Actinogen

XanaMIA Phase 1b trial achieves primary endpoints: topline results & strategic update

Dr. Steven Gourlay MBBS PhD MBA, CEO & MD

May 4, 2022

Authorised by the Board of Directors of Actinogen Medical Limited

Disclaimer

This presentation has been prepared by Actinogen Medical Limited. ("Actinogen" or the "Company") based on information available to it as at the date of this presentation. The information in this presentation is provided in summary form and does not contain all information necessary to make an investment decision.

This presentation does not constitute an offer, invitation, solicitation or recommendation with respect to the purchase or sale of any security in Actinogen, nor does it constitute financial product advice or take into account any individual's investment objectives, taxation situation, financial situation or needs. An investor must not act on the basis of any matter contained in this presentation but must make its own assessment of Actinogen and conduct its own investigations. Before making an investment decision, investors should consider the appropriateness of the information having regard to their own objectives, financial situation and needs, and seek legal, taxation and financial advice appropriate to their jurisdiction and circumstances. Actinogen is not licensed to provide financial product advice in respect of its securities or any other financial products. Cooling off rights do not apply to the acquisition of Actinogen securities.

Although reasonable care has been taken to ensure that the facts stated in this presentation are accurate and that the opinions expressed are fair and reasonable, no representation or warranty, express or implied, is made as to the fairness, accuracy, completeness or correctness of the information, opinions and conclusions contained in this presentation. To the maximum extent permitted by law, none of Actinogen its officers, directors, employees and agents, nor any other person, accepts any responsibility and liability for the content of this presentation including, without limitation, any liability arising from fault or negligence, for any loss arising from the use of or reliance on any of the information contained in this presentation or otherwise arising in connection with it.

The information presented in this presentation is subject to change without notice and Actinogen does not have any responsibility or obligation to inform you of any matter arising or coming to their notice, after the date of this presentation, which may affect any matter referred to in this presentation.

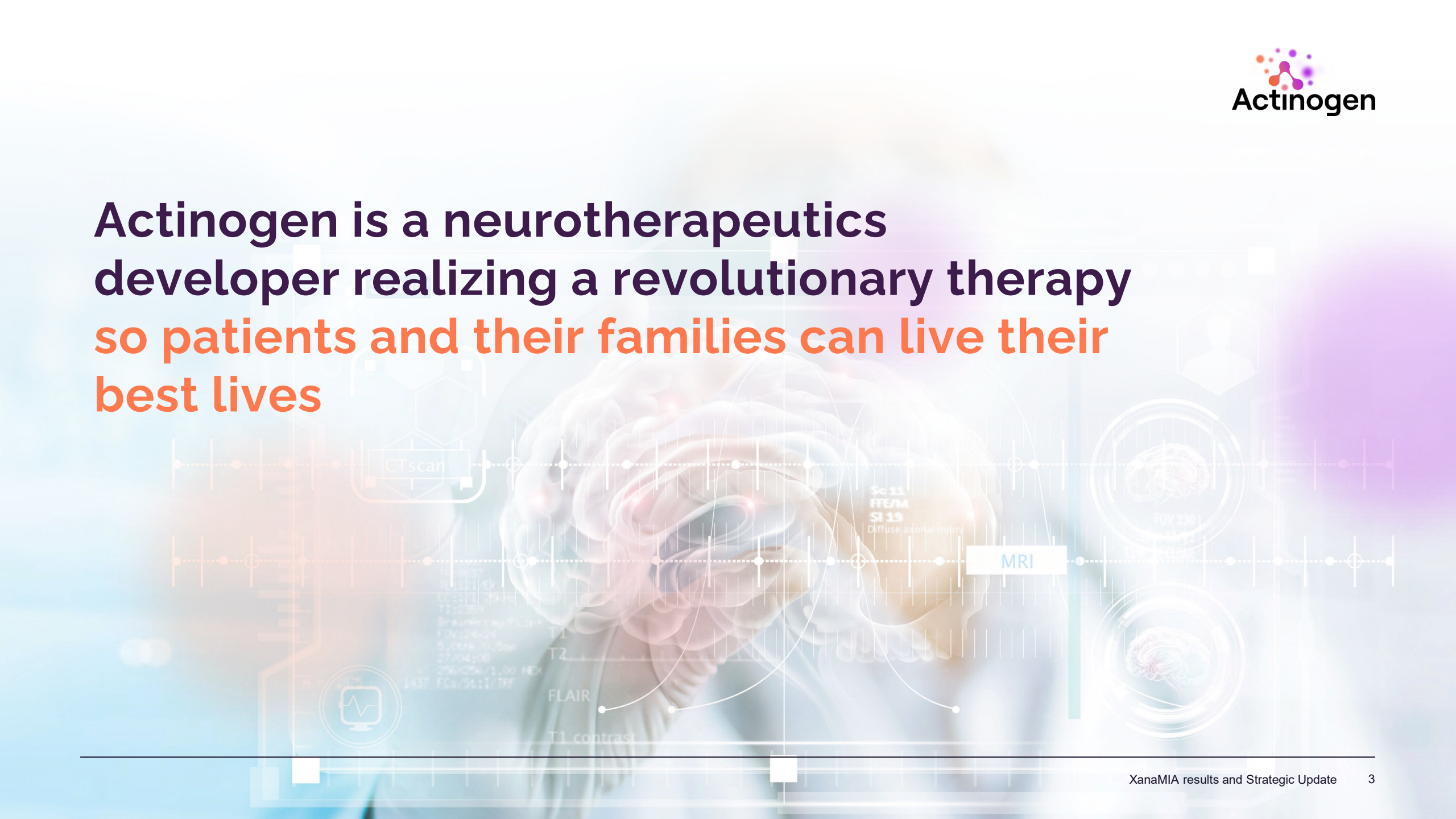
This presentation is not for general distribution or third party reliance or use.

This presentation contains certain budget information, forecasts and forward looking statements that are based on the Company's management's beliefs, assumptions and expectations and on information currently available to management in respect of which there is **NO guarantee of future performance**. Such budget information, forecasts and forward looking statements involve known and unknown risks, uncertainties, and other factors which may cause the actual results or performance of Actinogen to be materially different from the results or performance expressed or implied by such forward looking statements. These risks and uncertainties include, but are not limited to the performance of Actinogen in its clinical trials including whether it's technology proves to be a safe and effective treatment, market penetration, competition from any other similar products, intellectual property risks (including securing rights in technology and patents) and global economic conditions. Furthermore, Actinogen's research, product development, testing, pricing, marketing and other operations are subject to extensive regulation by domestic and foreign government regulatory authorities. There is no guarantee that Actinogen will obtain the required approvals, licences and registrations from the relevant authorities in jurisdictions in which it operates. Actinogen or others could identify product and efficacy issues relating to the safety of our technology. Accordingly, all forward looking statements are based on numerous assumptions regarding the Company's present and future business strategies and the political and economic environment in which Actinogen will operate in the future, which are subject to change without notice. Past performance is not necessarily a guide to future performance and no representation or warranty is made as to the likelihood of achievement or reasonableness of any forward looking statements or other forecast. There is no guarantee that Actinogen will achieve its stated objectives/milestones, that any of its forecasts will be met or that forward looking statements will be realised. You are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and we do not undertake any obligation to revise and disseminate forward-looking statements to reflect events or circumstances after the date hereof, or to reflect the occurrence of or non-occurrence of any events.

Neither Actinogen nor any other entity or person in or associated with Actinogen guarantee any return (whether capital or income) or generally the performance of Actinogen or the price at which its securities may trade. Any investment in Actinogen is subject to investment risks including the possibility of loss of capital invested and no return of income or payment of any dividends.

To the maximum extent permitted at law, Actinogen and all of its representatives, directors, officers, partners, employees or professional advisers (**Parties**) exclude all direct and indirect liability arising out of or in connection with any use or reliance of the information contained or described within this presentation. Other than to the extent required by law (and only to that extent), the Parties do not make any representation or give any assurance, guarantee or warranty (express or implied) as to, nor assume any responsibility or liability for, the authenticity, origin, validity, accuracy, suitability or completeness of, or any errors in or omissions from, any information, statement or opinion contained in this presentation or any accompanying, previous or subsequent material or presentation.

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



Actinogen snapshot

Actinogen Medical (ASX:ACW) is 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, ≤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 XanaMIA trial in healthy older volunteers at 5 mg and 10 mg dose levels

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[1]
- ✓ Cash position A$19M at 31 Mar 2022

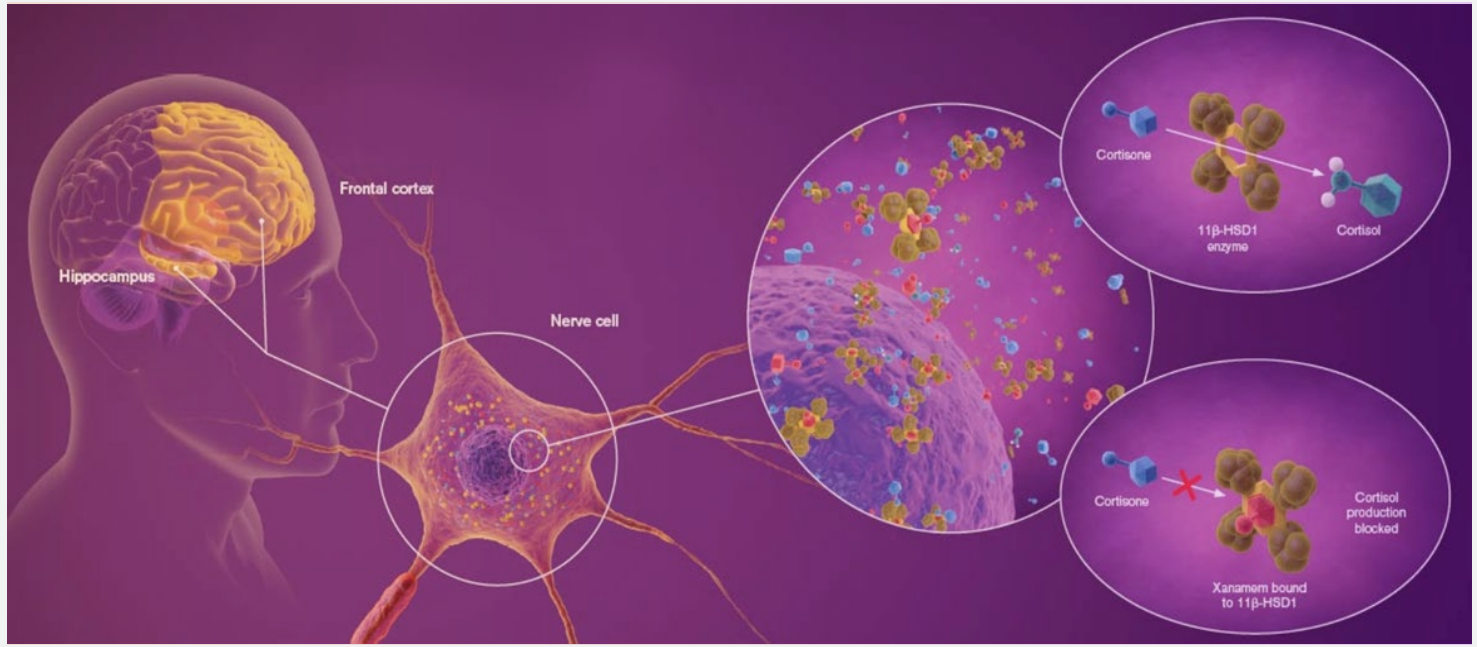
1. Composition of matter to 2031 plus 5-year extension in most countries, new patents in process

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)



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

Cognition Clinical Advisory Board

Renowned 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

Key implications from the new XanaMIA results

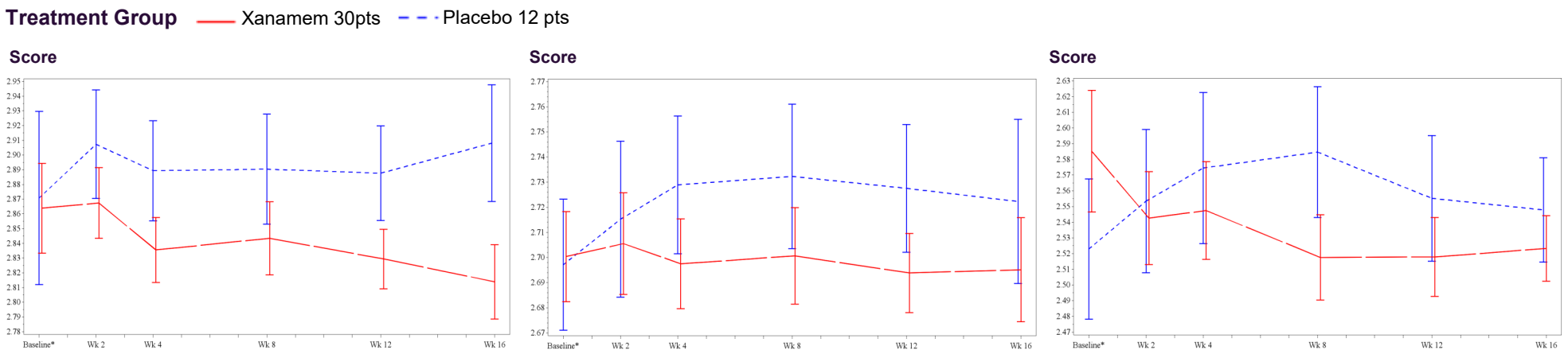
- Trial met its primary safety, efficacy (cognition) and pharmacodynamic endpoints
- Second consecutive double-blind trial to show improvement in attention and working memory with Xanamem
- Confirms the target dose range of ≤10 mg suggested by imaging of Xanamem action in the brain
- Demonstrates Actinogen can efficiently conduct trials like this in under 12 months in Australia
- Sets Actinogen up for success in future trials, including near-term Phase 2 trials in multiple diseases associated with dysregulated brain cortisol

1. "Attention" domains were individual and composite scores of working memory (one back test), visual identification (identification test), psychomotor function (detection test); other domains were a one card learning test, a delayed recall test and continuous paired learning test.

Previously

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

PET data supports exploring a lower Xanamem dose range of ≤10mg daily

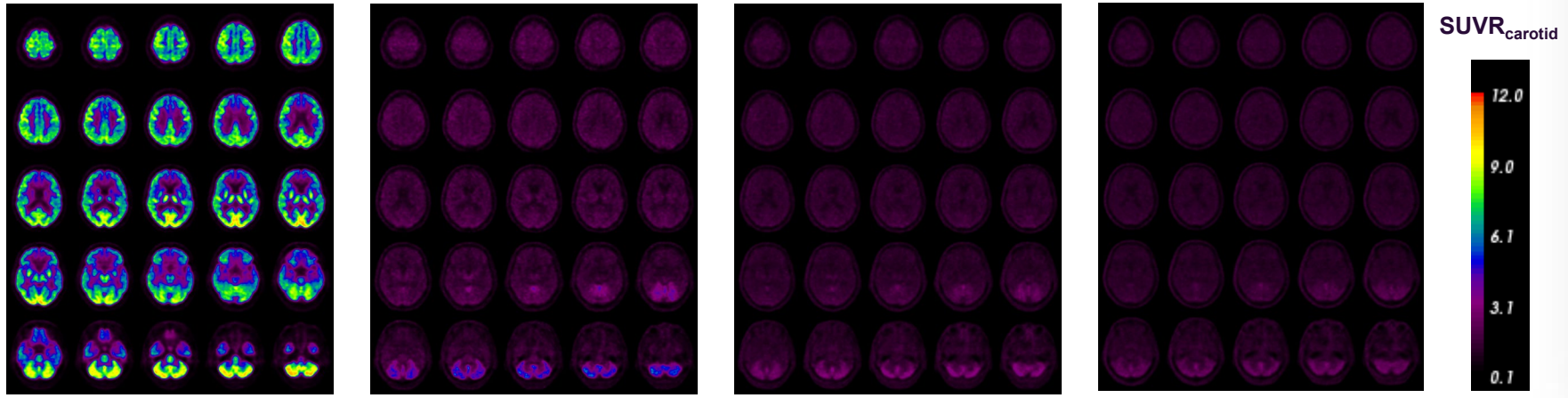
Baseline

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.

XanaMIA Phase 1b/2 trial design

Targeting the first stages of Alzheimer's Disease (AD)

XanaMIA - Part A: Double-blind Phase 1b	XanaMIA - Part B: Phase 2
H12022: *minimally effective dose level*	**2023: experimental study design in patients with early stages of Alzheimer's Disease**
107 healthy older subjects with normal cognition, 50-80 years of age • 10 mg & 5 mg daily vs. placebo • designed to measure effect sizes in cognition rather than statistical significance	**Final design to be determined.**
6-week duration of therapy, 4-week follow up	
Primary dose-response objectives: 1. Safety of 5 mg and 10 mg dose levels 2. Pharmacodynamics of ACTH[1] response 3. Cognition: especially attention effects seen previously in Cogstate CTB	

1. ACTH: adrenocorticotropic hormone; ACTH levels are a measure of the pharmacodynamic action of Xanamem to reduce intracellular cortisol

Statistical methods

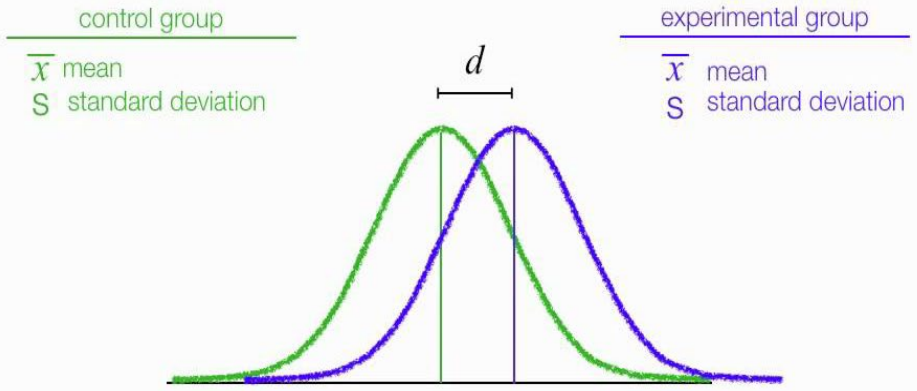
- Double-blind, randomized design, industry best standard statistical analysis for smaller sample size trials: computerized cognitive testing with the Cogstate CTB[1] with International Digit Symbol Substitution Test - Symbols (IDSST-S)
- “Intention-to-treat” analyses with no imputation for missing data, no “last observation carried forward”
- Linear Mixed-Effects Model for Repeated Measures (MMRM) with treatment group, visit, and treatment-by-visit interaction as fixed effects. Baseline score was included as a covariate and subject-specific intercept as a random effect
- Effect Sizes (ES) vs. placebo were estimated from modelled data as Z scores and raw data as Cohen’s d statistics
- For cognitive data the a priori criterion for effect detection was Cohen’s d ≥ 0.3 in one or more tests (≥ 0.2 is regarded as clinically meaningful in Alzheimer’s Disease)

1. “Attention domains were individual and composite scores of working memory (one back test), visual identification (identification test), psychomotor function (detection test); other domains were a one card learning test, a delayed recall test and continuous paired learning test.

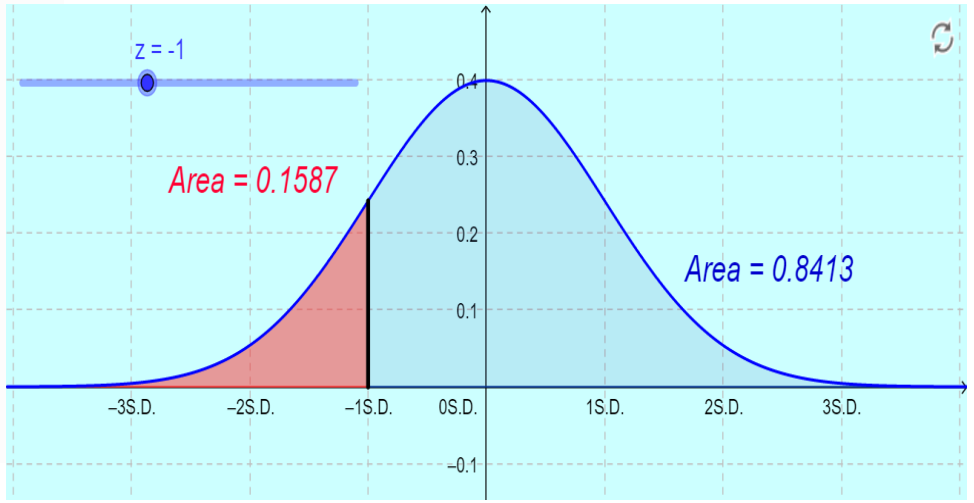
Effect size statistics measure “signal to noise”

Ratios commonly used in trials of Alzheimer’s Disease using raw or statistical model data

$$d = \frac{\overline{x} - \overline{x}}{S}$$



Cohen’s d



Z-score is a standardization method for a normal distribution

1. ADASCog endpoint using ES as Cohen’s d (Aduhelm: estimated from Biogen presentation 2021) or Cohen’s d or Modelled Standardized Mean (AChE inhibitors: Rockwood 2004)

XanaMIA dose-ranging topline results

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)

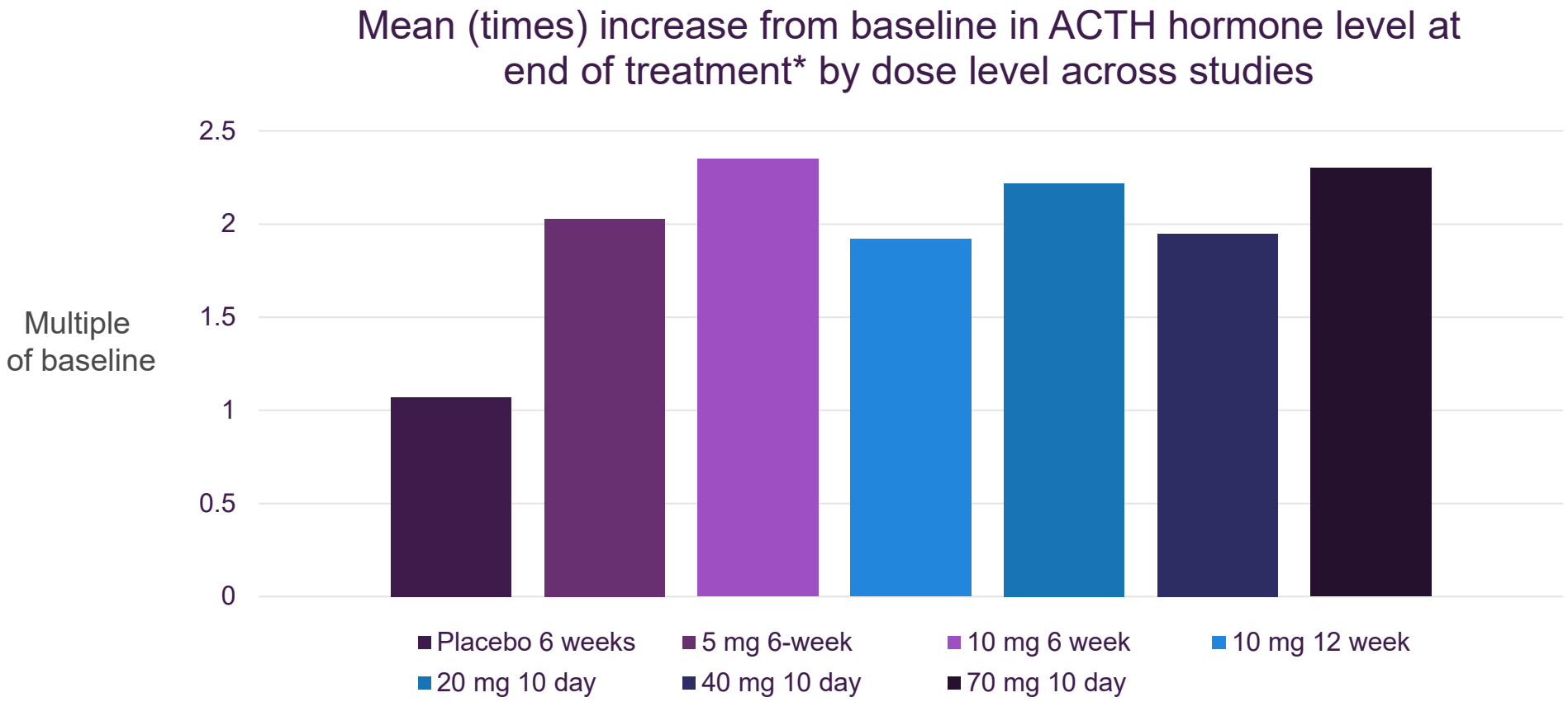
- Xanamem was safe and well-tolerated over the 6-week treatment period in this cognitively normal population aged 50-80 years (mean age 64 years, mixed female and male population)

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

ACTH hormone response suggests similar Xanamem biological activity at 5 mg and 10 mg dose levels

ACTH is the brain hormone that regulates cortisol production in the adrenal gland

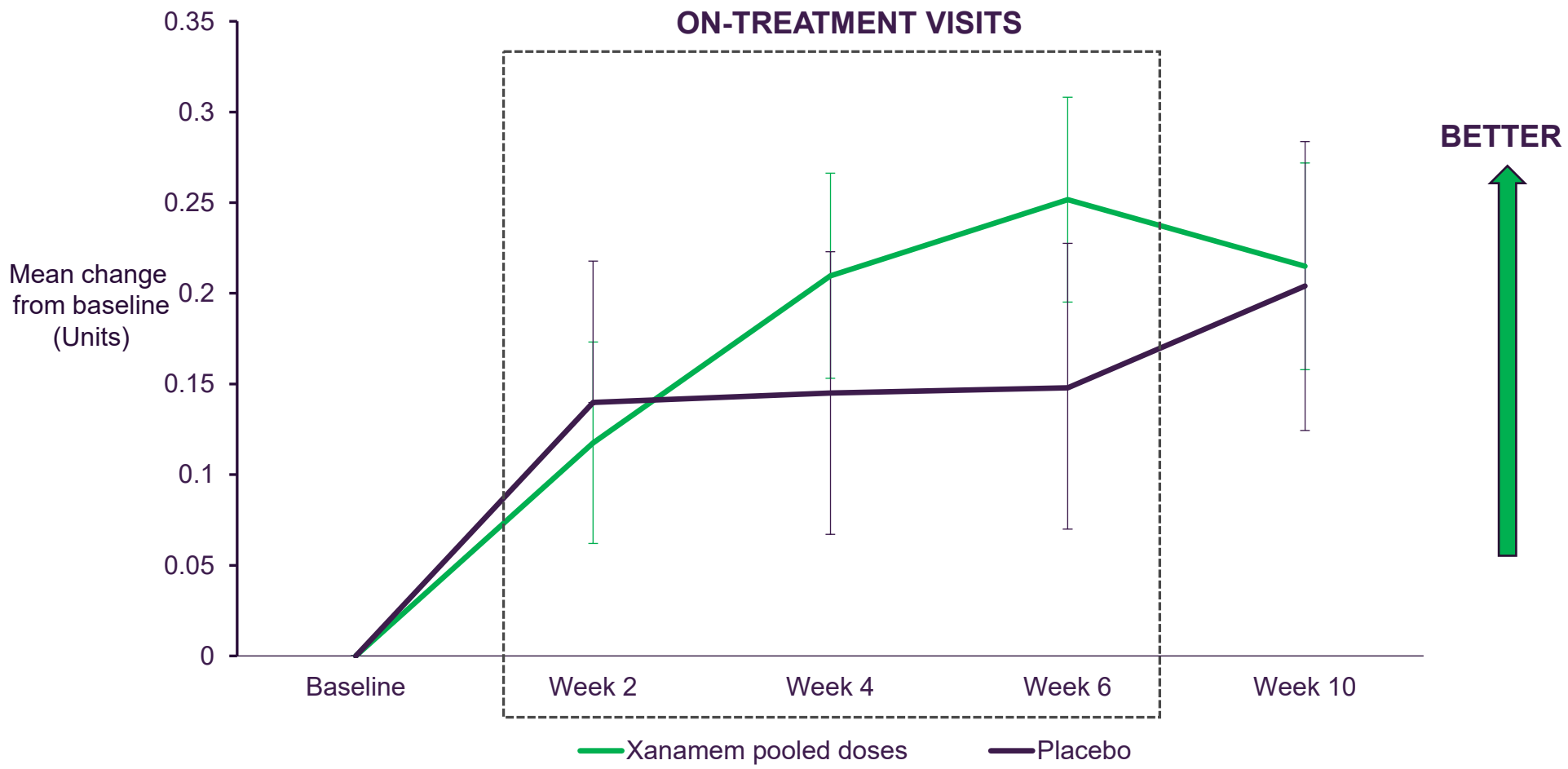


* steady-state plasma levels are achieved after 3 days: Webster et al. 2017, Actinogen data on file

Actinogen

Attention Composite improved at Week 4 and 6 vs. placebo

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



Actinogen

Effect Sizes Attention Composite & domains

Magnitude of treatment effect (on-treatment MMRM ES[1] > 0.9 in green)

XanaMIA trial Cognitive Evaluation (Test)	Desired improvement	Effect size[1] 5 mg			Effect size[1] 10 mg		
		Week 4 N=35	Week 6 N=35	Follow up N=33	Week 4 N=30	Week 6 N=29	Follow up N=29
Attention Composite	Positive	0.52	1.29	0.51	0.65	0.48	-0.38
Working Memory (One Back Test)	Positive	0.19	1.11	1.11	0.42	0.98	1.07
Visual Attention (Identification Test)	Positive	0.45	1.97[2]	-0.31	-0.48	0.29	-1.99
Psychomotor Function (Detection Test)	Positive	0.95	0.27	0.83	1.61	0.30	0.65

1. Z-score of standardized treatment effect (mean difference in MMRM model change from baseline vs. placebo/standard error of change) ; Z > 0.9 ~ one-sided 80% confidence interval or greater
2. p < 0.05 by MMRM, Cohen's d (raw mean change/pooled raw standard deviation of change) = 0.32

Previous XanaHES trial[3]	Week 4	Week 8	Week 12	Follow up
Attention Composite ES[1]	1.11	1.20	1.27	1.36

3. XanaHES Phase 1 clinical trial treated healthy elderly patients with 20mg Xanamem daily (n=30 active, n=12 placebo). MMRM ES Z-score calculated by a similar model to the XanaMIA trial

Effect Sizes non-attentional domains, IDSST-S

Mixed positive & negative effects similar to previous XanaHES trial; no effect on IDSST-S (on treatment MMRM ES[1] > 0.9 in green and -0.9 in pink)

XanaMIA trial Cognitive Evaluation Test	Desired Improvement	Effect Size[1] 5 mg			Effect Size[1] 10 mg		
		Week 4 N=35	Week 6 N=35	Follow up N=33	Week 4 N=29	Week 6 N=29	Follow up N=29
Composite	Positive	-0.60	-1.34	-0.67	-1.34	-0.09	-0.12
Paired Associate Learning (CPAL Test)	Positive	-0.17	1.07	0.47	-1.11	0.41	0.38
Delayed recall (CPAR)	Positive	-0.74	-1.83	-0.86	-0.98	-0.36	-1.42
Visual Learning (One Card Learning Test)	Positive	-0.15	-1.22	-0.57	-0.69	-0.19	0.77
IDSST-S	Positive	-0.19	0.04	0.07	-0.84	-0.20	-0.69

1. Z-score of standardized treatment effect (mean difference in MMRM model change from baseline vs. placebo/standard error of change); Z > 0.9 ~ one-sided 80% confidence interval or greater

Previous XanaHES trial	Week 4	Week 8	Week 12	Follow up
Non- Attention Composite ES[2]	0.56	0.11	0.13	-0.20

2. XanaHES Phase 1 clinical trial treated healthy elderly patients with 20mg Xanamem daily (n=30 active, n=12 placebo). MMRM ES Z-score calculated by a similar model to the XanaMIA trial

Xanamem was safe and well-tolerated

- No treatment-related serious adverse events
- Other predominantly mild events were generally equally distributed across the three groups including placebo
- No adverse events of concern, consistent with program safety database of over 300 people studied in trials to date

Summary

- There is a strong unmet need for new and safer treatments for many diseases where dysregulated cortisol is a target - Xanamem is designed to reduce cortisol inside brain cells
- Xanamem is potentially a rapidly-acting cognitive enhancer and, in the longer term, a disease modifier
- This Phase 1b trial in cognitively normal, older volunteers met its primary objectives of safety, pharmacodynamics and clinically significant effects on cognition:
  - ✓ Rapid improvements in cognition for attention tests highly consistent with the prior XanaHES trial
  - ✓ Met primary cognitive endpoint of Cohen's d > 0.3 and other clinically significant effects in test domains of "attention" (working memory, visual attention, psychomotor function)
  - ✓ Biological activity confirmed for 5 mg and 10 mg dose levels based on ACTH hormonal response
  - ✓ ACTH and cognition findings were consistent with high target engagement in the brain at low doses visualized with PET imaging

Next steps

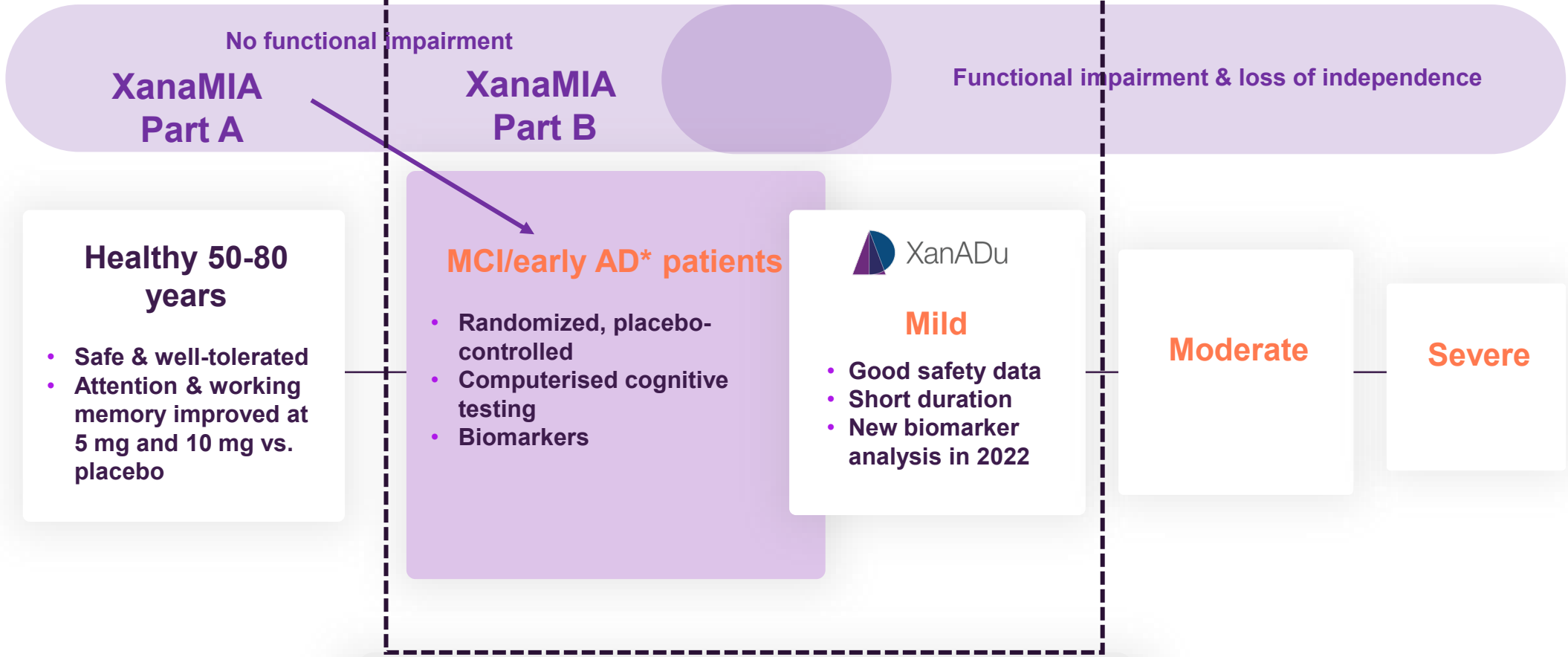
Actinogen continues its Phase 2 trial program with greater confidence:

- In its choice of a lower minimally effective dose range of ≤ 10 mg
- Utility of the Cogstate CTB to measure cognitive effects of Xanamem

The next steps for Alzheimer's Disease include:

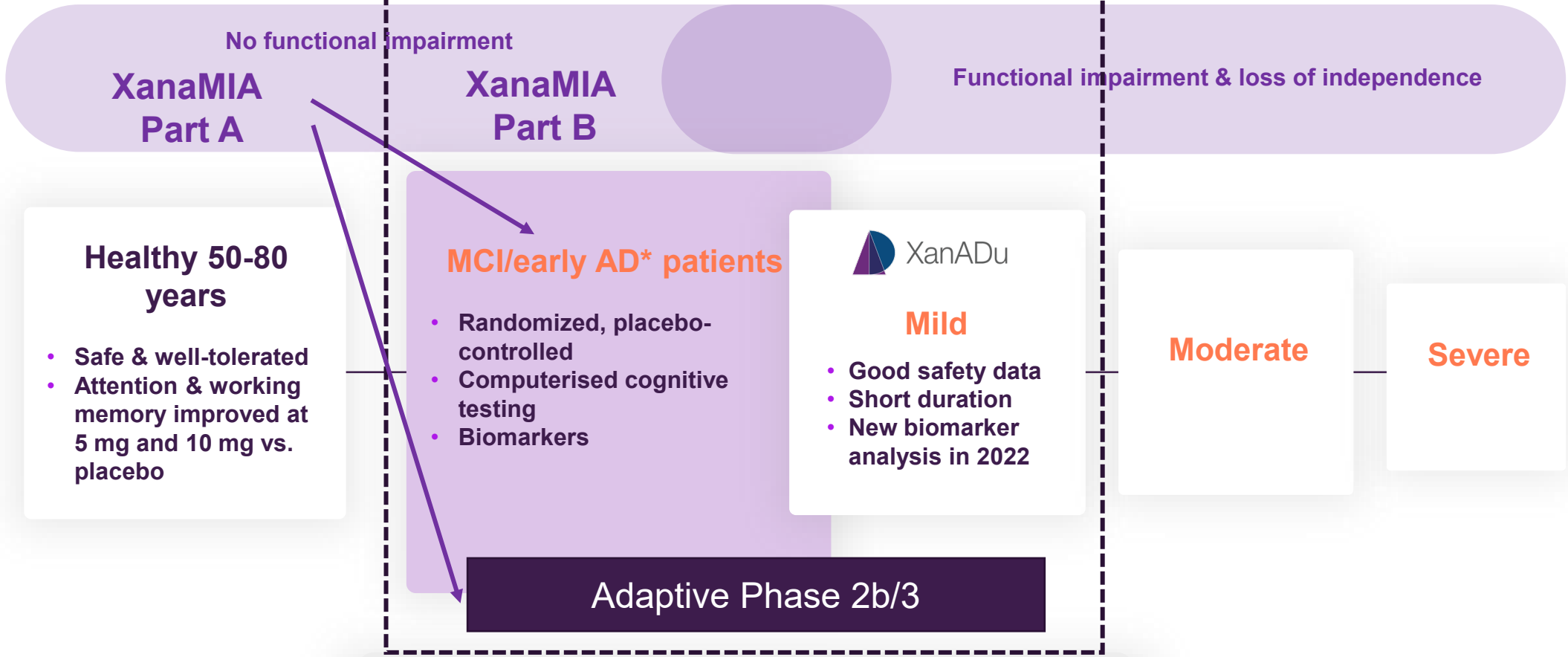
- Full analysis of trial data
- Consultation with Australian and international Alzheimer's Disease experts
- Design of the XanaMIA Part B trial in patients with early stages of Alzheimer's Disease

Next: Moving Xanamem trials into AD patients with a focus on cognitive enhancement



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

Next: Moving Xanamem trials into AD patients with a focus on cognitive enhancement



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

Actinogen Strategy

Accelerate clinical development

- ***Focus on cognitive enhancement***:
  - Early stages of Alzheimer's Disease
  - Implement XanaMIA Part B
  - Depression Phase 2 trial
  - 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

Regulatory engagement

- Seek early US FDA and EMA interactions on cognitive enhancement development programs

Xanamem Clinical Development Pipeline

	Phase 2 Pathway	Outlook
 Cognitive impairment in early **Alzheimer's disease**	**XanaMIA (IND)** **Part A:** 10mg, 5mg, Placebo Older Volunteers: Cognition **Part B:** Patients with early stage AD: Cognitive enhancement & supporting assessments	*"Big-to-market"* *Multiple Phase 2b/3 trials*
 **Depression** with cognitive impairment	**Study preparation** → **XanaMDD** Phase 2 randomised trial measuring depression & cognition	*Potential to treat both depression and related cognitive impairment*
 Anxiety, sleep & behavioural problems in **Fragile X Syndrome**	**XanaFX (IND)** **Proof-of-concept in adolescent and young adult males**	*Pending alternative funding or partnership*

Key catalysts

- **Clinical trials**

  Alzheimer's Disease

  - **XanaMIA Part A cognition & safety results positive**
  - Expert review of XanaMIA data and next steps
  - Commence XanaMIA Part B trial in patients in 2022, results 2023-4
  - Regulatory interactions

  Depression

  - Commence trial setup
  - Commence program later in 2022, results 2023-4

- **Publications and collaborations**

  - XanaMIA Part A scientific presentation later in 2022
  - PET study manuscript submitted
  - Other key peer-review publications

Thank you and Questions