ASX ANNOUNCEMENT

ACW Alzheimer’s Disease biomarker study clinical results presentation slides

Sydney, 10 October 2022. Actinogen Medical ASX: ACW (“ACW” or “the Company”) is pleased to release the attached presentation slides relating to the positive Phase 2a clinical data from its Alzheimer’s Disease (AD) biomarker study announced this morning on the ASX platform.

Webcast today at 11am AEDT

Actinogen CEO Dr Steven Gourlay and CMO Professor Paul Rolan will present the slides at a webcast at 11am AEDT today to review the positive clinical results from the biomarker study.

Register for the webcast by clicking on the link below or copying it into a web browser:

https://us02web.zoom.us/webinar/register/WN__5Yufq4xQ4-upem9WPnHwQ

A full recording of the webcast will be made available on the Actinogen website www.actinogen.com.au as soon as practicable following the conclusion of the webcast.

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. 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.
Alzheimer’s Disease biomarker study validates Xanamem® program
Positive Phase 2a clinical data

Dr. Steven Gourlay MBBS PhD MBA, CEO & MD
Professor Paul Rolan MD FRACP, CMO
10 October 2022
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Phase 2a clinical biomarker results
Online Q&A

1. Click on the Q&A icon

2. Type your question in the new Q&A window

3. Hit enter on your keyboard to submit your message

To contact support:
Please call 1300 816 159 (within Australia) or +61 2 8072 1479 (outside of Australia)
Alzheimer’s Disease biomarker study validates Xanamem® program

Positive Phase 2a clinical data

Dr. Steven Gourlay MBBS PhD MBA, CEO & MD
Professor Paul Rolan MD FRACP, CMO

10 October 2022
Alzheimer’s Disease (AD) key clinical findings

Major points

• Phase 2a placebo-controlled trial of Xanamem 10 mg vs. placebo over 12 weeks was re-run in 72 biomarker-positive patients with mild AD

• Used a pre-specified protocol & analysis plan to avoid bias

• Patients with elevated blood pTau showed a clinically significant Xanamem effect on the CDR-SB endpoint representing a 60% relative reduction in progression of disease

• CDR-SB effect of 0.6 – 0.8 points is larger than the 0.45 points reported recently for a successful Phase 3 trial of lecanemab¹ (amyloid antibody)

• Positive trends in a Neurologic Test Battery (NTB) of executive function & Mini Mental State Exam (MMSE)

• Regulatory path to approval clear and uncontroversial with FDA-approved CDR-SB

• Findings significantly de-risk and improve AD program efficiency

Xanamem Phase 2 & 3 program

Building on four independent Phase 1 and 2 studies showing activity

Current Phase 1 & 2a, biomarker
Safety, cognition activity (n~300)

Phase 2b
Alzheimer’s Disease (AD)

Phase 3
Alzheimer’s Disease with focus on cognitive enhancement

Phase 2a
Cognitive Impairment in Depressive Disorder (CIDD)

Phase 3
Cognitive Impairment in Depression
AD biomarker study fundamentals

Assessment of efficacy in the Xanamem AD program is based on the proven use of clinical endpoints of cognition and function for regulatory approvals without reliance on biomarkers.

However, as a supplement to clinical data, biomarkers have one major and two lesser potential uses:

- **Choosing patients with a disease likely to get treatment benefit**
  - Confirming patients who have “real” AD and are likely to progress and thus have measurable treatment benefits.

- **Confirming biologic activity & dose**
  - Biologic activity at a given dose to indicate potential use as a surrogate endpoint with suitable validation.

- **In regulatory submissions as “surrogate” endpoints prior to more definitive Phase 3 trials**
  - e.g. accelerated approvals to shave time off marketing approvals for serious diseases like cancer.
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 processes¹,²

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
Xanamem’s mechanism is different to anti-amyloid antibodies

Proteins may be a secondary phenomena not related to biological causation

Corticosterone Releasing Factor

ACTH

Neuro-inflammation

Xanamem

Cortisone → Cortisol

GABA, glutamate

Dendritic spine pruning

Cognitive impairment

Amyloid & pTau proteins

Neuron death

Phase 2a clinical biomarker results
Previously: evidence of Xanamem activity in cognition from multiple sources

- Protection against cognitive decline in animal model of AD using a Xanamem analogue independent of amyloid plaque
- Human 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
A brief history of Alzheimer’s Disease drug development

See also Actinogen Clinical Trials
Science Forum 03 August 2022
https://youtu.be/Bm9ATZx1zEk
A small number of drugs to tackle cognition have worked and been approved in AD

Approved on clinical scales\(^1\) in mild-moderate AD, 6-month trials

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>First Approval</th>
<th>Benefit</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral anticholinesterase inhibitors</td>
<td>1996</td>
<td>Cognitive &amp; functional scales</td>
<td>Gastrointestinal side effects Multiple trials</td>
</tr>
<tr>
<td>e.g. donepezil, rivastigmine, galantamine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral NMDA inhibitors</td>
<td>2003</td>
<td>Cognitive &amp; functional scales</td>
<td>Gastrointestinal side effects Multiple trials</td>
</tr>
<tr>
<td>e.g. memantine, some in development</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral oligomannate</td>
<td>2019</td>
<td>Cognitive &amp; functional scales</td>
<td>Single positive trial</td>
</tr>
<tr>
<td>(GV-971, brown algae)</td>
<td>China only</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The primary Xanamem strategy is to follow this proven clinical pathway

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1. Clinical scales measure how a patient feels, performs and functions.
## Clinical Dementia Rating – Sum of Boxes (CDR-SB) endpoint to assess dementia in early-stage AD

<table>
<thead>
<tr>
<th>Test domain</th>
<th>Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
</tr>
<tr>
<td>------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Memory</td>
<td>0</td>
</tr>
<tr>
<td>Orientation</td>
<td></td>
</tr>
<tr>
<td>Judgment &amp; Problem Solving</td>
<td></td>
</tr>
<tr>
<td>Community Affairs</td>
<td></td>
</tr>
<tr>
<td>Home &amp; Hobbies</td>
<td></td>
</tr>
<tr>
<td>Personal Care</td>
<td></td>
</tr>
</tbody>
</table>

Score is sum of each line i.e. score between 0 and 18 (0 = normal)
Amyloid antibodies are “disease modifying” based on Positron Emission Tomography (PET) brain scan and CDR-SB

Use of blood and cerebrospinal fluid (CSF) levels is in development

<table>
<thead>
<tr>
<th>Predictive biomarker</th>
<th>How measured</th>
<th>Observations</th>
<th>FDA</th>
<th>Impact of drug treatment for target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain amyloid</td>
<td>PET scan</td>
<td>Aducanumab - major amyloid reduction(^1)</td>
<td>✓</td>
<td>Clinically significant benefit 0.4 points on CDR-SB</td>
</tr>
<tr>
<td></td>
<td>PET scan</td>
<td>Lecanemab – under consideration by FDA</td>
<td>✓</td>
<td>Statistically and clinically significant benefit 0.45 points on CDR-SB</td>
</tr>
<tr>
<td>CSF amyloid</td>
<td>Spinal tap</td>
<td>Part of ATN(^2) diagnostic criteria for AD, prediction evolving</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood amyloid</td>
<td>Blood test</td>
<td>Promising as alternative to spinal tap for CSF or imaging</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CDR-SB is an accepted endpoint for pivotal trials in early-stage AD

1. Aduhelm US Product Information
2. ATN: Amyloid, Tau, Neurodegeneration
Elevated pTau181 diagnostic for AD type dementia

Blood pTau proposed to select patients with confirmed AD in Phase 2b

1. Data shown from Thijssen et al 2020; ADpath Alzheimer’s Disease pathology diagnosis; FTLD Frontotemporal Dementia pathology diagnosis; TAU FTLD type dementia; TDP a different type of FTLD dementia

Phase 2a clinical biomarker results
Elevated blood pTau is the single best predictor of progression in AD\textsuperscript{1}

Blood pTau proposed to select AD patients likely to progress in Phase 2b

1. Data shown from Cullen et al. 2022; Thijssen et al 2020 showed similar findings for pTau181; similar findings Cullen et al. 2021, Aβ amyloid beta; P-tau phosphorylated tau protein; NFL neurofilament light (a nerve protein); GFAP Glial Fibrillary Acidic Protein (only in brain)
Phase 2 biomarker study methods and results
Phase 2 blood biomarker study design & methods

Uses a pre-specified protocol and analysis plan

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)

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

Creates valuable data relating to patient selection and efficacy in a mild AD population
Baseline characteristics of patients confirms similar populations

Slightly higher ADASCog14, CDR-SB & ADCOMS, lower MMSE in biomarker study

<table>
<thead>
<tr>
<th></th>
<th>Biomarker Study N=72</th>
<th>XanADu Phase 2a N=185</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD)</td>
<td>71 (8)</td>
<td>71 (8)</td>
</tr>
<tr>
<td>% female</td>
<td>54%</td>
<td>57%</td>
</tr>
<tr>
<td>ADASCog14 (mean, SD)</td>
<td>33 (8)</td>
<td>29 (9)</td>
</tr>
<tr>
<td>ADCOMS (mean, SD)</td>
<td>0.52 (0.19)</td>
<td>0.50 (0.20)</td>
</tr>
<tr>
<td>MMSE (mean, SD)</td>
<td>22 (3)</td>
<td>23 (3)</td>
</tr>
<tr>
<td>CDR-SB (mean, SD)</td>
<td>3.9 (1.6)</td>
<td>3.8 (1.7)</td>
</tr>
<tr>
<td>pTau pg/mL (mean, SD)</td>
<td>7.7 (6.8)</td>
<td>-</td>
</tr>
<tr>
<td>% pTau &gt; 10.2 pg/mL</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Aβ42/40 ratio (mean, SD)</td>
<td>21.9 (15.5)</td>
<td>-</td>
</tr>
<tr>
<td>GFAP pg/mL (mean, SD)</td>
<td>118 (73)</td>
<td>-</td>
</tr>
</tbody>
</table>

Study population is similar to overall “mixed” non-AD and AD Phase 2a population.
Higher pTau (> 6.74 pg/mL\(^1\)) subgroup shows clinically significant effect on CDR-SB (n=34)

Group most likely to have pathological AD

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Desired change</th>
<th>Xanamem (n=16)</th>
<th>Placebo (n=18)</th>
<th>Cohen’s d</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADASCog14 total (mean)</td>
<td>Down</td>
<td>1.5</td>
<td>0.8</td>
<td>0.00</td>
<td>0.74</td>
</tr>
<tr>
<td>ADCOMS (mean)</td>
<td>Down</td>
<td>0.07</td>
<td>0.09</td>
<td>0.13</td>
<td>0.57</td>
</tr>
<tr>
<td>ADASCog14 167 units (mean)</td>
<td>Down</td>
<td>1.0</td>
<td>0.9</td>
<td>0.06</td>
<td>0.93</td>
</tr>
<tr>
<td>MMSE units (mean)</td>
<td>Up</td>
<td>-0.9</td>
<td>-1.2</td>
<td>0.16</td>
<td>0.80</td>
</tr>
<tr>
<td>CDR-SB units (mean)(^1)</td>
<td>Down</td>
<td>0.4</td>
<td>1.0</td>
<td>0.41</td>
<td>0.09</td>
</tr>
<tr>
<td>CDR-SB units (median)</td>
<td>Down</td>
<td>0.0</td>
<td>0.8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>NTB units (mean)</td>
<td>Up</td>
<td>0.5</td>
<td>-2.3</td>
<td>0.26</td>
<td>0.48</td>
</tr>
<tr>
<td>RAVLT units (mean)</td>
<td>Up</td>
<td>0.7</td>
<td>0.5</td>
<td>0.02</td>
<td>0.91</td>
</tr>
<tr>
<td>NPI units (mean)</td>
<td>Down</td>
<td>1.3</td>
<td>0.5</td>
<td>-0.18</td>
<td>0.42</td>
</tr>
</tbody>
</table>

1. Median value in this study

Clinically significant effect size of CDR-SB 0.6 – 0.8 units
## Benefit on CDR-SB in both high pTau subgroups

Groups most likely to have pathological AD

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Desired change</th>
<th>Xanamem</th>
<th>Placebo</th>
<th>Cohen’s d</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pTau &gt;6.74 pg/mL(^1) (mean)</td>
<td>34</td>
<td>Down</td>
<td>0.4</td>
<td>1.0</td>
<td>0.41</td>
<td>0.09</td>
</tr>
<tr>
<td>pTau &gt;6.74 pg/mL (median)</td>
<td>34</td>
<td>Down</td>
<td>0.0</td>
<td>0.8</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>pTau &gt;10.2 pg/mL(^1) (mean)</td>
<td>9</td>
<td>Down</td>
<td>0.1</td>
<td>0.8</td>
<td>0.62</td>
<td>0.33</td>
</tr>
<tr>
<td>pTau &gt;10.2 pg/mL (median)(^1)</td>
<td>9</td>
<td>Down</td>
<td>-0.3</td>
<td>0.5</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Clinically significant effect size of CDR-SB 0.7 - 0.8 units in very high pTau group

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1. Published cutoff of 10.2 pg/mL\(^2\) cutoff by Cullen et al. 2022 for progression to clinical AD. 6.74 pg/mL represents the median value of the dataset.
Xanamem doubled rate of disease stabilization

Response analysis in pTau-positive patients

Twice as many patients in the Xanamem group had stable or improved disease compared with placebo¹

56% of patients treated with Xanamem were stable or improved

0.6-point effect size represents a 60% 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%)
### MMSE shows Xanamem effect measurable in more impaired dementia

More clinically impaired subgroup

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Desired change</th>
<th>MMSE score</th>
<th>Cohen’s d</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE 20-23 (mean)</td>
<td>46</td>
<td>Up</td>
<td>1.7</td>
<td>-0.3</td>
<td>0.93</td>
</tr>
<tr>
<td>MMSE 20-23 (median)</td>
<td>46</td>
<td>Up</td>
<td>2.0</td>
<td>-1.0</td>
<td>-</td>
</tr>
</tbody>
</table>

Clinically & statistically significant effect size of MMSE +2.0 to 3.0 units
No change observed over 12 weeks consistent with non-amyloid mechanism

10mg vs. placebo, mean (standard error bars), published test-retest range in boxes

Longer duration studies needed to evaluate potential disease modification effects
Efficacy conclusions

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

- Clinical activity of Xanamem in 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
- Complements positive prior trial findings on cognition
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

XanaMIA Phase 1b
- Healthy 50-80 years
  - Safe & well-tolerated
  - Attention & working memory improved at 5 mg and 10 mg vs. placebo

XanaMIA Phase 2b
- MCI/early AD¹ patients
  - N=330, placebo-controlled
  - pTau patient selection
  - 5 mg & 10 mg dose levels
  - 6 month duration
  - Cogstate computerised cognitive testing & CDR-SB
  - Various secondary endpoints

FDA/EMA meetings then Pivotal Trial(s)

Rapid path to multi-billion dollar market alone or as combination therapy

Functional impairment & loss of independence

XanADu
- Mild
  - 10 mg vs. placebo
  - Good safety data
  - Short (12 weeks)
  - Biomarker analysis shows clinical activity in likely AD subset

Phase 2a clinical biomarker results

1. Mild Cognitive Impairment (MCI): memory, executive function deterioration with retained functional abilities; very mild AD with some functional impairment
XanaMIA Phase 2b trial design & implementation model: selecting AD patients by blood pTau level

Key inclusion/exclusion criteria
- Clinical diagnosis of MCI or mild dementia due to AD (NIA-AA)
- Elevated blood p-tau181
- Cognitive impairment relative to demographic norms
- Excluded vascular cause of dementia

Primary Endpoints
- CDR-SB
- Cogstate CTB attentional composite (attention and working memory)

Key Secondary Endpoints
- Amsterdam Activity of Daily Living scale
- Cogstate Executive Function & Episodic Memory Function Composites
- Individual tests
- Carer questionnaire / Patient Global Improvement

Key Implementation Features
- Australian trial sites plus selected international locations
- Actinogen “hands-on” operational model
- Optimized for scalable addition of international sites as required
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

**Key inclusion/exclusion criteria**
- Primary diagnosis of **MDD**
- Persistent depressive symptoms despite existing therapy
- Cognitive impairment relative to demographic norms

**Primary Endpoints**
- Cogstate CTB attentional composite (attention and working memory)

**Key Secondary Endpoints**
- Montgomery-Åsberg Depression Rating Scale (**MADRS**)
- **Executive Function** Cognitive Composite
- **Memory Function** Cognitive Composite

**Key Implementation Features**
- Australian trial sites
- Actinogen “hands-on” operational model
- First patient enrollment planned for 2022
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

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Stage</th>
<th>Cognitive endpoint</th>
<th>Company market cap. ($AU)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral Xanamem</strong> to lower brain cortisol</td>
<td>Phase 2</td>
<td>Cognitive test battery, CDR-SB, NTB</td>
<td>170 million</td>
</tr>
<tr>
<td>(Actinogen)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Oral inhibition filamin A</strong> to stop Aβ42 amyloid signal to TLR/α7nicR (Cassava Sciences)</td>
<td>Phase 3</td>
<td>Cognitive test battery</td>
<td>2.5 billion</td>
</tr>
<tr>
<td><strong>Oral QPCT inhibitor</strong> to prevent toxic amyloid formation (Vivoryon)</td>
<td>Phase 2</td>
<td>Cognitive test battery</td>
<td>315 million</td>
</tr>
</tbody>
</table>

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

1. at 9 Oct 2022
Xanamem Strategy & Timeline
Actinogen strategy validated by new results

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

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

Forward planning

- Scale up and optimise manufacturing to prepare for commercially viable, large scale production
- Ancillary clinical and nonclinical studies
- Commercial planning
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
Eminent world-leading authority on dementia, Associate Professor Michael Woodward, commented:

“The positive data for CDR-SB and other endpoints are encouraging and indicate a likely therapeutic effect of Xanamem in patients with the early stages of Alzheimer’s Disease.

The use of pTau blood levels to confirm the diagnosis of Alzheimer’s Disease in future trials represents a practical and efficient method to select patients at risk of disease progression and in whom a treatment effect is more likely to be observed.”
Questions
Online Q&A

1. Click on the Q&A icon

2. Type your question in the new Q&A window

3. Hit enter on your keyboard to submit your message

To contact support:
Please call 1300 816 159 (within Australia) or +61 2 8072 1479 (outside of Australia)
Thank you

If you have any questions following the webcast please contact:

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Appendix
### Xanamem Clinical Development Pipeline

#### Phase 2 Pathway

<table>
<thead>
<tr>
<th>Area</th>
<th>Description</th>
</tr>
</thead>
</table>
| **Cognitive impairment in early Alzheimer’s disease** | *Biomarker/efficacy analysis in patients with mild AD*  
- Phase 2 dataset of 10mg vs. placebo over 12 weeks, October 2022  
*Cognitive benefit in patients with early stages of AD*  
- Phase 2 XanaMIA Part B commencing H1 2023 |

| **Cognitive Impairment in Depressive Disorder** | *Depression and cognitive impairment placebo-controlled trial*  
- Phase 2 XanaCIDD trial to commence in Q4 2022 |

| **Anxiety, sleep & behavioural problems in Fragile X Syndrome** | *XanaFX (open IND with Phase 2 protocol)*  
- Phase 2 proof-of-concept in adolescent and young adult males |

#### Outlook

- “Big-to-market”  
  Multiple Phase 2b/3 trials
- Potential to treat both depression and related cognitive impairment
- Pending alternative funding or partnership
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>11β-HSD1</td>
<td>11 beta HydroxySteroid Dehydrogenase-1 enzyme</td>
</tr>
<tr>
<td>Aβ</td>
<td>Amyloid beta – a type of amyloid protein associated with Alzheimer’s Disease, 42 and 40 are different forms</td>
</tr>
<tr>
<td>ACTH</td>
<td>Adrenocorticotropic hormone that regulates blood levels of cortisol</td>
</tr>
<tr>
<td>ADAS-Cog</td>
<td>Alzheimer’s Disease Assessment Score - Cognition</td>
</tr>
<tr>
<td>ApoE4</td>
<td>Apoptoprotein genotype associated with genetic risk of Alzheimer’s Disease</td>
</tr>
<tr>
<td>ATN</td>
<td>Amyloid, Tau, Neurodegeneration</td>
</tr>
<tr>
<td>Clinical scales</td>
<td>Measure how a patient feels, performs and functions</td>
</tr>
<tr>
<td>CDR-SB</td>
<td>Clinical Dementia Rating “Sum of Boxes” scale measuring cognition and function on an 18-point scale (high worse)</td>
</tr>
<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>CSF</td>
<td>Cerebrospinal fluid</td>
</tr>
<tr>
<td>CTAD</td>
<td>Clinical Trials on Alzheimer’s Disease (conference)</td>
</tr>
<tr>
<td>CTB</td>
<td>Cognitive Test Battery of computerized tests</td>
</tr>
<tr>
<td>Double-blind</td>
<td>Investigators, participants and company do not know who has active vs placebo treatment during a trial</td>
</tr>
<tr>
<td>EMA</td>
<td>European Medicines Agency</td>
</tr>
<tr>
<td>FDA</td>
<td>US Food &amp; Drug Administration</td>
</tr>
<tr>
<td>GFAP</td>
<td>Glial Fibrilliary Acidic Protein – a marker of microglial cell activation in the brain</td>
</tr>
<tr>
<td>Filamen A</td>
<td>a protein believed to relate to amyloid toxicity</td>
</tr>
<tr>
<td>IDSST</td>
<td>International Digit Symbol Substitution Test of cognition</td>
</tr>
</tbody>
</table>
**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