ASX ANNOUNCEMENT

Actinogen CEO presentation to Bell Potter Healthcare Conference

Sydney, 09 November 2022. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that CEO and Managing Director Dr Steven Gourlay will present to the Bell Potter *Healthcare Conference* this afternoon.

Dr Gourlay will provide an overview of Actinogen and focus on the Company's recent positive Phase 2a data from its Alzheimer's Disease (AD) biomarker study that showed a strong clinical effect from its lead compound Xanamem® and a major validation of the 'cortisol hypothesis' for AD.

He will also outline how the Company is rapidly moving forward into its upcoming Phase 2 trials in Depression and Alzheimer's Disease.

A copy of Dr Gourlay's presentation slides is attached.

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.

® Xanamem is a registered trademark of Actinogen Medical Limited

New Alzheimer's Disease study validates Xanamem® activity & program

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

Dr. Steven Gourlay MBBS PhD MBA, CEO & MD

Bell Potter Heathcare Conference, 09 November 2022

Authorised by the Board of Directors of Actinogen Medical Limited

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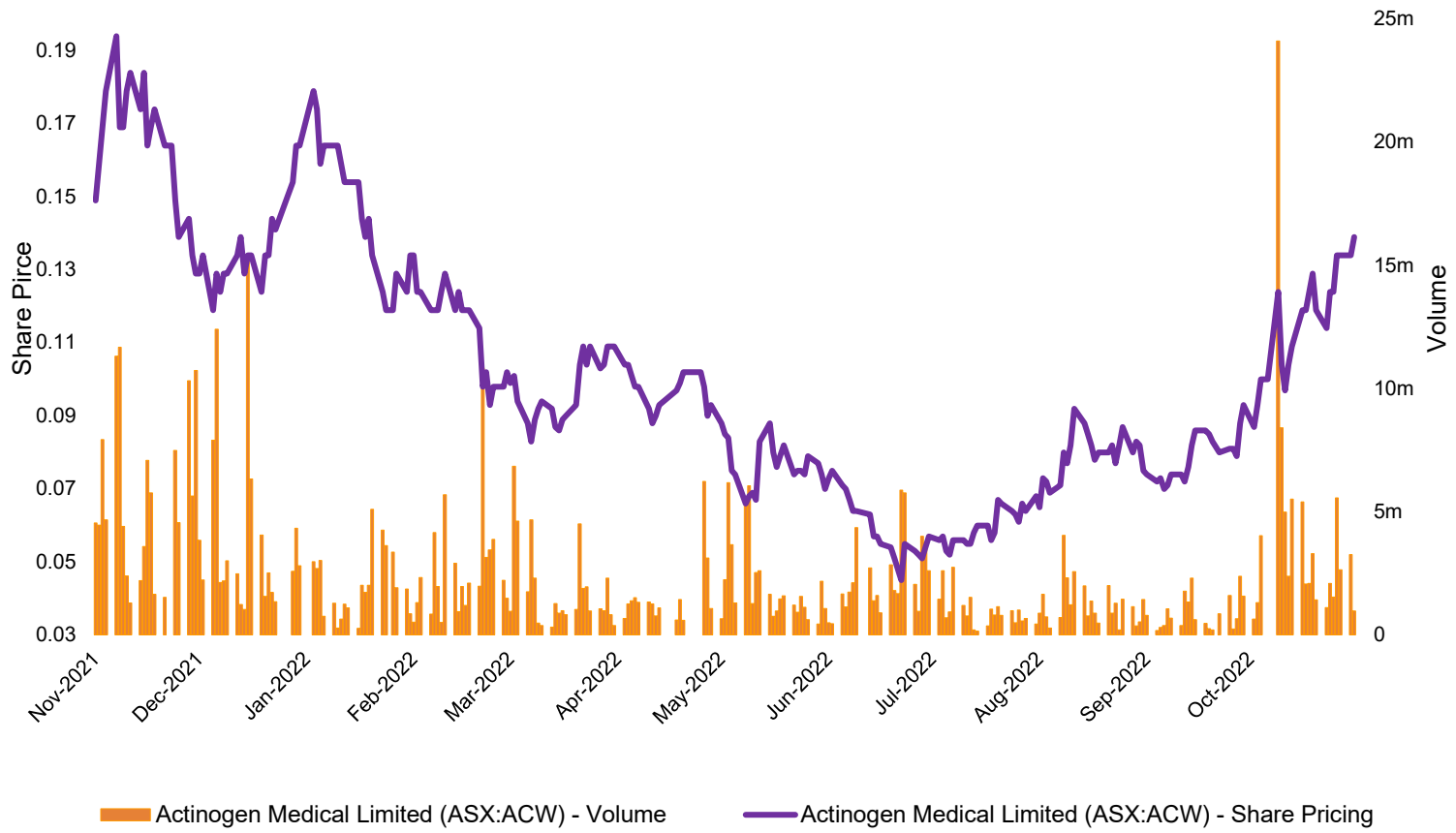
ACW top stockholders and stock price

Share price chart at 01 November 2022

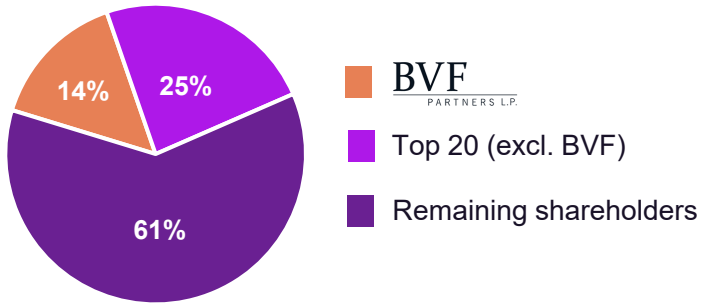


Trading Information

52 week high	A$0.20
52 week low	A$0.04
Number of issued shares	1,796M
Market capitalisation (01 Nov 2022)	A$242M
Cash Balance at 30 Sep 2022	A$17M[1]

Major Shareholders

BVF Partners	13.9%
Steven Gourlay	3.7%
Edinburgh Technology Fund	2.7%



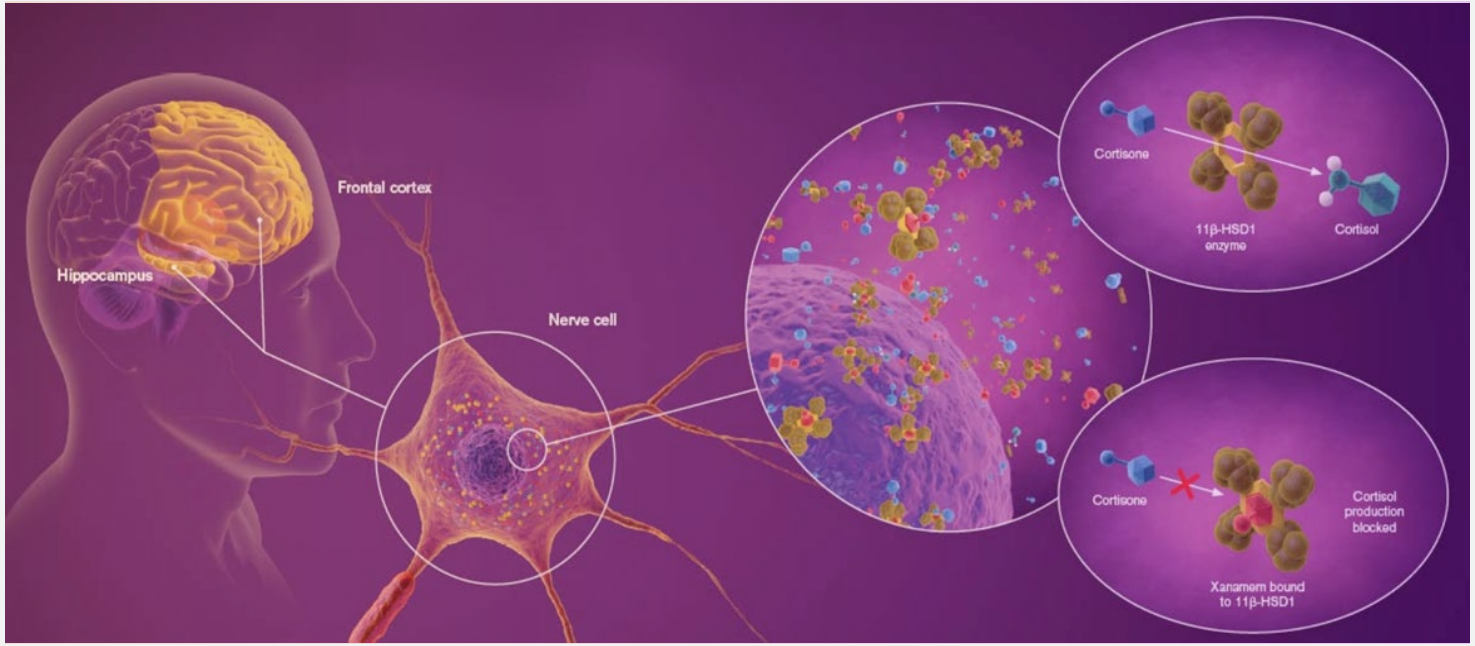
[1] Including receivable of A$4 million for R&D tax credit

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

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

Leadership and Management

Extensive drug development and commercial experience

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

…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

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

Jeff Carter

Chief Financial Officer

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

Tamara Miller

SVP Product Development

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

Dr Paul Rolan

Chief Medical Officer

MD, FRACP

Cheryl Townsend

VP Clinical Operations

RN, M Health Law

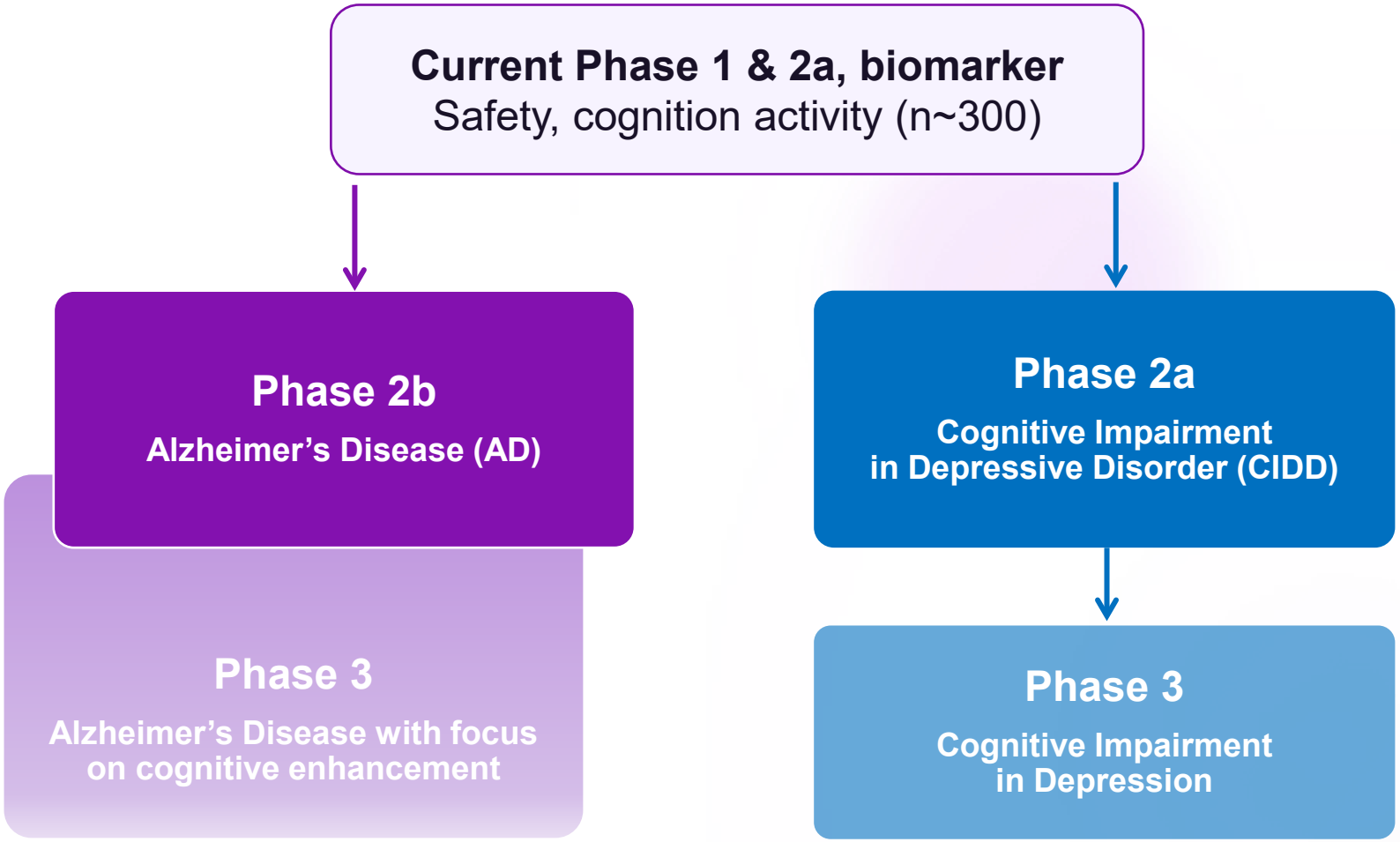
Dr Christian Toouli

Head of Business Development

PhD; GAICD

Xanamem Phase 2 & 3 program

Building on four independent Phase 1 and 2 studies showing activity



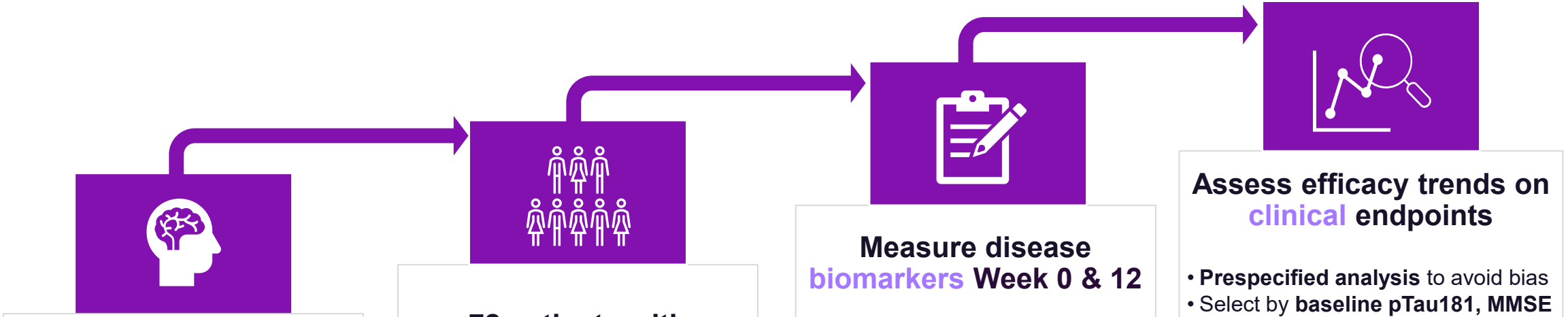
Previously: evidence of Xanamem activity in cognition from multiple sources

- ✓ **In animals**
  - ✓ **Protection against cognitive decline in animal model of AD using a Xanamem analogue independent of amyloid plaque**
- ✓ **In humans**
  - ✓ **PET scan study showing high levels of target binding at doses of 5 mg and above**
  - ✓ **Consistent target engagement measured by ACTH response**
  - ✓ **XanaHES trial in cognitively normal older volunteers – Cogstate attention & working memory**
  - ✓ **XanaMIA trial in cognitively normal older volunteers – Cogstate attention & working memory**

Human and animal data support Xanamem activity at doses of 5 to 10 mg daily

Phase 2 blood biomarker study design & methods

Uses a pre-specified protocol and analysis plan to avoid bias



Phase 2a trial (XanADu)

- **185 people with mild AD** (MMSE 20-26)
- No amyloid imaging or biomarkers
- Placebo-controlled
- 12 weeks
- 10 mg Xanamem vs. placebo

72 patients with stored blood samples

- Available plasma stored at -80°C
- Evaluated by expert biomarker laboratory blinded to treatment assignment

Measure disease biomarkers Week 0 & 12

- **pTau181**
- **Amyloid 42/40 ratio**
- **GFAP**
- **tTau (insufficient volume)**
- **NfL (insufficient volume)**

Assess efficacy trends on clinical endpoints

- **Prespecified analysis** to avoid bias
- Select by **baseline pTau181, MMSE and amyloid ratio levels to reassess** efficacy
- Focus on **endpoints most sensitive to change** in a MCI/mild AD population (**CDR-SB**)

Creates valuable data relating to patient selection and efficacy in a mild AD population

Clinical Dementia Rating – Sum of Boxes (CDR-SB)
functional endpoint to assess dementia in 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)

Xanamem doubled rate of disease stabilization on FDA-approved CDR-SB endpoint

Response analysis in pTau-positive patients with "real AD" likely to progress

Twice as many patients in the Xanamem group had stable or improved disease compared with placebo[1]

56% of patients treated with Xanamem were stable or improved vs. 28% in placebo

Large effect size represents a 60-80% relative reduction of disease progression vs. placebo

Xanamem protected the majority of patients from progression

1. Where CDR-SB decreased or was unchanged - Xanamem 9 of 16 (56%) vs. Placebo 5 of 18 (28%)

Bedside cognition test (MMSE) shows Xanamem effect measurable in more severe dementia

More clinically impaired subgroup

	N	Change in MMSE score				
Group		Desired change	Xanamem	Placebo	Cohen's d	p value
MMSE 20-23 (mean)	46	Up	1.7	-0.3	0.93	0.02
MMSE 20-23 (median)	46	Up	2.0	-1.0	-	-

Clinically & statistically significant effect size of MMSE +2.0 to 3.0 units

Efficacy conclusions

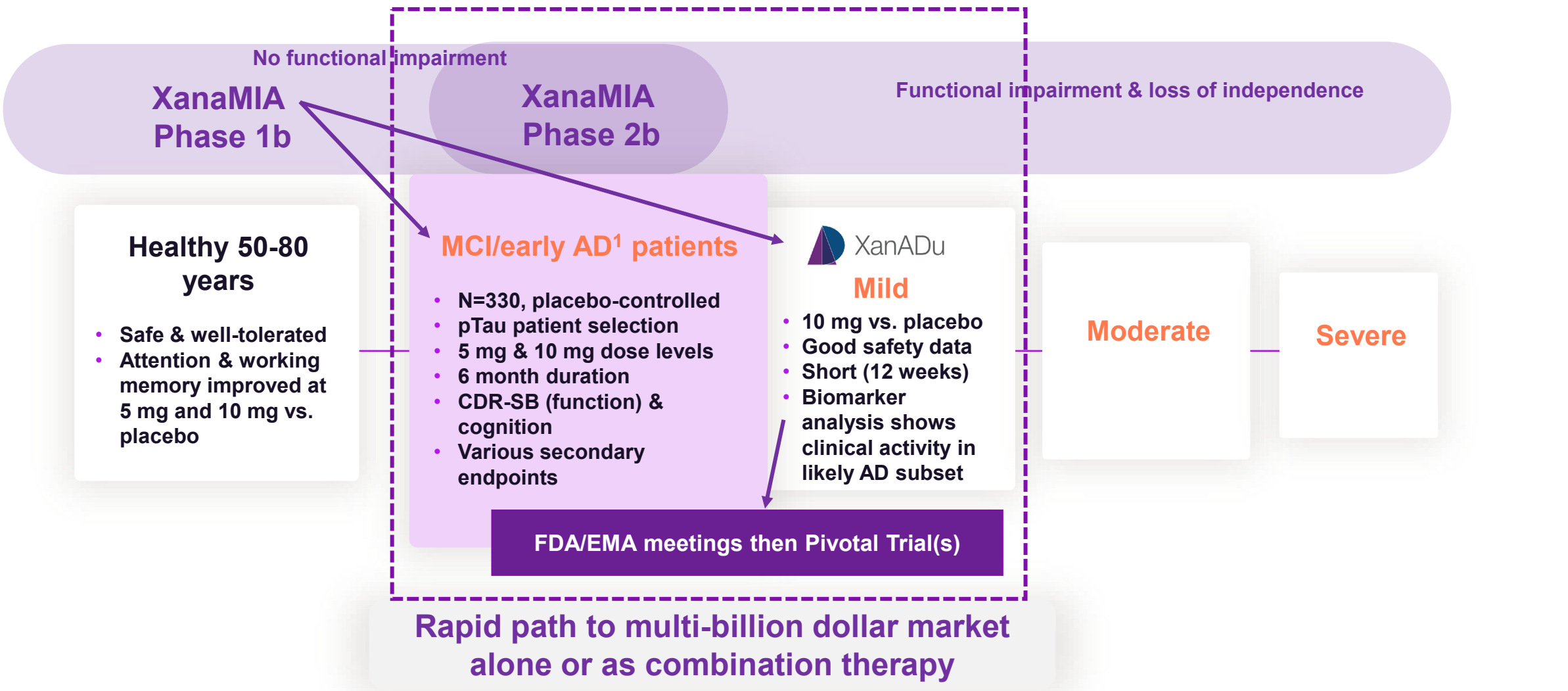
This analysis validates and de-risks the AD program by showing:

- ✓ **Clinical activity of Xanamem in mild AD patients**
- ✓ **Large clinical effect size**
- ✓ **Utility of blood pTau levels to select suitable patients for next Phase 2b trial**
- ✓ **Utility of CDR-SB to measure the benefit of Xanamem in future trials**
- ✓ **Potential utility of tests of executive function in future trials**
- ✓ **Complements positive prior trial findings on attention & working memory**

Moving forward rapidly in Cognitive Impairment in AD and Depression

Biomarker data validate planned Phase 2b protocol in Mild Cognitive Impairment / mild AD with positive blood pTau

Focus on speed to market as a cognitive enhancing treatment



1. Mild Cognitive Impairment (MCI): memory, executive function deterioration with retained functional abilities; very mild AD with some functional impairment

Science Behind the Xanamem Depression Program

- ✓ 80-90% report neurocognitive symptoms[1]
- ✓ Cognitive symptoms often persist during remission[1]
- ✓ Elevated cortisol associated with severe, melancholic depression[2]
- ✓ Cortisol associated with treatment outcomes, relapse, & cognition[3]
- ✓ Positive effects with GR receptor antagonism with mifepristone[4]
- ✓ Meta-analysis of clinical cortisol approaches[5]
- ✓ Xanamem & improved human cognition[6]

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 biopolar disorder, Young et al. 2004; Evidence from clinical studies with CRH_1 receptor antagonists, Holsboer & Ising 2008
5. Meta-analysis of prior trials aimed at reducing cortisol, Ding et. al 2021
6. Xanamem placebo-controlled trial working memory & attention (Actinogen data on file)

Market characteristics of Major Depressive Disorder (MDD)

Actinogen

MDD is common[1,2]

~5% prevalence globally, 1 in 7 lifetime risk

Neurocognitive symptoms are a typical feature (>80%)[3]

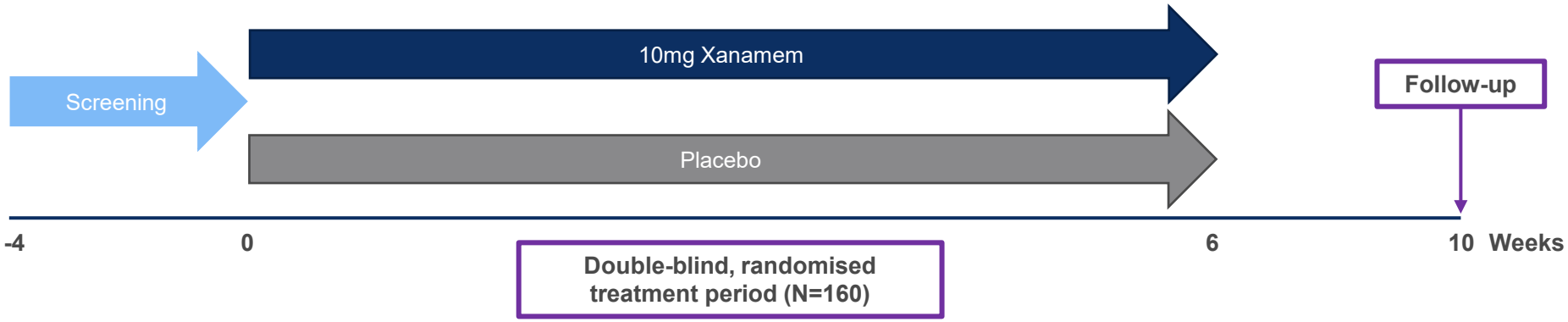
Difficulty thinking and concentrating, unable to make decisions

Only one anti-depressant has a cognitive benefit in its label

Vortioxetine sales US$500m[4]

1. World Health Organization, Depression. 2021.
2. Kessler & Bromet 2013
3. Conradi et al. 2011, *Psychol Med,* 41(6):1165-74.
4. Lundbeck financial reports 2020

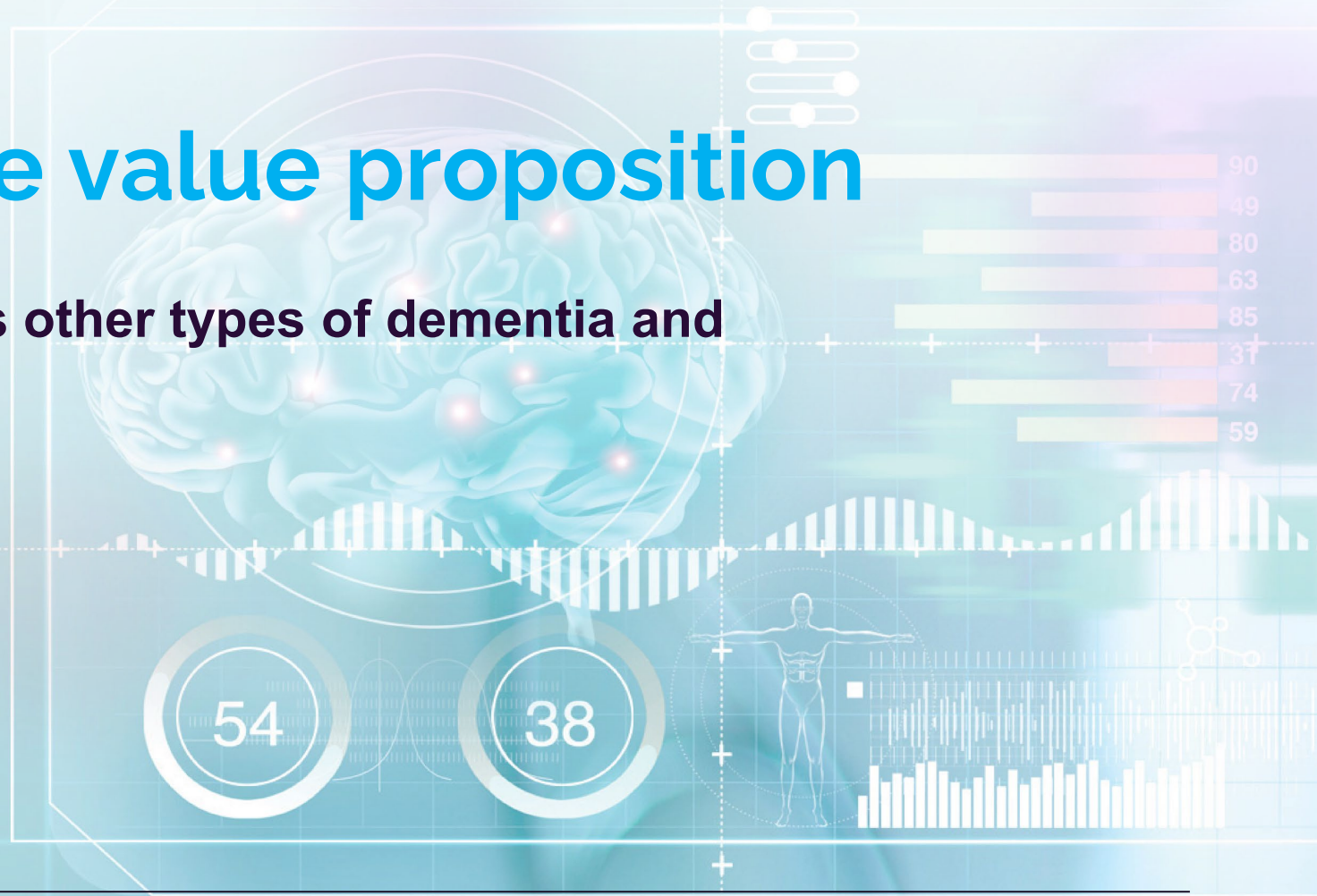
XanaCIDD trial design & implementation model



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 CTB 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** • **First patient enrollment planned for 2022**

Xanamem's unique value proposition

Many other opportunities such as other types of dementia and neuropsychiatric conditions



Actinogen has the only non-amyloid mechanism drug in development with credible cognitive data

It is one of only three worldwide AD clinical trial programs for an oral medication with credible cognitive activity data

Mechanism	Stage	Cognitive endpoint	Company market cap. ($AU)[1]
Oral Xanamem to lower brain **cortisol** (**Actinogen**)	Phase 2	Cognitive test battery, **CDR-SB, NTB**	230 million
Oral inhibition filamin A to stop Aβ42 **amyloid** signal to TLR/α7nicR (**Cassava** Sciences)	Phase 3	Cognitive test battery	2.3 billion
Oral QPCT inhibitor to prevent toxic **amyloid** formation (**Vivoryon**)	Phase 2	Cognitive test battery	280 million

Xanamem is unique with 3 independent trials now showing cognitive and clinical benefits relevant to AD and other diseases

1. at 1 Nov 2022

The Xanamem opportunity in depression is large

Current anti-depressants

work slowly (3 weeks) and initial suicide risk

do not target cognition

multiple adverse effects
blood pressure, sexual function, appetite…

Xanamem improves cognition quickly

Xanamem may improve both depression and cognitive impairment

Xanamem Strategy & Timeline

Actinogen strategy validated by new 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

Xanamem timeline & catalysts

2022

- October **multiple partnering presentations of new results**
- November **CTAD XanaMIA presentation**
- Trial **enrollment starts for XanaCIDD** trial in Depression
- Key global **regulatory submissions** in AD with FDA, EMA, other
- Phase 2b XanaMIA **AD trial preparation**

2023

- **Partnering discussions**
- **XanaMIA Phase 2b** enrollment starts H1
- **XanaCIDD** enrollment ± results
- **Presentations & publications**

2024

- XanaMIA **Phase 2b results**
- **Expand Cognitive/Depression** program
- **Expand Alzheimer's Disease** program

Appendix

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

GFAP Glial Fibrilliary Acidic Protein – a marker of microglial cell activation in the brain

Filamen A a protein believed to relate to amyloid toxicity

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