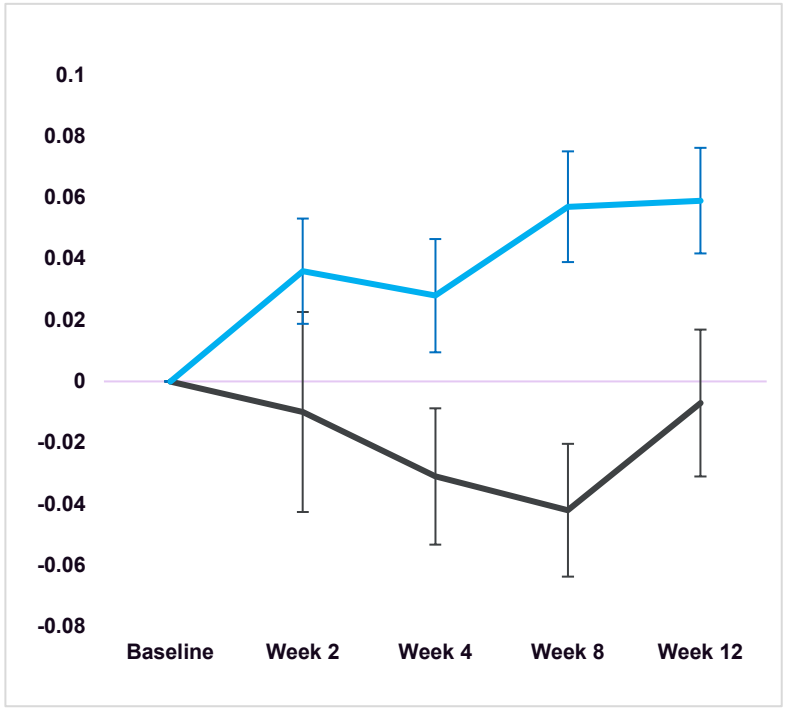
Detection Test (psychomotor function)



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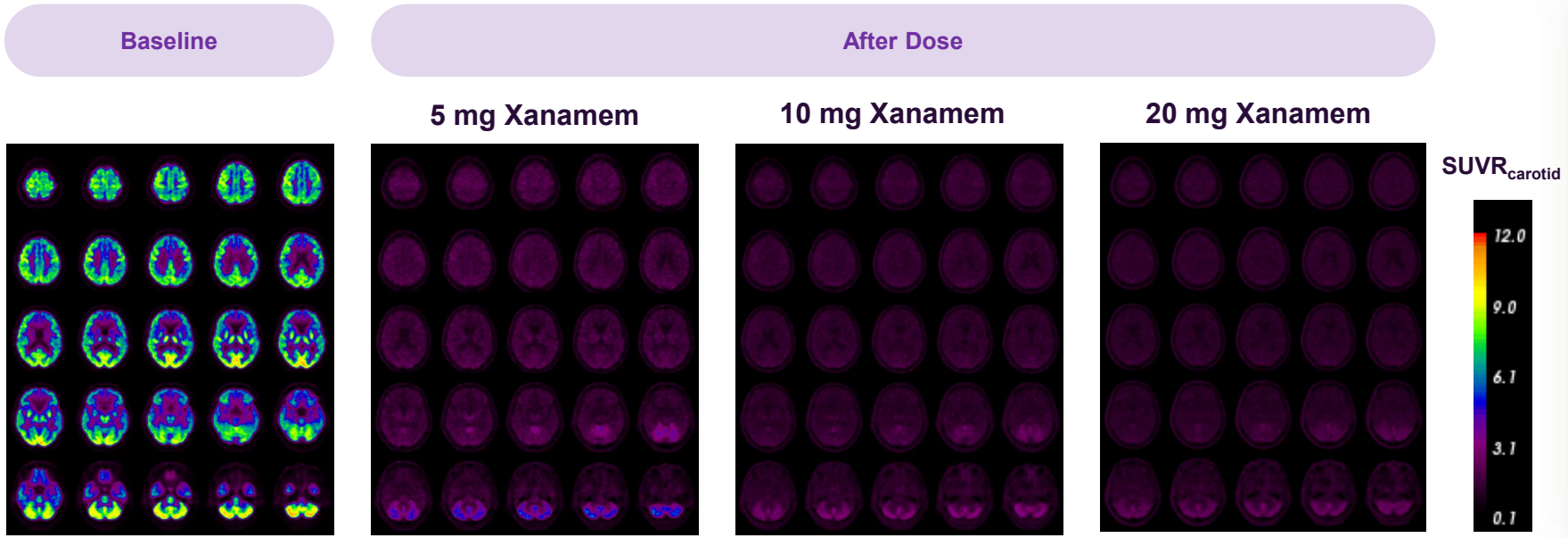
Xanamem Placebo

* XanaHES trial, n = 30 Xanamem 20mg vs n = 12 Placebo (Actinogen data on file)

2020: PET data shows full target engagement in the brain at low doses

Previous enzyme inhibitors have not achieved adequate brain concentrations



PET data 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.

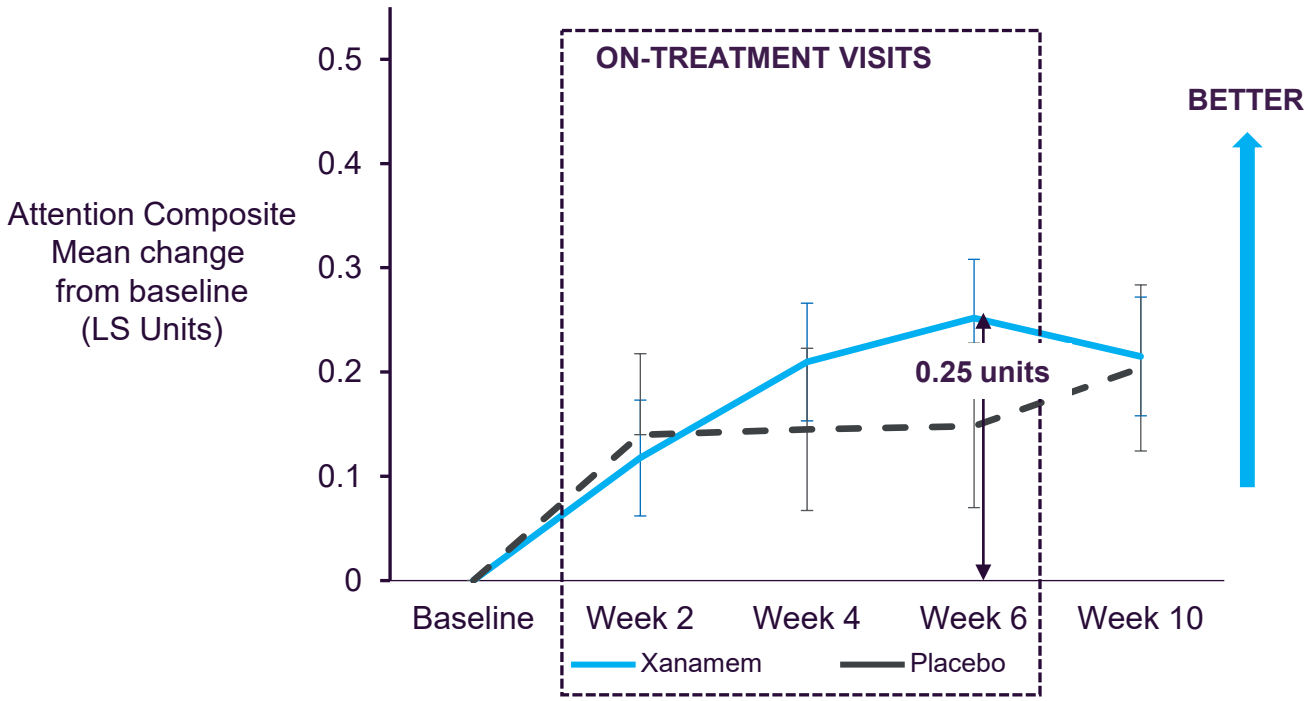
This is consistent with full hormonal pharmacodynamic activity seen with 10 mg in clinical trials. 5 and 10 mg show excellent clinical tolerability and safety.

Note: 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.

2022: Attention/Working Memory improved by 4-6 weeks* at lower doses

Computerized cognitive testing using Cogstate system in cognitively normal older people[1,2]

XanaMIA Phase 1b trial (n=107, Xanamem 10 mg & 5 mg)[1]



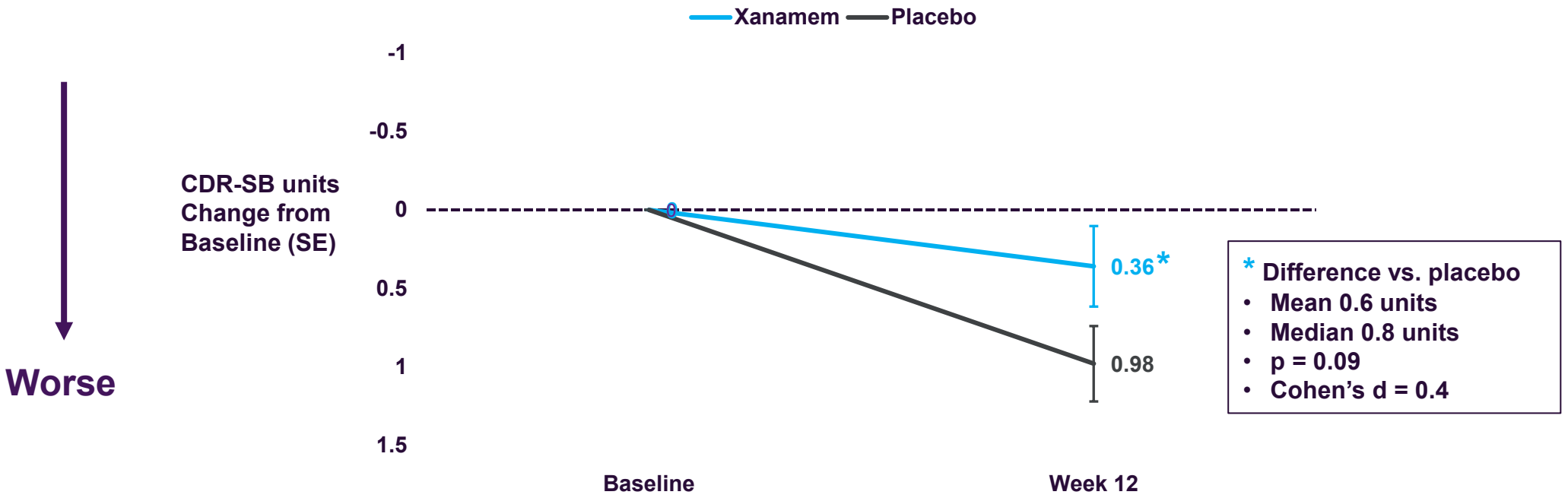
Attention composite improved in two prior independent, randomized trials

* "Attention composite" of working memory/visual attention/psychomotor speed (mean, SE)

1. XanaMIA trial in healthy volunteers aged 50-80 years: n = 36 10 mg, n = 34 5 mg, n = 37 placebo; pooled data for 5 mg and 10 mg groups; reported in 2022
2. XanaHES trial, n = 30 Xanamem 20mg vs n = 12 Placebo (Slide 8, Actinogen data on file)

2022: Topline result from pre-specified analysis in AD patients with plasma pTau181 > median of 6.74 pg/mL

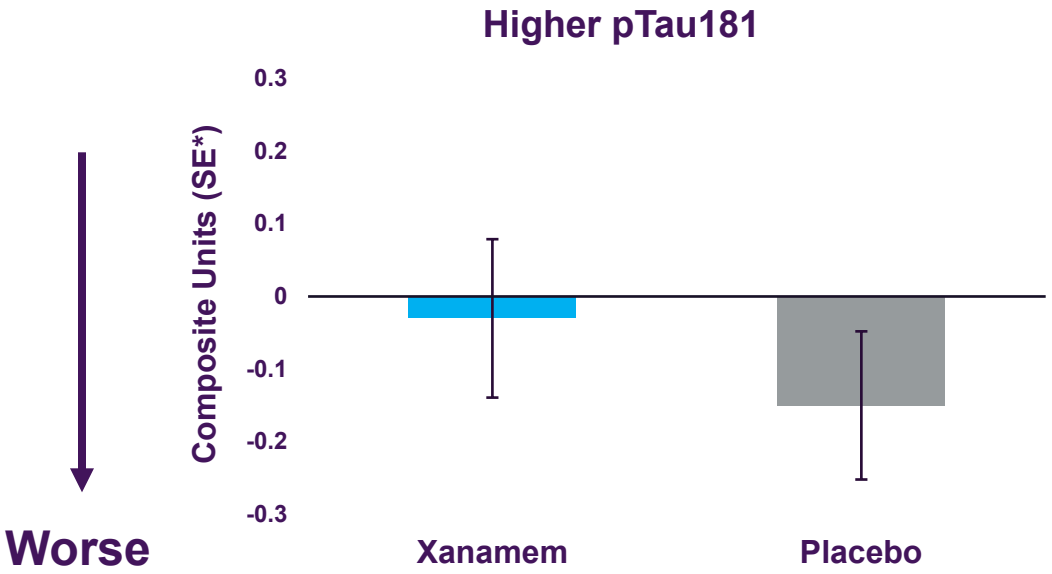
Using pre-specified protocol, statistical analysis plan and blinded biomarker analysis

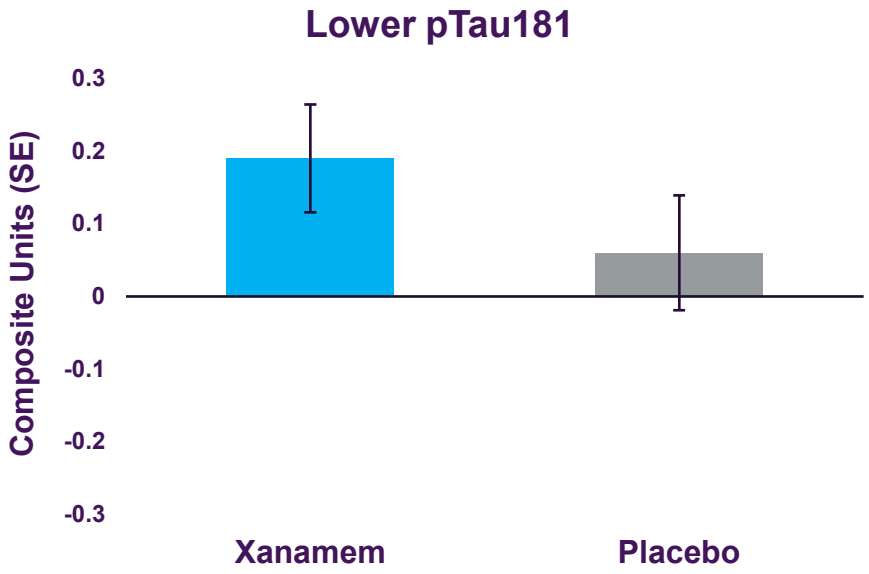


Oral Xanamem 10 mg largely prevented progression over 12 weeks

Exploratory: Change from baseline in cognitive composite

Positive trends in both high and low plasma pTau181 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

Promising safety profile

10mg daily well tolerated over 12 weeks in patients with mild AD

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

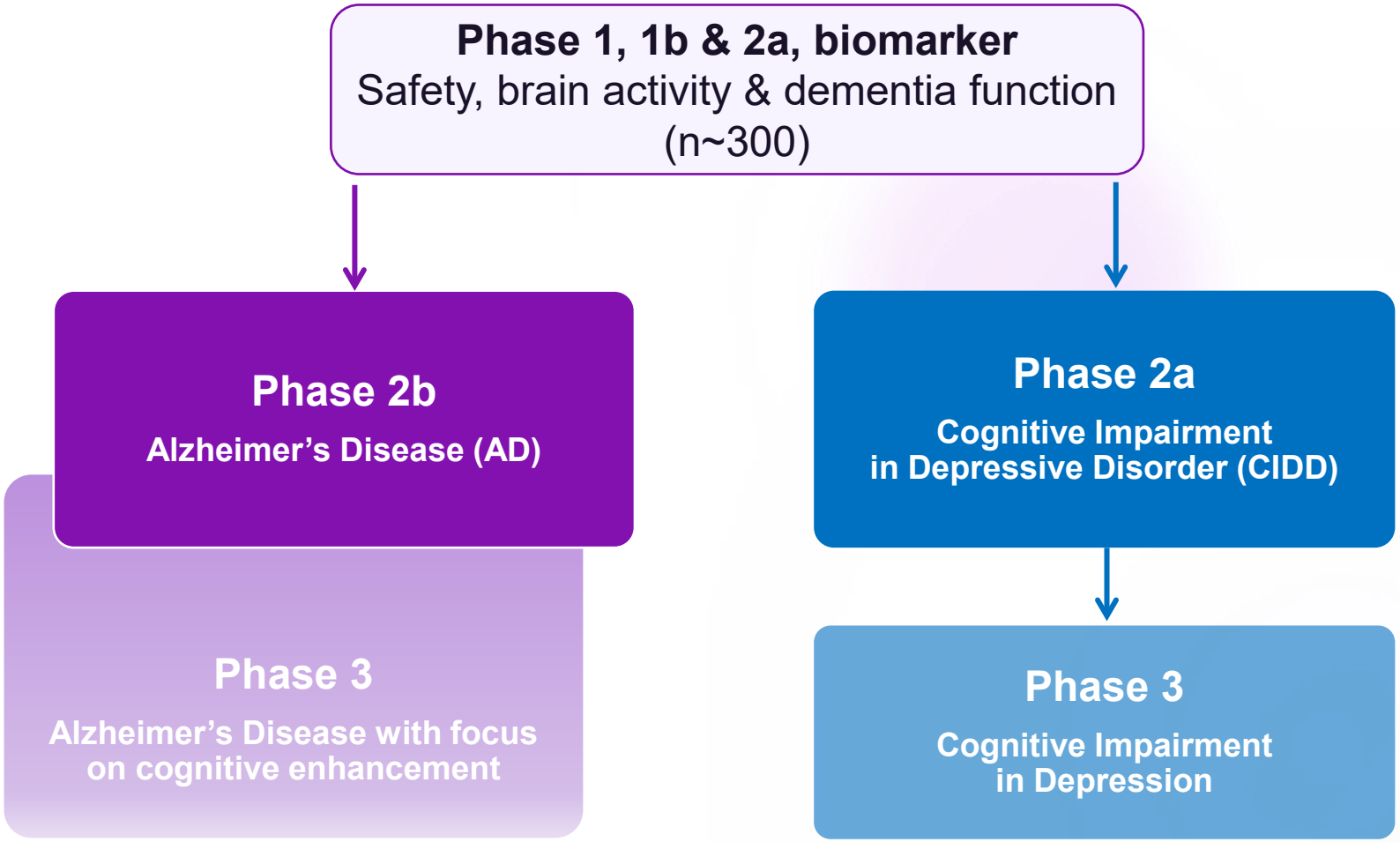
✓ No treatment-related Serious Adverse Events in whole program (n=301)

Moving forward rapidly in Cognitive Impairment in AD and Depression

Phase 2a data validate planned Phase 2b protocol in patients with Mild Cognitive Impairment / mild AD and elevated blood pTau biomarker

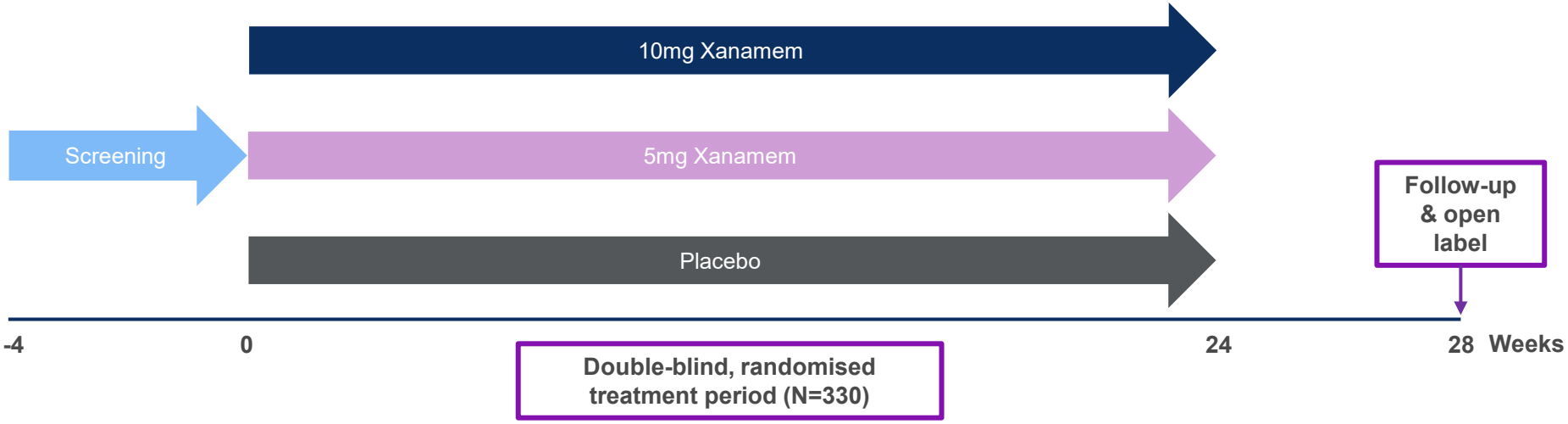
Xanamem clinical program overview

Building on four independent Phase 1 and 2 studies showing safety and activity



XanaMIA Phase 2b trial in Alzheimer's Disease

Selecting patients with early AD likely to progress during the trial

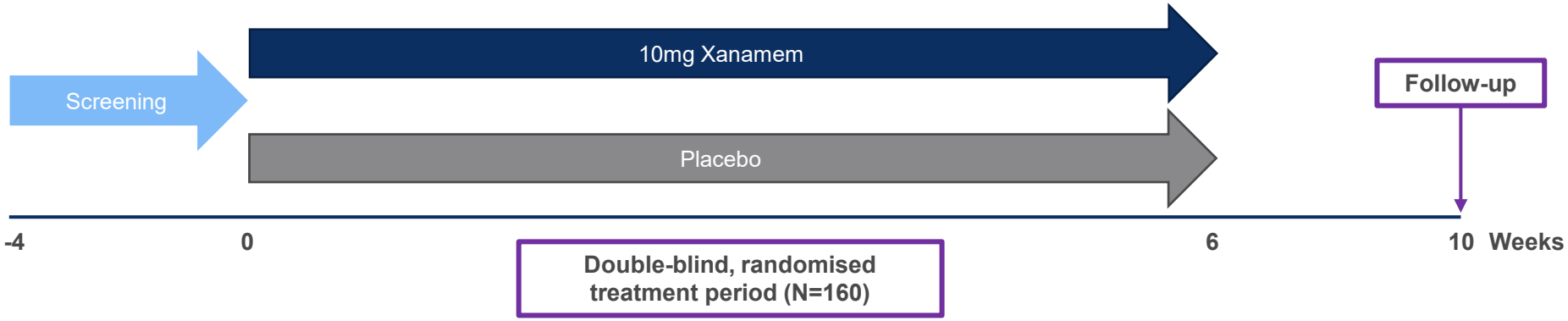


Key inclusion/exclusion criteria	Primary Endpoints	Key Secondary Endpoints	Key Implementation Features
• Clinical diagnosis of **MCI or mild dementia** due to AD (NIA-AA) • Blood **p-tau181** to confirm progressive AD • **Cognitive impairment** test	• **CDR-SB (functional)** • **Cognitive Test Battery (cognitive)**	• **Amsterdam Activity of Daily Living** scale • **Executive Function & Episodic Memory** Function Composites • Carer questionnaire / Patient Global Improvement	• **Australian trial sites plus scalable selected international locations** • **Actinogen "hands-on" operational model**

MCI=mild cognitive impairment; 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

Confirmatory trial designed to show improved cognition and improved 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	• **Australian trial sites** • **Actinogen "hands-on" operational model** • **Enrollment Commenced Dec 2022**

Xanamem Development: Strategy & Timelines

Actinogen strategy validated by new trial results

Backed by strong balance sheet and intellectual property

Accelerate clinical development

- ***Focus on cognitive enhancement***:
  - **Patients with early Alzheimer's Disease**
    - **Use pTau for patient selection**
    - **Phase 2b will use commercial tablets**
  - **Cognitive enhancement Depression** Phase 2
  - Trial **operations based in Australia** and selected other countries

Forward planning

- Scale up and optimise **manufacturing** to prepare for commercially viable, large scale production
- **Ancillary clinical and nonclinical** studies
- **Commercial** planning

Create value from partnerships

Pharma/biotech engagement

- **Actively engage large and mid-size potential partners with new results**
  - Seek value-add partnerships
  - Evaluate regional opportunities

Regulatory engagement

- Seek early **US FDA and EMA** interactions to agree endpoints for pivotal, approvable trials in AD

Two major phase 2 trials of Xanamem in 2023-24

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2022

- Two positive, independent clinical trials
- Commercial tablet manufacturing
- Started enrolment in XanaCIDD Depression trial
- FDA “clear to proceed” with 6-month Phase 2b trial in AD

2023

- XanaMIA Phase 2b AD enrollment starts Q2
- XanaCIDD enrollment ± depression results
- Peer-review publications
- Key FDA/EMA meetings

2024

- XanaMIA Phase 2b enrollment ± AD results
- Further Expand both clinical programs

Appendix

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Clinical Dementia Rating – Sum of Boxes (CDR-SB) functional endpoint to assess dementia in MCI/early-stage AD

Test domain	Impairment				
	None	Questionable	Mild	Moderate	Severe
	0	0.5	1	2	3
Memory					
Orientation					
Judgment & Problem Solving					
Community Affairs					
Home & Hobbies					
Personal Care					

Score is sum of each line i.e. score between 0 and 18 (0 = normal)

Selected glossary 1

11β-HSD1 11 beta HydroxySteroid Dehydrogenase-1 enzyme

Aβ Amyloid beta – a type of amyloid protein associated with Alzheimer's Disease, 42 and 40 are different forms

ACTH Adrenocorticotropic 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 Fibrilliary 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 Glutaminyl-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