ASX ANNOUNCEMENT

Actinogen CEO presentation for non-deal roadshow investor meetings

Sydney, 11 August 2022. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce that the Company's CEO, Dr Steven Gourlay will be meeting with investors in Singapore on a two-day non-deal roadshow arranged by Spark Plus Singapore, commencing today.

A copy of Dr Gourlay's presentation materials used for meeting discussions is attached.

While in Singapore, Dr Gourlay will also meet with a key opinion leader in dementia for the Asia Pacific region.

ENDS

Investors

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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. 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.

Actinogen

A clinical-stage company progressing Phase 2 trials for Alzheimer's Disease, Depression & other diseases

Dr. Steven Gourlay MBBS PhD MBA, CEO & MD

Spark Plus investor roadshow 11-12 August 2022

Disclaimer

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Actinogen snapshot

Actinogen Medical (ASX:ACW) is developing a novel oral treatment with rapid onset of clinical activity to improve cognition 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** (attention & working memory) confirmed in two consecutive well-controlled trials (5 mg, 10 mg & 20 mg dose levels vs. placebo)

Attractive disease indications and rationale

- ✓ **Strong cortisol rationale** for treatment of multiple diseases: early stages of Alzheimer's Disease; Depression & related cognitive impairment; Fragile X Syndrome; and many others

Protected and funded

- ✓ Molecule in-licensed from U Edinburgh in 2014
- ✓ Comprehensive patents in place[2]
- ✓ **Cash position A$16.4M at 30 Jun 2022**

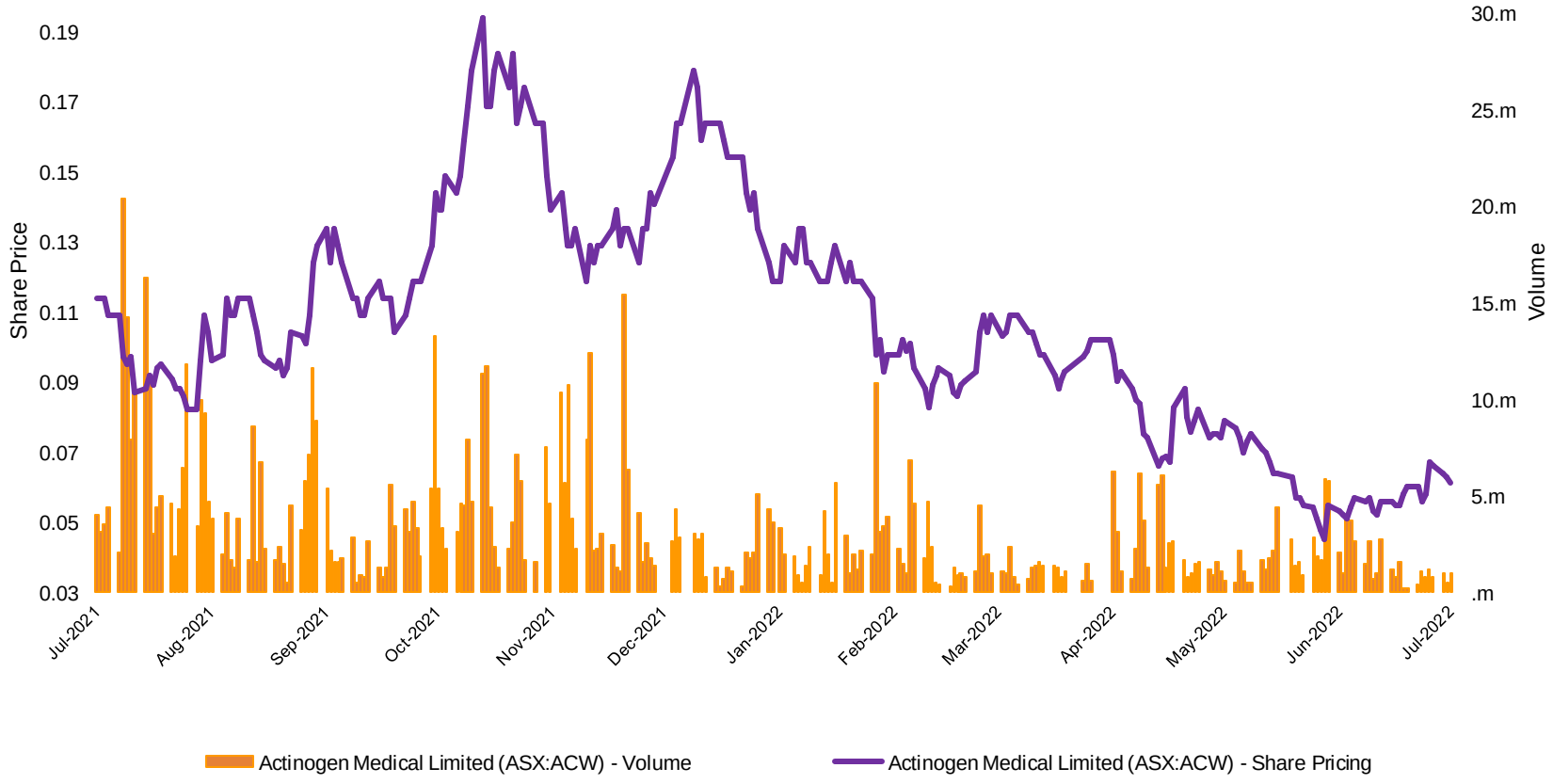
High functioning semi-virtual company model

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

ACW top stockholders and stock price

Share price chart at 27 July 2022

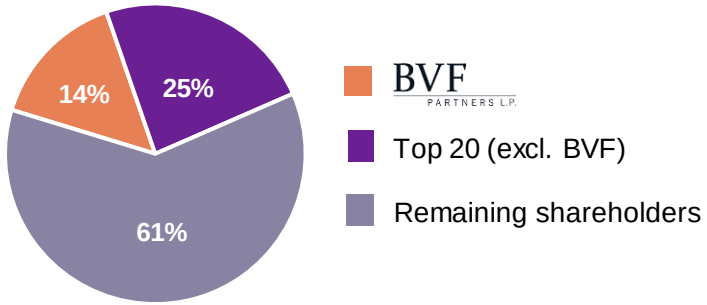


Trading Information

52 week high	A$0.20
52 week low	A$0.044
Number of issued shares	1,796M
Market capitalisation (27 July 2022)	A$102M
Cash Balance at 30 Jun 2022	A$16.4M

Major Shareholders

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



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

International Cognition Clinical Advisory Board

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

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

International Scientific Advisory Boards

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 INSTITUTE OF NEUROSCIENCE & MENTAL HEALTH · 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

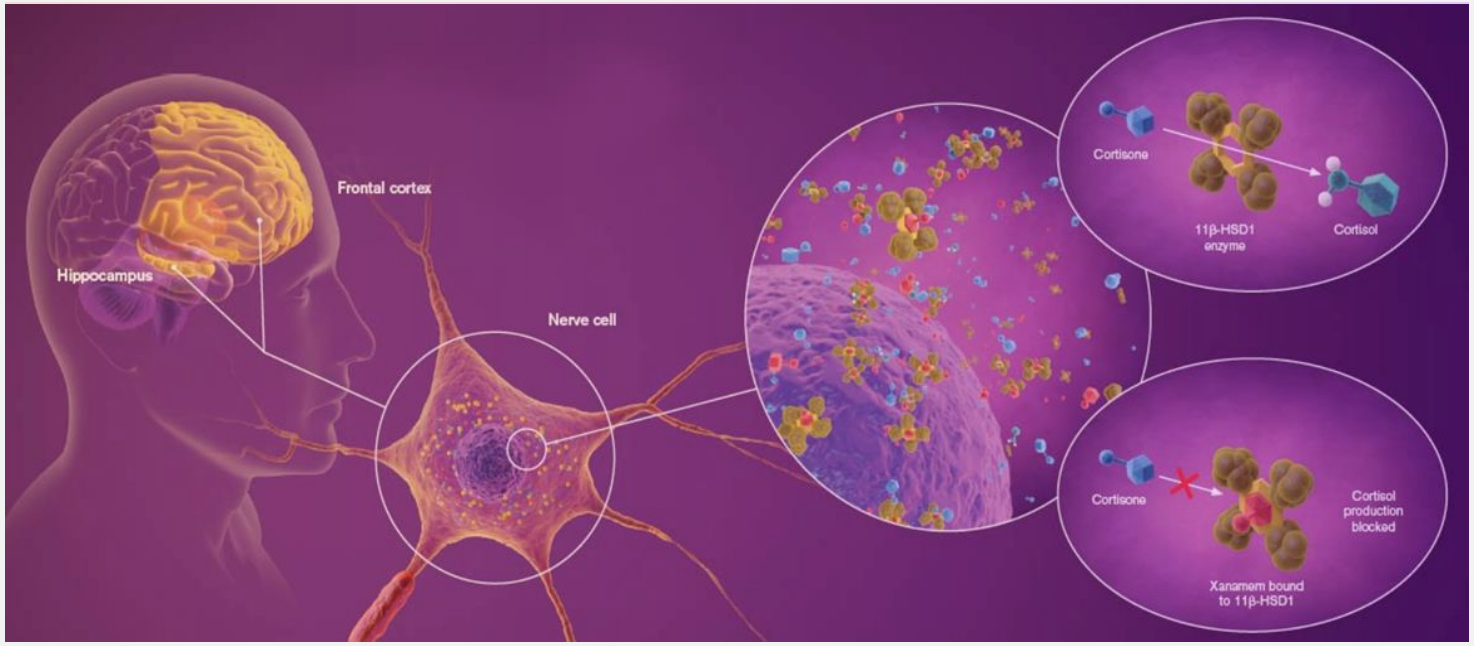
- Chair of Medicines at the Centre of Cardiovascular Science, University of Edinburgh
- Former positions across both biotech and academia
- Founder and Chief Scientific Officer at Kynos Therapeutics

Xanamem®: oral, low dose, once-a-day treatment with a unique 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:

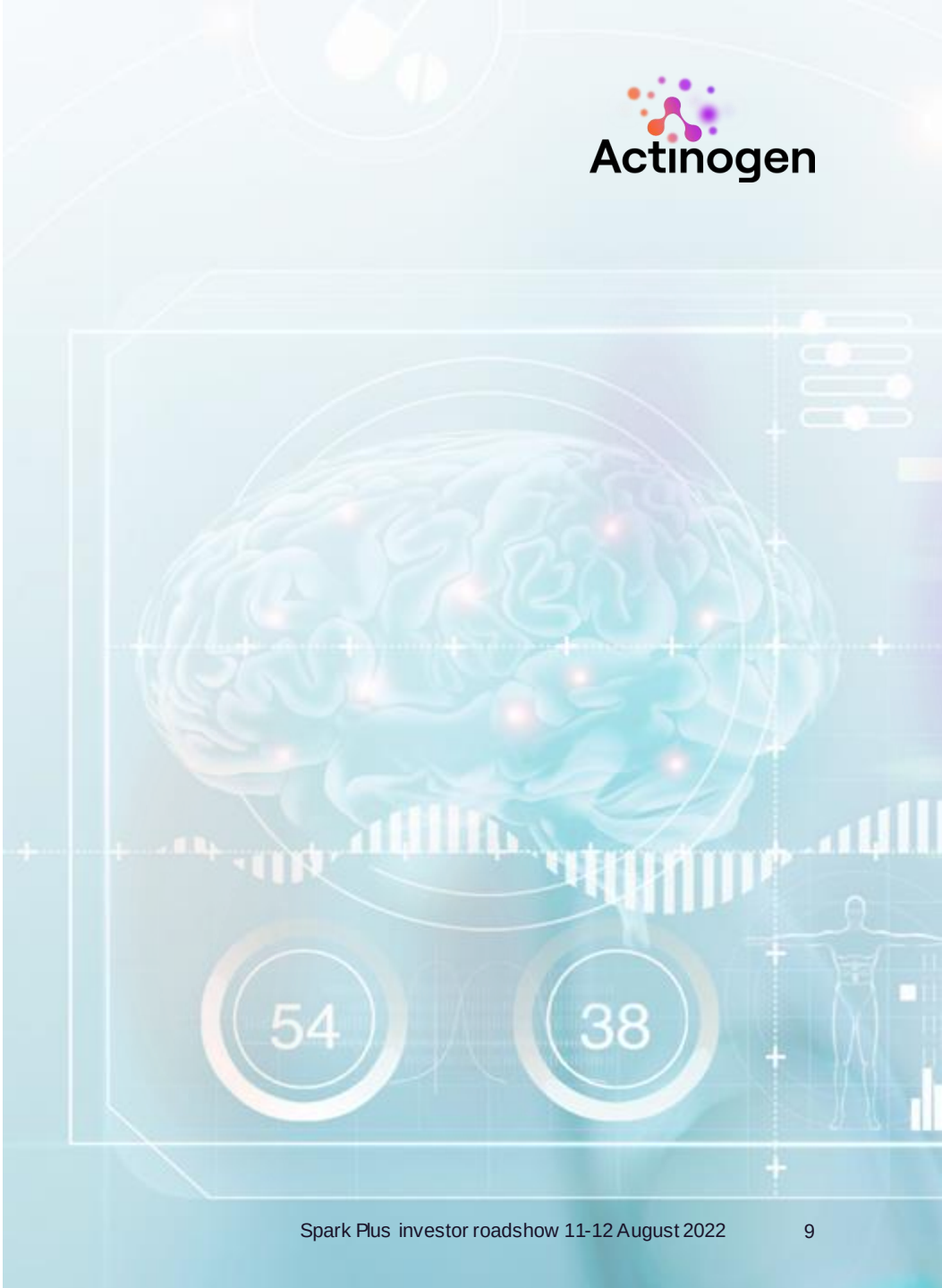
- Rapidly cognitive enhancing
- Disease-modifying (slow or halt progression) in AD



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

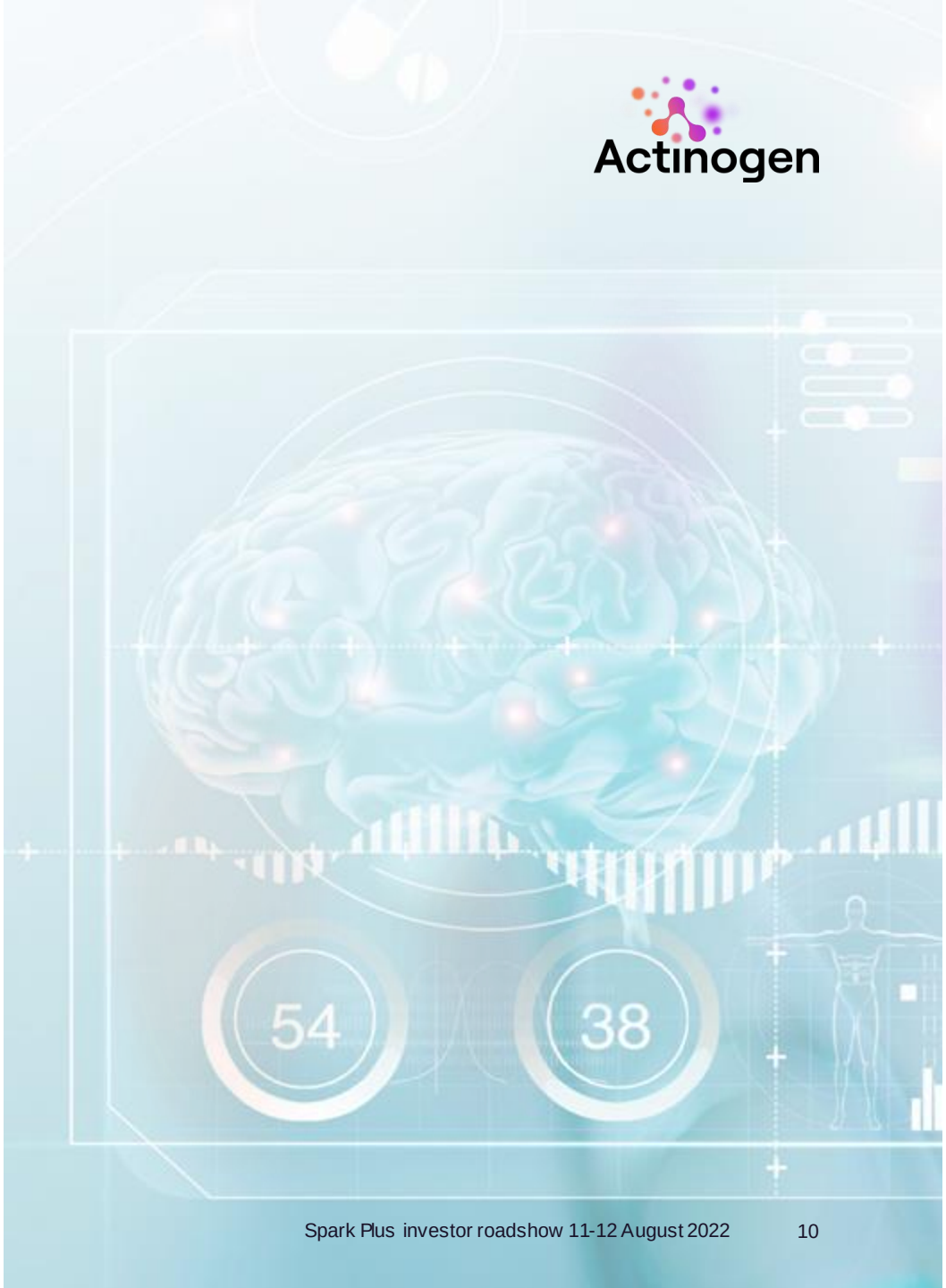
The role of cortisol in health

- Cortisol is an essential hormone for health in humans
- Its key function is to modulate the response to stress:
  - physical stress such as infection
  - psychological stress
- Outside the brain, cortisol controls the amount of inflammation due to disease, infection
- Inside the brain, role is complex and modulates mood, attention, memory
- Elevated cortisol is known to be toxic to brain tissue and associated with shrinkage of key areas for memory



Xanamem highly suited to development in brain diseases

- Well absorbed, small dose (5-10 mg), once-a-day dosing
- Penetrates brain well
- High binding to target enzyme from 5mg
- Safe and very well tolerated
- Good candidate for combination therapy due to low potential for drug interactions



High target engagement confirms brain activity at Xanamem doses of ≤10mg in 2020

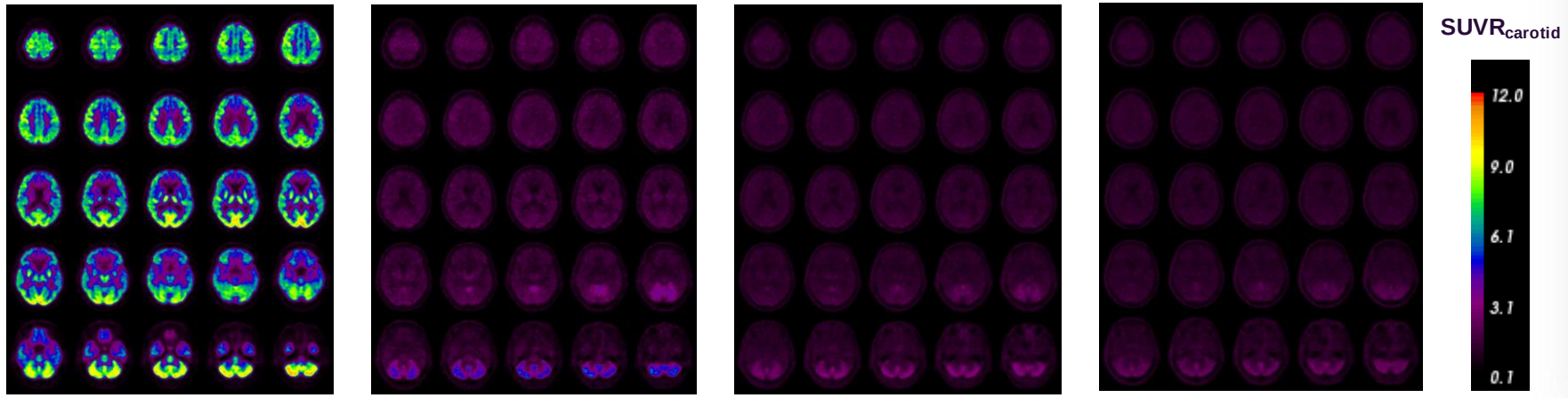
Baseline

After Dose

5 mg Xanamem

10 mg Xanamem

20 mg Xanamem



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.

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.

Promising safety profile in > 300 individuals to date

Phase 2 trial 10mg daily over 12 weeks in patients with mild AD (MMSE* 20-26)

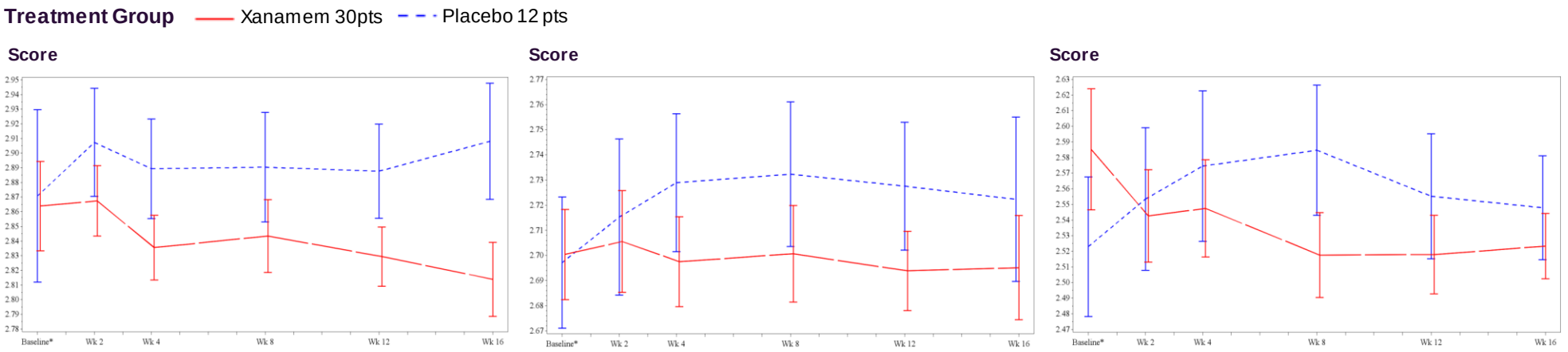
TEAE** term	Xanamem (n=91)	Placebo (n=94)	Total (n=185)
Headache	5 (5.5%)	2 (2.1%)	7 (3.8%)
Dizziness	4 (4.4%)	3 (3.2%)	7 (3.8%)
Diarrhoea	1 (1.1%)	4 (4.3%)	5 (2.7%)
Fatigue	3 (3.3%)	1 (1.1%)	4 (2.2%)
Nerve conduction abnormal	1 (1.1%)	3 (3.2%)	4 (2.2%)
Somnolence	1 (1.1%)	3 (3.2%)	4 (2.2%)
Decreased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

* Mini Mental State Examination
** Treatment Emergent Adverse Events possibly related to Xanamem reported by more than one patient in any group: all mild-moderate

✓ **No treatment-related Serious Adverse Events in whole program**

Cognitive improvement vs. placebo in healthy, older volunteers in XanaHES trial (2019)

- Cogstate Cognitive Test Battery (CTB) with 20 mg daily, 12-week treatment; effect size (ES) estimated with the same MMRM statistical model as the current trial[1]
- Clinically significant effects on "attention" domains of cognition (ES[2] attention composite = 1.2)



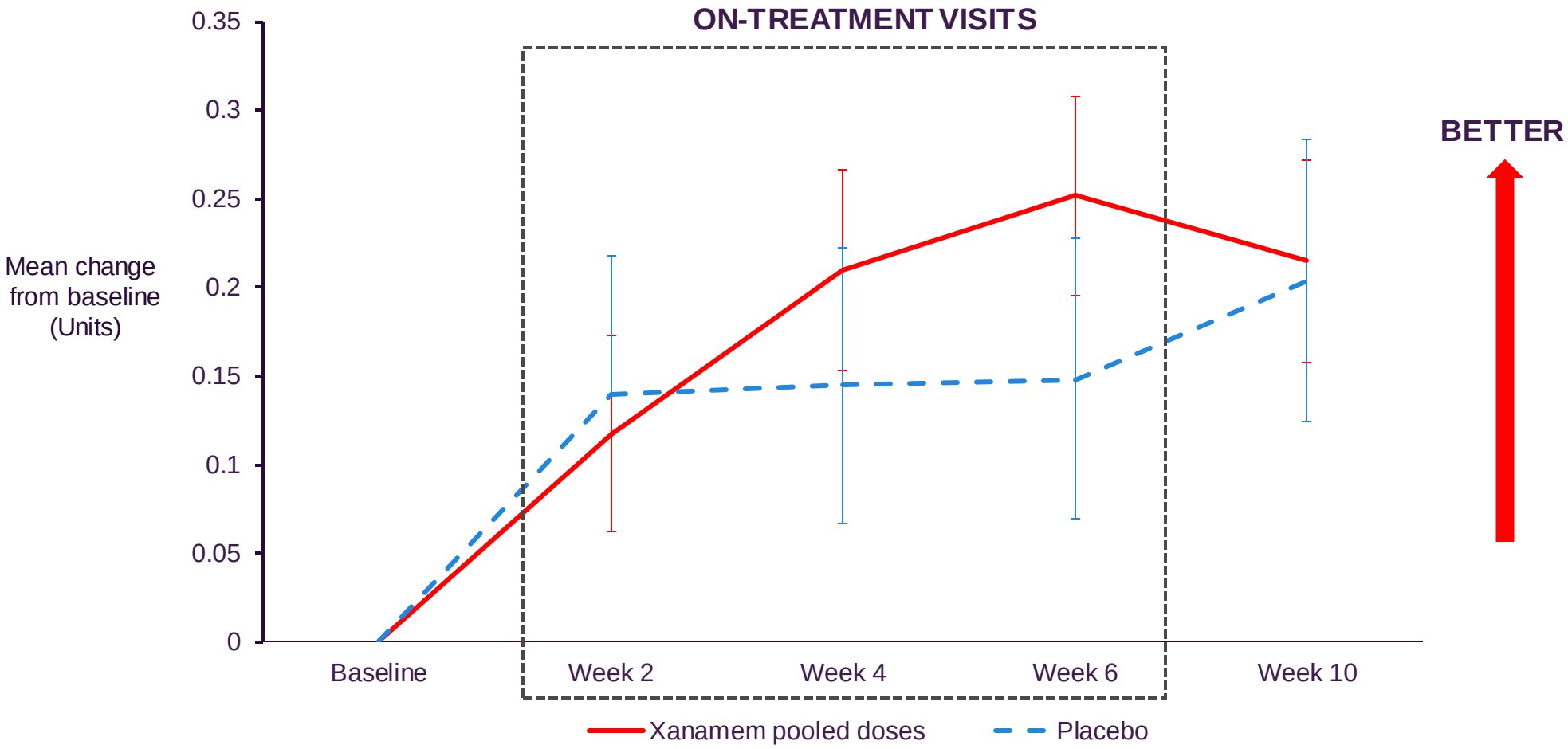
Working memory (One Back Test) | Visual attention (Identification Test) | Psychomotor function (Detection Test)

Lower Xanamem scores in red are better

1. XanaHES Phase 1 clinical trial treated healthy elderly patients with 20mg Xanamem daily (n=30 active, n=12 placebo). All plotted values are the means of observed data
2. Z-score of standardized treatment effect (mean difference in MMRM model change from baseline vs. placebo/standard error of change).

Attention composite improved at weeks 4 and 6 vs. placebo in a second clinical trial (2022)

Pooled working memory / visual attention / psychomotor speed (mean, SE)



The XanaMIA Part A trial met its objectives

- **Clinically significant** improvements were seen in the **attentional domains, including working memory**, of the Cogstate CTB with both doses, including visual attention with 5 mg at the end of treatment achieving the a priori primary endpoint criterion of Cohen's d > 0.3 (Cohen's d = 0.32, Z = 1.97, p < 0.05)

- Xanamem was **safe and well-tolerated** over the 6-week treatment period in this cognitively normal population aged 50-80 years (mean age 64 years, mixed female and male population)

- Both 5 mg and 10 mg dose levels showed **pharmacodynamic activity** by raising mean ACTH by 2.03 to 2.35 times, respectively, principally within the normal laboratory range and to a similar extent as higher doses in prior studies

- **Cognitive findings consistent with prior XanaHES trial and with high brain activity of 5 mg and 10 mg doses in a Positron Emission Tomography (PET) study**

Strategy & Next Trials

Actinogen Strategy

Accelerate clinical development

- ***Focus on cognitive enhancement***:
  - Early stages of Alzheimer's Disease
  - XanaMIA Part B Phase 2
  - Cognitive enhancement Depression Phase 2
  - Trial operations mainly in Australia
- Suspend global Fragile X Syndrome Phase 2 until alternative funding can be found

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 on cognitive enhancement development programs

Alzheimer's Disease

Targeting cognitive enhancement and disease-modification in the early stages of disease

Characteristics of early Alzheimer's Disease (AD)

AD is common[1]

~55 million people worldwide have dementia, with AD the commonest type

AD patients initially suffer memory loss

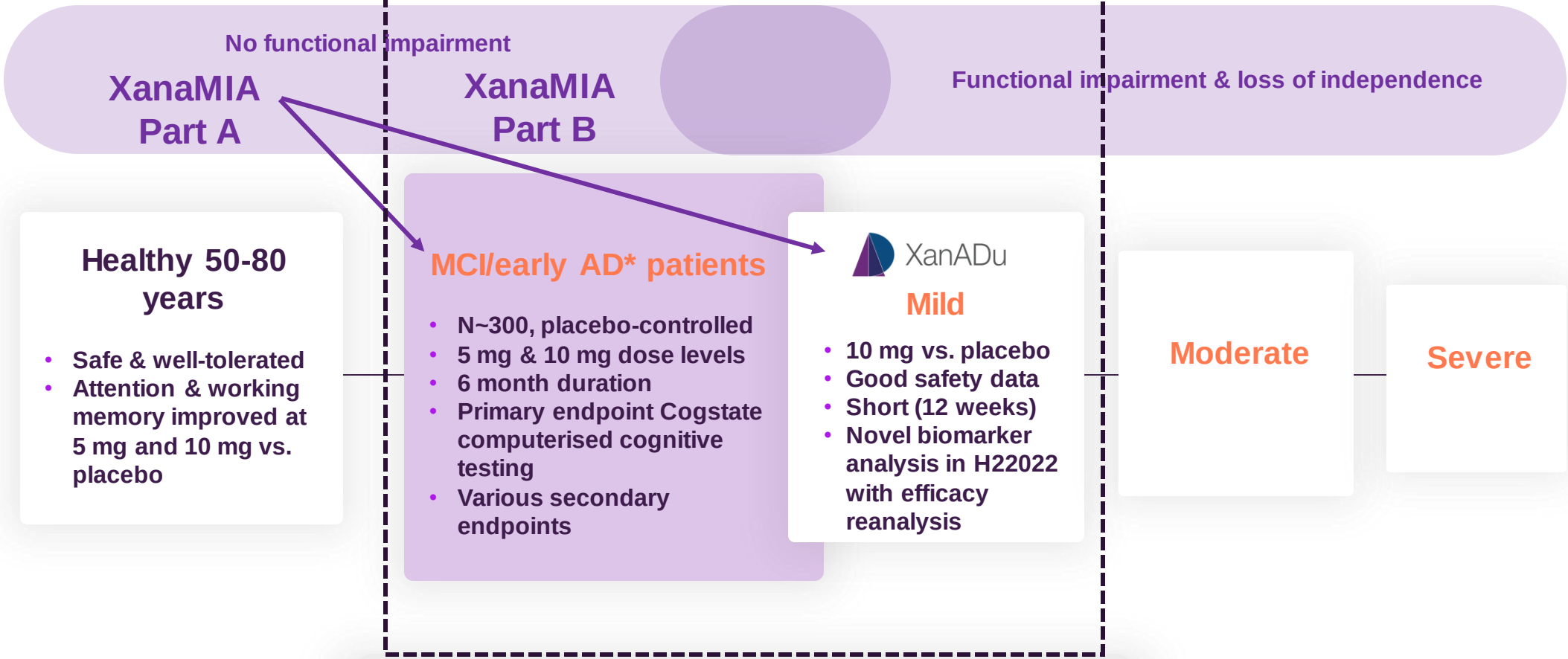
As AD progresses, memory worsens and other problems develop e.g. language, problem solving, ability to live independently

Existing treatments have minimal effectiveness and side effects

New treatments needed to improve memory and slow AD in its early stages

1. Dementia Australia

Moving Xanamem trials into AD patients with a focus on cognitive enhancement & biomarkers



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

October 2022: Planned analysis of Phase 2 plasma samples for Alzheimer's Disease biomarkers

Biomarker responses to treatment, reanalysis of efficacy in biomarker positive patients

XanADu Phase 2 Trial

~70/185 patients available for analysis

10mg daily

Mild Alzheimer's Disease without biomarker or imaging confirmation

We will now assess whether Xanamem improved AD blood biomarkers

We will also reassess efficacy trends in biomarker positive patients

XanaMIA Part B – Patients with early Alzheimer's Disease

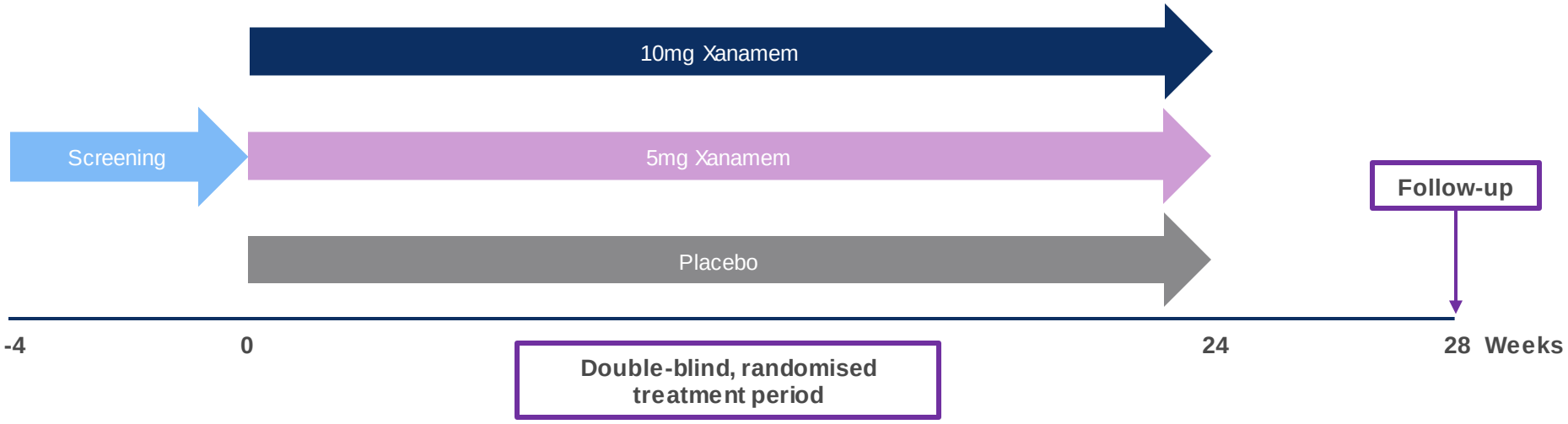
Key design considerations

Double-blind randomized parallel-groups design:

- Placebo, 5 and 10 mg Xanamem once daily
- Approx. 100 per group
- 24 weeks treatment

Patients with:

- Clinical diagnosis of early-stage AD
- Demonstrated cognitive impairment by coding test
- Elevated p-Tau181 (AD biomarker signature)



N~300 (~100 per group)

Key outcomes

Primary outcome

- Cogstate attention composite (same as XanaMIA Part A and XanaHES)

Secondary outcomes

- Amsterdam Activity of Daily Living scale (more sensitive than ADAS-Cog)
- Cogstate
  - Executive Function Composite
  - Episodic Memory Function Composite
- Individual tests
- Carer questionnaire / Patient Global Improvement

Cognitive Impairment associated with Major Depressive Disorder - XanaCIDD

Targeting dual cognitive enhancement and anti-depressant activity

Science Behind the Xanamem Depression Program

- ✓ 80-90% report difficulty with thinking (cognition)[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 effects, Ding et. al 2021
6. Xanamem placebo-controlled trial working memory & attention (Actinogen data on file)

Characteristics of Major Depressive Disorder (MDD)

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 statement re cognition

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

The Xanamem opportunity in depression

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

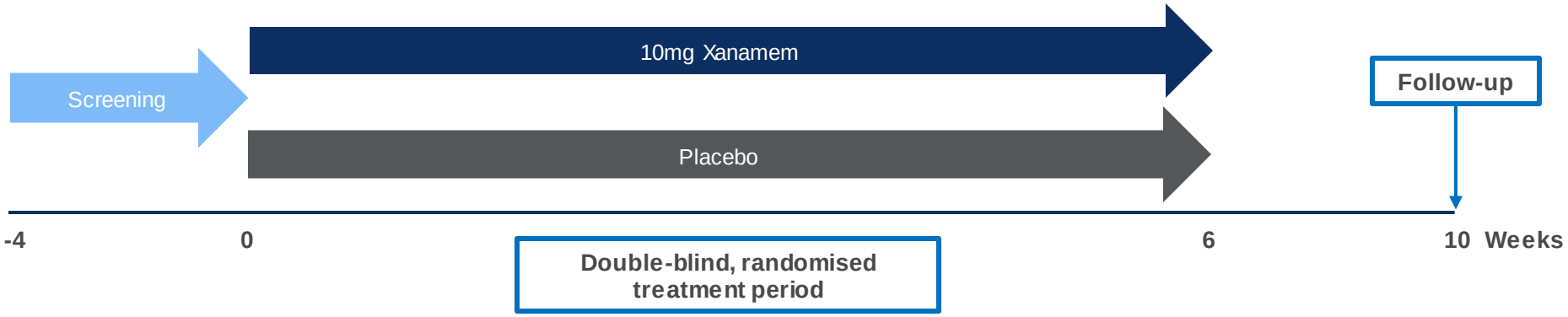
XanaCIDD trial design & implementation model

Double-blind randomized parallel-groups design:

- Placebo and 10 mg Xanamem once daily
- Approx. 80 per group
- 6 weeks treatment

Patients with:

- Clinical diagnosis of MDD
- Demonstrated cognitive impairment by coding test
- Persistent depressive symptoms despite first line therapy (SSRI/SNRI)



N~160 (~80 per group)

COWAT=Controlled Word Association Test; HVLT-R=Hopkins Verbal Learning Test–Revised; iDSST=international Digit Symbol Substitution Test; OCL=One card learning; SSRI=Selective serotonin reuptake inhibitor; SNRI=Serotonin and norepinephrine reuptake inhibitor;

Key outcomes

Primary outcome

- Cogstate CTB attentional composite (attention and working memory)

Secondary outcomes

- Montgomery-Åsberg Depression Rating Scale (**MADRS**)
- Executive Function Cognitive Composite (**One-Back**, **COWAT**, **iDSST**)
- Episodic Memory Cognitive Composite (**OCL**, **HVLT-R**)

Xanamem Clinical Development Pipeline

	Phase 2 Pathway	Outlook
Cognitive impairment in early **Alzheimer's disease**	**Biomarker analysis in** patients with mild AD - Phase 2 dataset of 10mg vs. placebo over 12 weeks, H2 2022 **Cognitive benefit** in patients with early stages of AD - Phase 2 XanaMIA Part B commencing H2 2022	*"Big-to-market"* *Multiple Phase 2b/3 trials*
Depression with cognitive impairment	**Depression and cognitive impairment placebo-controlled trial** - Phase 2 XanaCIDD trial to commence in H2 2022	*Potential to treat both depression and related cognitive impairment*
Anxiety, sleep & behavioural problems in **Fragile X Syndrome**	**XanaFX (IND)** - Phase 2 proof-of-concept in adolescent and young adult males	*Pending alternative funding or partnership*

Timeline for Xanamem data & catalysts

Actinogen

2022

- Ongoing pharma/biotech **partnering** meetings with new data
- Q4 **Biomarker data** to assess disease-modifying potential
- Q4 **CTAD XanaMIA presentation**
- Q4 New **trials commence** in Alzheimer's Disease and Depression
- Q4 Key global **regulatory** planning meetings with FDA, EMA

2023

- **XanaMIA Part B** enrolment
- **XanaCIDD** enrolment ± initial results

2024

- XanaMIA **Part B results**
- **Expand Depression** program
- **Expand Alzheimer's Disease** program

Contact

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