



## ASX ANNOUNCEMENT

### ACW CEO presents at Sachs 15<sup>th</sup> Annual European Life Sciences Conference

**Sydney, 1 March 2022.** Actinogen Medical ASX: ACW (“ACW” or “the Company”) CEO Dr Steven Gourlay will give a virtual presentation to the Sachs 15th Annual European Life Sciences CEO Forum for Partnering & Investment conference today.<sup>1</sup>

Dr Gourlay will also have the opportunity to conduct virtual business development and other stakeholder meetings during the main conference days, 1-2 March, through to the conference close on Friday 4 March. The information used for Dr Gourlay’s presentation and meetings is attached to this announcement.

The focus of Dr Gourlay’s presentation and meetings is to update the industry on recent developments in the Company’s clinical development pipeline, including:

- **Completion of the last patient visit in the XanaMIA Part A trial in Mild Cognitive Impairment (MCI) due to Alzheimer’s Disease (AD) in February 2022, with expected cognition results timeline narrowed from Q2 2022 to April 2022**
- **Retrospective analysis of the effects of Xanamem® on “disease modifying” biomarkers using stored samples from the prior Phase 2 study in mild AD, with results expected in H2 CY2022**
- **Expansion of the Phase 2 XanaFX clinical trial for patients with Fragile X Syndrome (FXS) to include sites in North America and a new 5mg dose group, with planned enrolment increased from 50 to 75. The trial is commencing following receipt of US FDA IND approval in November 2021, and results are expected in 2023**
- **Selection of Major Depressive Disorder (MDD) as the third indication for Xanamem trials, based on a strong scientific rationale, with a randomised phase 2 clinical trial scheduled to commence in 2022. Results are expected in 2023.**

**Dr Steven Gourlay, Actinogen CEO and MD, commented:**

*“We are delighted to update potential pharmaceutical industry partners on our expanded clinical development pipeline and its multiple near and medium-term milestones.*

*“It is pleasing to see strong ongoing interest and activity in the sector at the Sachs Associates European Life Sciences conference. This is especially true of the Alzheimer’s Disease field that was boosted by the 2021 accelerated approval by the FDA of the anti-amyloid antibody, Aduhelm.*

<sup>1</sup> The fully virtual conference will be held in the Central European Time Zone.

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*“Actinogen is actively exploring the effects of its lead molecule, Xanamem, on its ability to improve cognition in a range of diseases.*

*“Actinogen’s clinical development pipeline is designed to fulfil our vision of making a material difference to the quality of life for people and their families living with serious neurological conditions like Alzheimer’s Disease, Fragile X Syndrome, and Depression.”*

## 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 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.

We are currently developing our lead compound, Xanamem®, as a promising new therapy for Alzheimer’s Disease, Fragile X Syndrome, Depression and other neurological diseases where reducing cortisol inside brain cells could have a positive impact. 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 works by blocking the production of intracellular cortisol 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, potentially linked to cognitive impairment and anxiety in Fragile X Syndrome, and cognitive impairment in Depression and other diseases.

The Company has studied 11β-HSD1 inhibition by Xanamem in more than 300 volunteers and patients, so far finding a statistically significant improvement in cognition over placebo in healthy, older volunteers. A series of Phase 2 studies in multiple diseases is being conducted to further confirm and characterise 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.**



# Sachs 15th Annual European Life Sciences CEO Forum

**Dr. Steven Gourlay MBBS PhD MBA: CEO & MD, CMO**

**March 1-2, 2022**

**NON-CONFIDENTIAL**

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**Actinogen is a neurotherapeutics developer realising a revolutionary therapy so neurology patients and their families can live their best lives**

CTscan

Sc 11  
FFEM  
SI 19  
Diffuse axonal injury

MRI



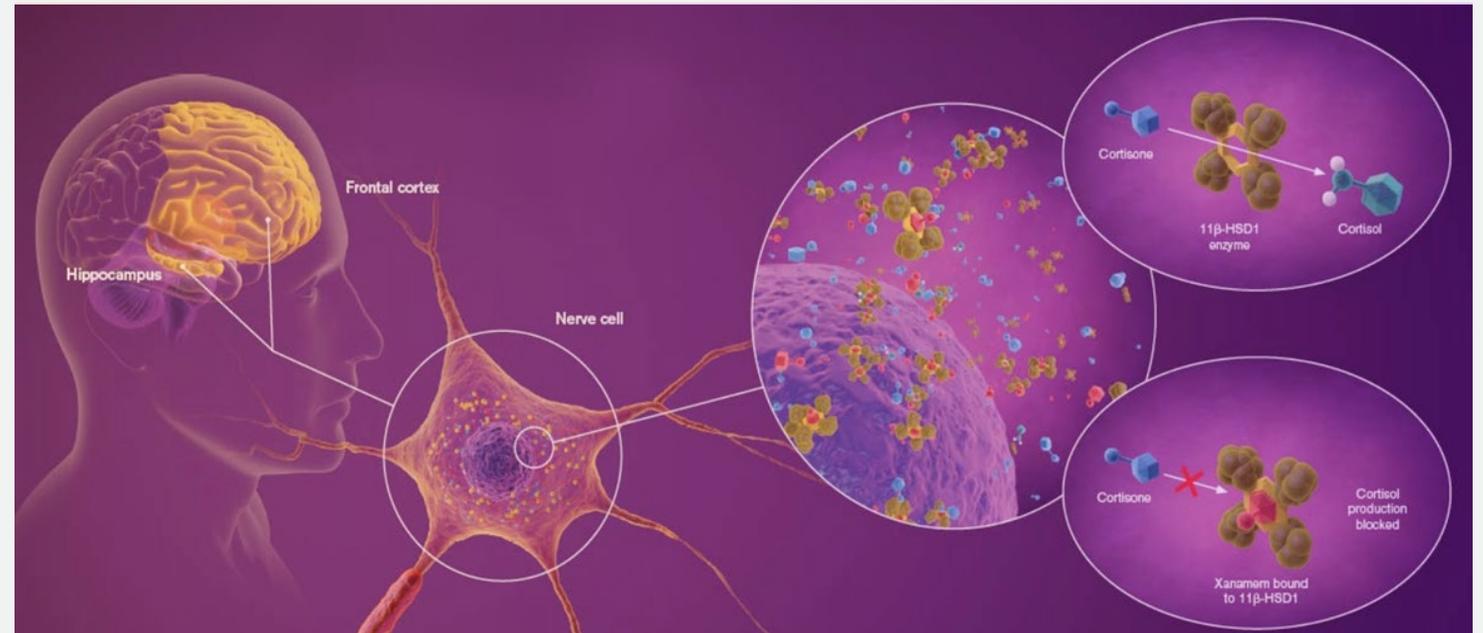
1437  
10/11/14  
11/2/14  
Brain/mri/FLAIR  
FOV24x24  
5.00x7.00Sec  
27/04/16  
256x256/1.00 MMX  
1437 FC019411/TF

T1  
T2  
FLAIR  
T1 contrast



# Xanamem®: oral treatment and novel mechanism

Brain penetrant, oral, once-a-day, 11 $\beta$ -HSD1 enzyme inhibitor reduces cortisol inside brain cells - modulating signalling pathways and underlying disease processes<sup>1,2</sup>



1. Xanamem® is a CNS (Central Nervous System) penetrant small molecule based on human PET evidence and 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

# Actinogen snapshot

Actinogen Medical (ASX:ACW) is a clinical-stage company developing a novel oral treatment with rapid onset of clinical activity to address a range of central nervous system (CNS) diseases



**Favourable pharmaceutical properties**

- ✓ Demonstrated target engagement in brain and HPA axis in human trials
- ✓ Low dose,  $\leq 10\text{mg}$
- ✓ Low drug-drug interaction potential



**Substantial clinical data**

- ✓ >300 subjects or patients safely treated
- ✓ Large Phase 2 safety database with 12 weeks therapy (N=185)
- ✓ Cognitive enhancement activity shown in healthy older volunteers



**Attractive first target indications and rationale**

- ✓ Strong cortisol rationale for treatment of multiple CNS diseases: early stages of Alzheimer's Disease; Fragile X Syndrome; and depression/related cognitive impairment



**Protected and funded**

- ✓ Molecule in-licensed from U Edinburgh in 2014
- ✓ Comprehensive patents in place<sup>1</sup>
- ✓ Pro-forma cash A\$22.2M at 31 Dec 2021

1. Composition of matter to 2031 plus 5-year extension in most countries, new patents in process

# Xanamem Clinical Development Pipeline

## Diseases to be studied in 2022/23

## Phase 2 Pathway

## Outlook



Mild cognitive impairment due to **Alzheimer's disease**

**XanaMIA (IND)**

**Part A:** 10mg, 5mg, Placebo Older Volunteers: cognition

**Part B:** Patients with MCI due to AD: cognition & biomarkers

*"Big-to-market"*  
*Multiple Phase 2b/3 trials*



Anxiety, sleep & behavioural problems in **Fragile X Syndrome**

Open  
IND Nov  
2021

**XanaFX**  
Phase 2 trial

*"Fast-to-market" single  
pivotal Phase 3*



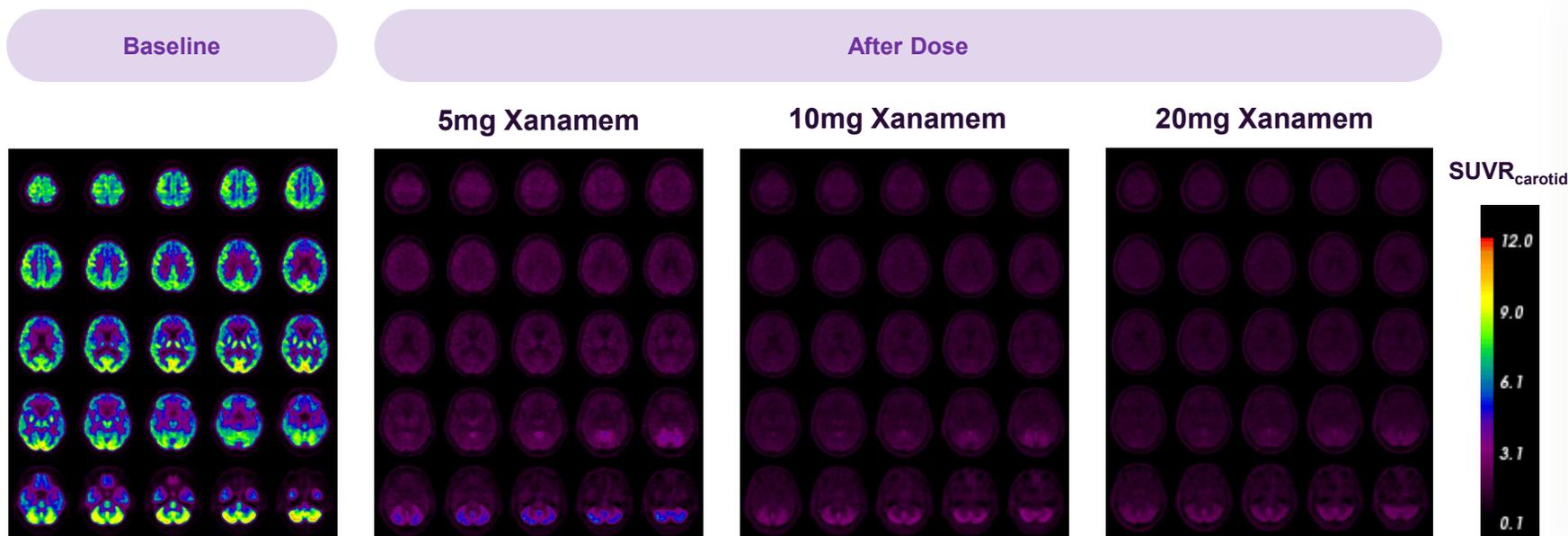
**Depression** with cognitive impairment

Study  
preparation

**XanaMDD**  
Phase 2 randomised trial

*Portfolio diversification  
and optionality*

# High brain occupancy PET data supports a low Xanamem dose $\leq 10\text{mg}$ daily



PET data demonstrates that Xanamem extensively binds to the  $11\beta\text{-HSD1}$  enzyme throughout the brain, with high post-treatment effects (absence of colour) after 7 days at all doses, slightly less at a 5mg dose.

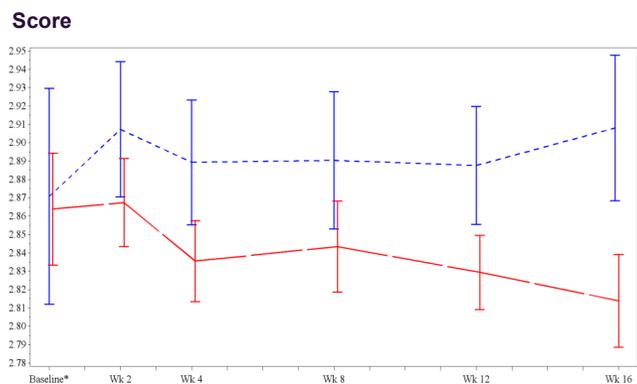
This is consistent with full hormonal pharmacodynamic activity seen with 10mg in clinical trials.

Note: Study population consisted of ~50% healthy subjects (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.

# Cognitive improvement shown in healthy, older volunteers

Phase 1 XanaHES study demonstrated statistically significant cognitive efficacy signal in multiple cognition domains based on Cogstate Cognitive Test Battery as early as 2 weeks<sup>1</sup>

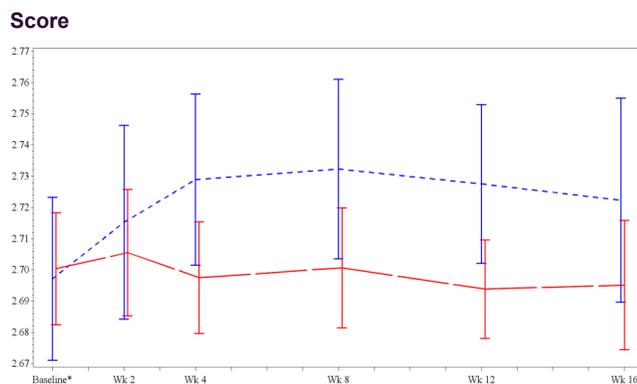
Treatment Group — Xanamem 30pts — Placebo 12 pts



P<0.01

**Working memory (One Back Test)**

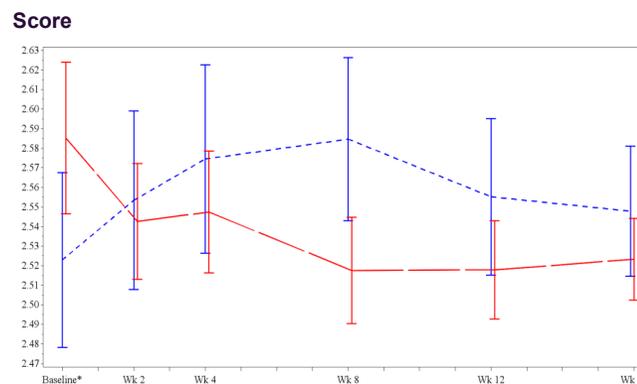
Strongly statistically significant result



P=0.05

**Visual attention (Identification Test)**

Statistically significant result



P=0.09

**Psychomotor function (Detection Test)**

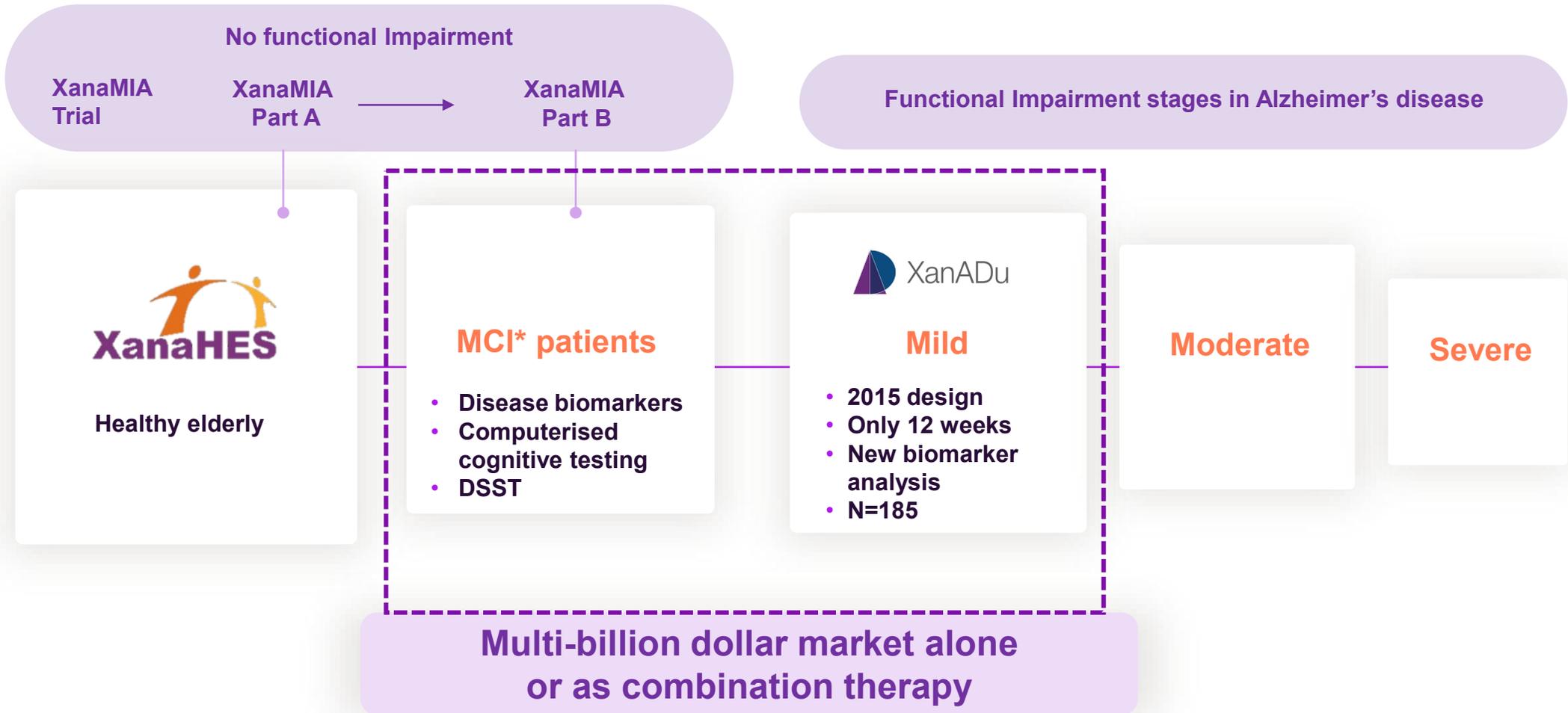
Good trend to a positive result

Large effect sizes seen in working memory and attention, trends in other domains

1. XanaHES Phase 1 clinical trial treated healthy older volunteers, aged 50-75 years, with 20mg Xanamem daily (n=30 active, n=12 placebo). All values are the means of observed data. p values were calculated with an ANCOVA (analysis of covariance) model using Baseline values as a covariate.



# Target population is the early stages of dementia

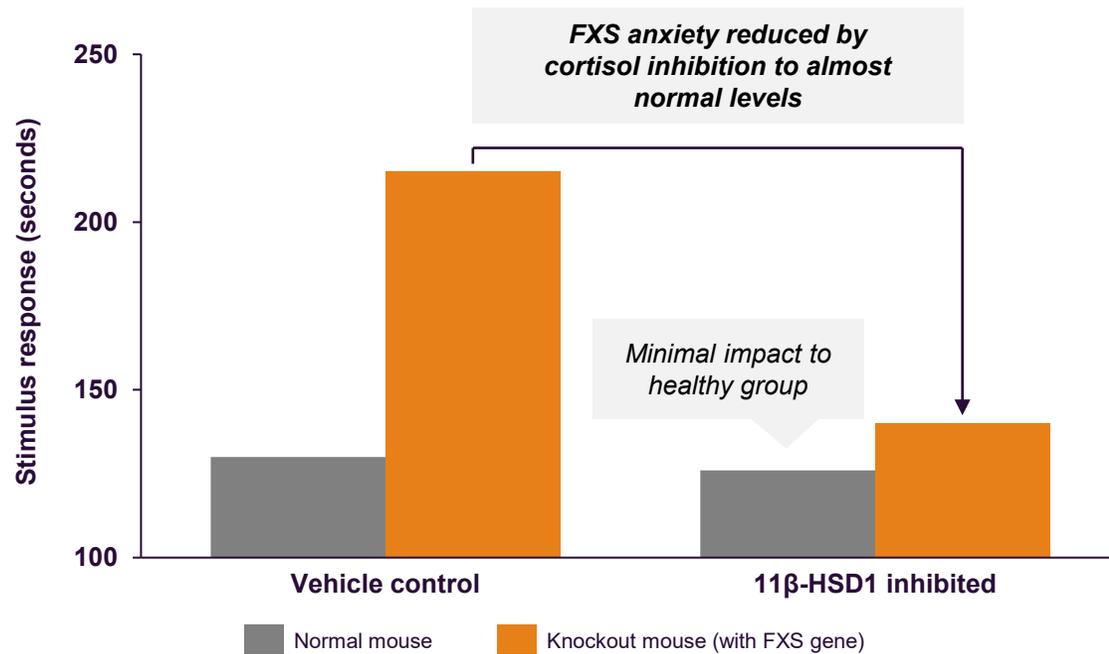


\* Mild Cognitive Impairment (MCI): memory, executive function deterioration with retained functional abilities



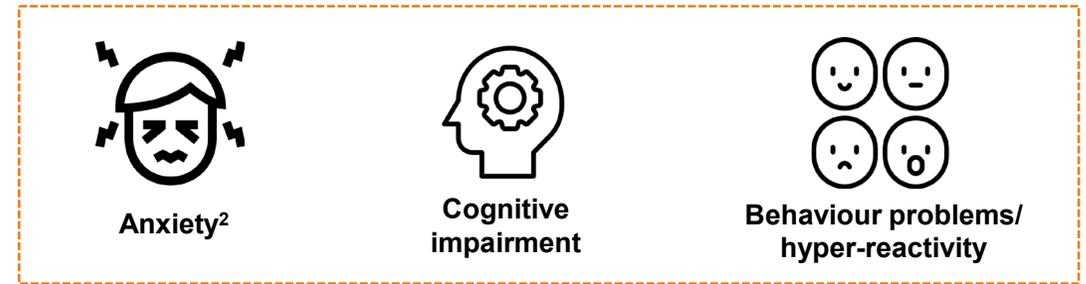
# Xanamem may treat multiple symptom domains in Fragile X Syndrome (FXS)

## Normalisation of anxiety in the FXS KO mouse<sup>1</sup>



## Symptoms of FXS are all potentially amenable to Xanamem therapy

### XanaFX trial target symptoms



Three icons are shown within a dashed orange box, representing target symptoms: Anxiety<sup>2</sup> (a person with lightning bolts), Cognitive impairment (a head with a gear), and Behaviour problems/hyper-reactivity (four faces with various expressions).

### Other FXS symptoms potentially amenable to Xanamem therapy



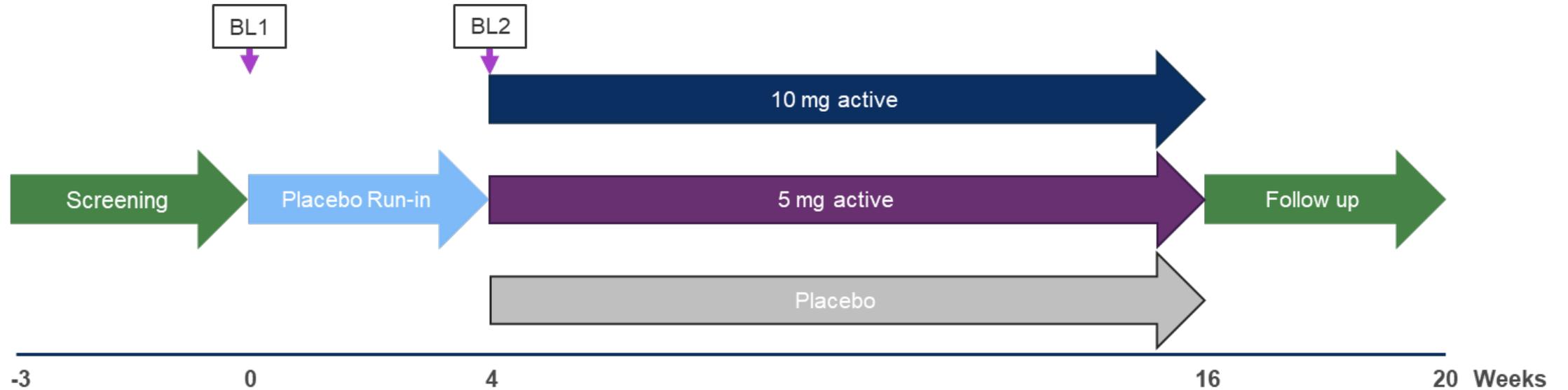
Three icons are shown below the dashed box, representing other potential target symptoms: Sleep problems (a person in bed), Learning disabilities (a person reading a book), and Speech and language deficits (a person speaking into a microphone).

1. Pre-clinical FMR1 knock-out mouse model using BVT 2733 as the 11β-HSD1 inhibitor showed highly significant results (\*\*p<0.0001). Normal mouse is a wild-type mouse. (Source: Vanderklish PW. 2019. Compounds for treatment of emotional/psychological symptoms in fragile x syndrome, WO 2019/075394 A1.)

2. ~90% of FXS patients suffer symptoms of anxiety

# Fragile X Syndrome Phase 2 trial design

Commencing currently, results planned for late 2023



N=25 per group

Sites in USA, Australia, NZ and UK

Implementation partnership with Worldwide Clinical Trials who specialize in pediatric, rare diseases

# Xanamem Targets Depression and its Associated Cognitive Impairment

**Major Depressive Disorder is common<sup>1,2</sup>**

**~5% prevalence globally, 1 in 7 lifetime risk**

**Neurocognitive symptoms are a typical feature (>80%)<sup>3</sup>**

**Difficulty thinking and concentrating, unable to make decisions**

**Only one anti-depressant has a cognitive benefit claim**

**Vortioxetine sales US\$500m<sup>4</sup>**

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

# Strategy to drive growth

## Accelerate clinical development

- Commencing Fragile X Syndrome trial
- Expanding pipeline with depression Phase 2 program
- Creating optionality for development and partnerships

## Forward planning

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

## Value from partnerships



### Pharma/biotech engagement

- Actively engaging with large and mid-size potential partners



### 2 open INDs, FXS Priority Review

- Priority review granted by FDA
- PRVs recently traded for US\$100M-US\$125M



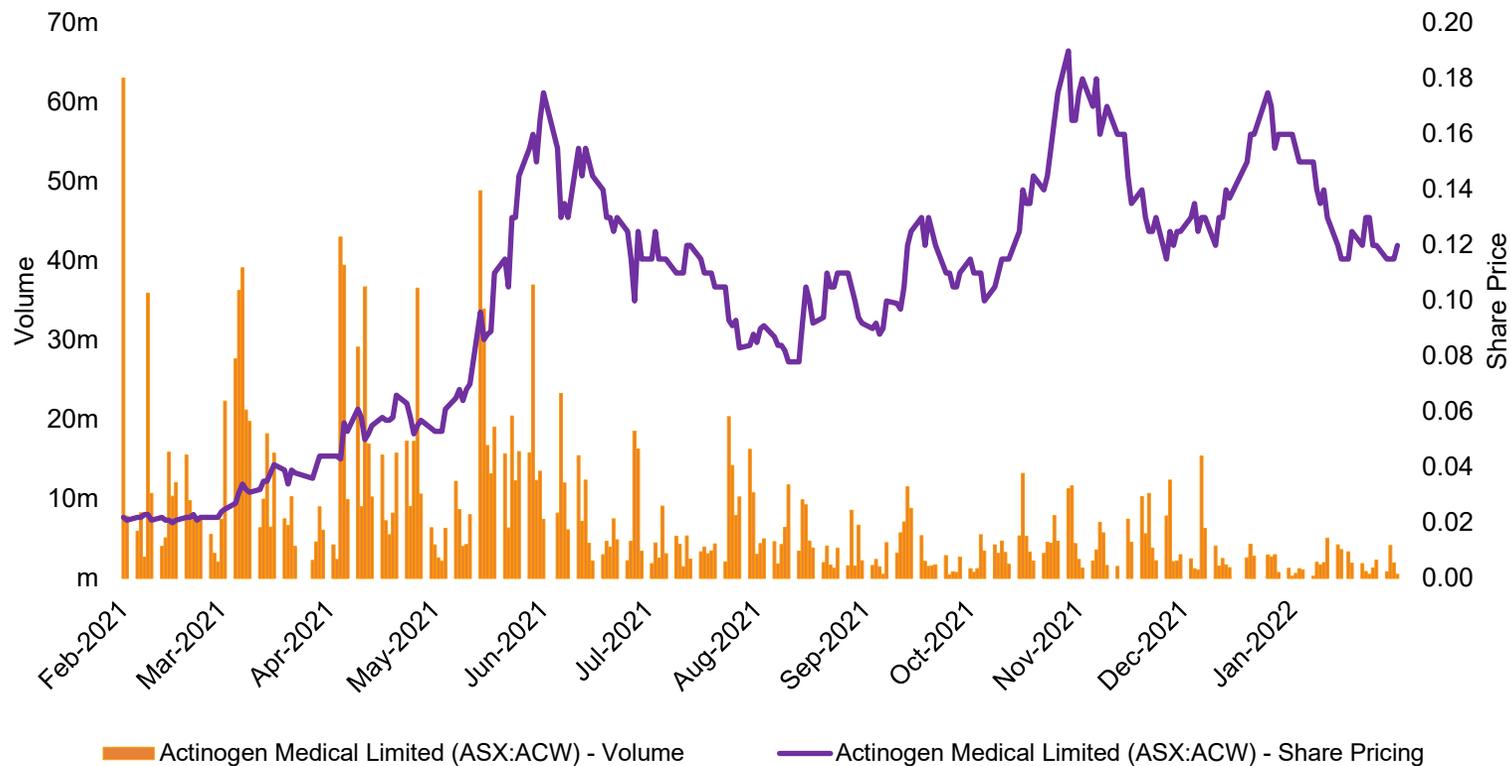
### Peer AD company valuations reflect growth potential

- Peer companies in phase 2 or 3 for AD: valuations ~US\$126M-\$2.1B<sup>1</sup>

1. Vivoryon Therapeutics, phase 2a/b AD lead asset (EURONEXT Amsterdam: 245m euro); Athira Pharma, phase 2 AD lead asset (NASDAQ GS:~US\$382m); Cassava Sciences, AD lead asset phase 2 asset with positive biomarker and cognition data (NASDAQ GS:~US2.1B); Annovis Bio, very early phase 2 data AD, PD (NASDAQ US\$126m). All companies' value primarily attributed to their lead AD asset. Market capitalisations as of February 10 2022.

# ACW stock performance 12 months

## Share price chart at 11 Feb 2022

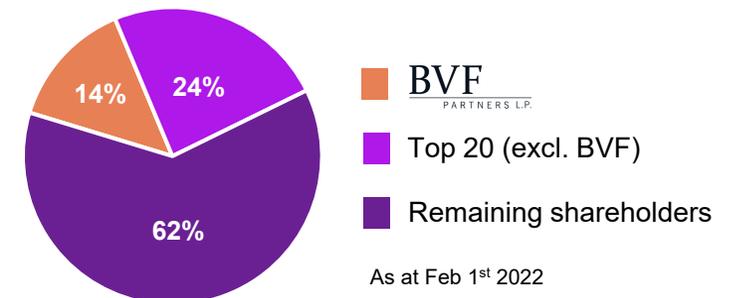


## Trading Information

52 week high	A\$0.20
52 week low	A\$0.02
Number of issued shares	1,779M
Market capitalisation (11 Feb 2022)	A\$213M
Pro-forma cash at 31 Dec	A\$22M

## Major Shareholders

BVF Partners	13.9%
Steven Gourlay	3.6%
Edinburgh Technology Fund	2.7%



# Key catalysts in 2022 & 2023

## ❑ Clinical trials

### Alzheimer's Disease

- XanaMIA Part A cognition results April CY2022
- XanADu retrospective biomarker results H2 CY2022
- XanaMIA Part B patient biomarker/cognition data 2023

### Fragile X Syndrome

- Commenced in 2021
- XanaFX trial results 2023

### Depression

- Commence program immediately, results 2023

## ❑ Publications and collaborations

- Focus on PET study and other key peer-review publications
- Leverage academic collaborations including Mild Autonomous Cortisol Secretion (MACS) Trial with Oxford University researchers