

ASX ANNOUNCEMENT

**Cognitive improvement demonstrated with Xanamem™**

- Statistically significant results demonstrate cognitive improvement in healthy elderly subjects dosed with 20mg Xanamem daily in the XanaHES dose escalation study
- Statistically significant reduction in serum cortisol following treatment with Xanamem 20mg daily
- Xanamem 20mg daily continues to exhibit a good safety profile with no serious adverse events observed
- Results significantly enhance the Xanamem dataset and help shape Actinogen's drug development strategy for the treatment of Alzheimer's disease and other neurological and metabolic diseases associated with cognitive impairment
- Company to host a Conference Call on October 1<sup>st</sup>, 2019 (today) at 10:30am (AEST)

**Sydney 1 October 2019: Actinogen Medical ASX: ACW ('ACW' or 'the Company')** is delighted to announce results from the XanaHES (*Xanamem in Healthy Elderly Subjects*) trial. The results demonstrate a significant improvement in cognition in trial participants dosed with Xanamem 20mg daily for 12 weeks, compared to placebo. This is the first time Xanamem has shown such a clear, statistically significant cognitive improvement in humans.

These breakthrough results reinforce the hypothesis and science underpinning the discovery and development of Xanamem - that lowering persistently raised cortisol levels in the brain is expected to positively enhance cognition.

Results from the study also showed that Xanamem, at a dose of 20mg daily, significantly ( $p < 0.001$ ) reduced serum cortisol levels in the trial participants over the study period. Furthermore, Xanamem 20mg daily exhibited a good safety profile over the 12 weeks of treatment, with no reports of serious adverse events.

Professor Michael Woodward from the Austin Health in Melbourne and one of the leading investigators in the XanADu trial said: *"It is just so pleasing and encouraging to see this positive efficacy data for Xanamem, following the disappointment of the XanADu trial. There have been so many past failures with the development of Alzheimer's drugs, so these promising results offer renewed hope for a treatment breakthrough for this devastating disease"*.

As previously announced, the XanADu trial in mild Alzheimer's patients showed that Xanamem 10mg daily was safe and altered the cortisol pathway but did not demonstrate an improvement in cognition.

The XanaHES trial was primarily designed as a placebo-controlled study to investigate the safety of 20mg Xanamem in healthy elderly subjects, but also included an exploratory assessment of cognition to evaluate the cognitive efficacy of Xanamem, using the industry standard Cogstate Cognitive Test Battery. The Cogstate Battery evaluated six domains of cognition, with the goal of broadly investigating whether 20mg Xanamem daily could positively influence cognition. Results from this trial show cognitive improvement in three of the six domains investigated after 12 weeks treatment (see table 1 below for more detail):

- One Back Test: evaluating working memory - highly statistically significant ( $p < 0.01$  with an effect size of 0.83)
- Identification Test: evaluating visual attention – statistically significant ( $p = 0.05$  with an effect size of 0.67)

- Detection Test: evaluating psychomotor function – trend to statistical significance (p=0.09 with an effect size of 0.76).

Effect size is a quantitative measure of the magnitude of a result indicating that treatment with 20mg Xanamem daily has a potentially important impact on these cognitive domains. See table 1 below for more details.

These results demonstrate an encouraging clinical efficacy signal in cognitive domains that are core to cognitive evaluation across many diseases.

Actinogen Medical Clinical Advisory Board member, Professor Jeff Cummings from the Cleveland Clinic in the USA commented: *“These results from the XanaHES study provide Actinogen with evidence of Xanamem’s ability to enhance cognition and inhibit cortisol production. Considering the broad array of medical conditions presenting with cognitive impairment and an associated raised cortisol, these promising results provide many opportunities for the ongoing development of the drug.”*

Enhancement of cognition in the XanaHES trial supports Xanamem’s potential for the treatment of Alzheimer’s disease and other conditions associated with cognitive impairment, including mood disorders like bipolar disorder, and schizophrenia

Actinogen CEO Dr Bill Ketelbey said: *“These are the results we have been looking for. They are hugely important for the development of Xanamem and for the potential for Xanamem to treat Alzheimer’s disease and other conditions associated with cognitive impairment”*

*“As we gather and analyse more data from XanaHES and the other ongoing studies, we are building a much clearer picture of Xanamem’s pharmacology, potential efficacy, safety, and mechanism of action; all of which will aid substantially in planning the future clinical development and commercialisation strategy for the drug.”*

*“We look forward to sharing Actinogen’s future development plans for Xanamem once they have been reviewed alongside these very pleasing results.”*

**Table 1: Results summary**

| COGNITIVE EVALUATION<br>(Test)            | P value | Effect Size: Cohen’s d |                   |                   |                   |
|---|---------|------------------------|-------------------|-------------------|-------------------|
|   |         | Week 2                 | Week 4            | Week 8            | Week 12           |
| WORKING MEMORY<br>(One Back Test)         | <0.01*  | 0.64 <sup>#</sup>      | 0.78 <sup>#</sup> | 0.64 <sup>#</sup> | 0.83 <sup>Δ</sup> |
| VISUAL ATTENTION<br>(Identification Test) | 0.05*   | 0.19                   | 0.67 <sup>#</sup> | 0.62 <sup>#</sup> | 0.67 <sup>#</sup> |
| PSYCHOMOTOR FUNCTION<br>(Detection Test)  | 0.09    | 0.47                   | 0.65 <sup>#</sup> | 1.12 <sup>Δ</sup> | 0.76 <sup>#</sup> |

**Notes:** \* statistical significance achieved;  
 # effect size >0.5 (medium treatment effect);  
 Δ effect size >0.8 (large treatment effect)

**Conference Call at 10.30am today**

The Company will host a **conference call at 10:30am (AEST) on Tuesday 1<sup>st</sup> October 2019 (today).**

The presentation that will be referred to in the call, is attached to this announcement.

The Company invites participants to ask questions during the call. In addition, interested parties may submit questions prior to the call to [info@actinogen.com.au](mailto:info@actinogen.com.au).

Participants are encouraged to pre-register for the call here:

<https://s1.c-conf.com/DiamondPass/Actinogen-invite.html>


You will receive a PIN and diary note for fast-track entry to the call. Alternatively, participants may dial in at the scheduled time using the dial-in number below

**Conference ID: 10002238**

|                                |                   |
|--------------------------------|-------------------|
| AUSTRALIA:                     | 1800 870 643      |
| ALTERNATIVE AUSTRALIAN NUMBER: | 1800 809 971      |
| OTHER INTERNATIONAL (METERED): | +61 7 3145 4010   |
| SYDNEY:                        | 02 9007 3187      |
| NEW ZEALAND:                   | 0800 4530 55      |
| AUCKLAND:                      | 0992 9168 7       |
| CHRISTCHURCH:                  | 0397 4263 2       |
| WELLINGTON:                    | 0497 4773 8       |
| CHINA:                         | 4001 2006 59      |
| FRANCE:                        | 0800 9814 98      |
| GERMANY:                       | 0800 1827 617     |
| HONG KONG:                     | 8009 66806        |
| JAPAN:                         | 0053 1161 281     |
| SINGAPORE:                     | 8001 0127 85      |
| SOUTH KOREA:                   | 0079 8142 0632 75 |
| UK:                            | 0800 0518 245     |
| USA/CANADA:                    | 1855 8811 339     |
| CHICAGO:                       | 1815 3732 080     |
| LOS ANGELES:                   | 1909 2354 020     |
| NEW YORK:                      | 1914 2023 258     |

**ENDS**

**Actinogen Medical**

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## **About Actinogen Medical**

Actinogen Medical (ASX: ACW) is an ASX-listed biotechnology company focused on innovative approaches to treating cognitive decline that occurs in chronic neurological and metabolic diseases. Actinogen Medical is developing its lead compound Xanamem, as a promising new therapy for Alzheimer's disease, a condition with multibillion-dollar market potential and material human impact. In the US alone, the cost of managing Alzheimer's disease is estimated to be US\$250bn and is projected to increase to US\$2tn by 2050, outstripping the treatment costs of all other diseases. Alzheimer's disease is now the leading cause of death in the UK and second only to ischaemic heart disease in Australia. In addition, Actinogen is currently planning an expanded clinical development program for Xanamem in cognitive impairment in mood disorders and schizophrenia. In the US alone, the collective economic costs of mood disorders and schizophrenia are estimated to exceed \$550bn, with the burden increasing every year. The cognitive dysfunction associated with these conditions is significantly debilitating for affected patients, with a substantial unmet medical need for novel, improved treatments.

## **About Xanamem™**

Xanamem's novel mechanism of action sets it apart from other Alzheimer's treatments. Xanamem is brain penetrant and works by blocking the excess production of cortisol - the stress hormone – through the inhibition of the 11β-HSD1 enzyme. There is a strong association between chronic stress and excess cortisol that leads to changes in the brain affecting memory. The 11β-HSD1 enzyme is highly concentrated in the hippocampus and frontal cortex, the areas of the brain associated with cognitive impairment in neurological diseases, including Alzheimer's disease, mood disorders and schizophrenia.

## **About XanADu**

XanADu is a Phase II double-blind, 12-week, randomised, placebo-controlled study to assess the safety, tolerability and efficacy of 10mg Xanamem once daily in subjects with mild dementia due to Alzheimer's disease. XanADu has fully enrolled 186 patients from 25 research sites across Australia, the UK and the USA. The trial is registered on [www.clinicaltrials.gov](http://www.clinicaltrials.gov) with the identifier: NCT02727699, where more details on the trial can be found, including the study design, patient eligibility criteria and the locations of the study sites.

## **About XanaHES**

XanaHES is a Phase I, randomised, single blinded, central reader blinded, placebo-controlled, dose escalation study to assess the safety and tolerability of Xanamem™ 20mg & 30mg once daily in healthy elderly volunteers. The XanaHES trial randomised 42 healthy elderly participants to receive either 20mg Xanamem daily (30 subjects) or placebo daily (12 subjects) for 12 weeks. Changes in cognitive performance from baseline to end-of-treatment will be measured as an exploratory efficacy outcome.

**Actinogen Medical encourages all current investors to go paperless by registering their details with the designated registry service provider, Link Market Services.**

# Investor Conference Call

*A novel approach to treating cognitive impairment  
and Alzheimer's disease*

Dr. Bill Ketelbey: CEO & MD

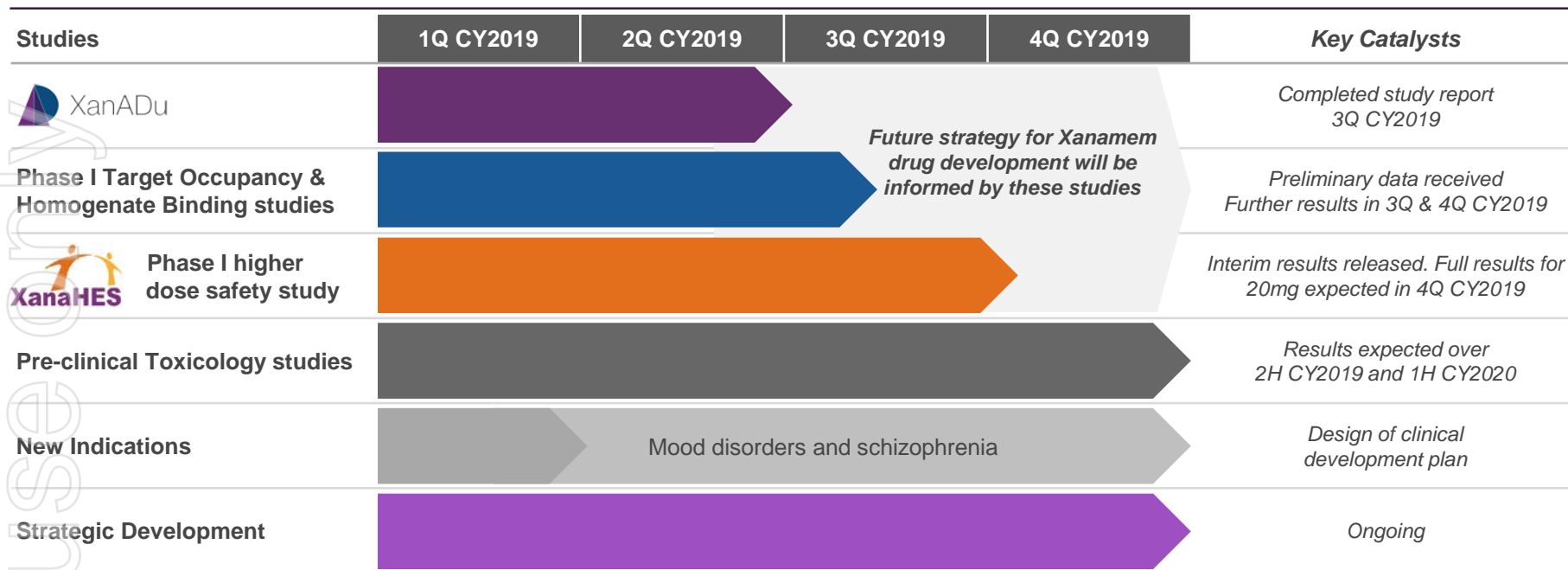
October 2019



**Actinogen**  
Medical

# Development Pipeline and Upcoming Catalysts

Multiple studies currently underway with significant upcoming milestones in the near term



**Actinogen is fully funded to complete all current studies**

# Comprehensive Xanamem Clinical Development Program

The ongoing comprehensive review of the data and results from XanADu and the additional studies will inform the optimal clinical development path



*Multiple endpoints and sub analyses will allow insight into Xanamem's potential and where it is most effective*



## Phase I Target Occupancy, & Homogenate Binding Studies

*Measures effects of different Xanamem doses on inhibiting the 11 $\beta$ -HSD1 enzyme in the brain*



**Totality of results**  
assessed by  
Actinogen and expert  
Clinical Advisory  
Board

## Key focus today



*Assess safety and tolerability of higher doses (to allow higher doses in future trials), with an efficacy assessment included*



## Additional Toxicology Studies

*Pre-clinical safety and toxicology studies to allow for longer treatment periods*

**The totality of results will inform further Xanamem development**

Single blind placebo-controlled, dose escalation study to assess safety, tolerability and efficacy of Xanamem in healthy elderly subjects – full results expected in 4Q CY2019



## 12 weeks

Xanamem treatment course  
Trial conducted at 1 site in Australia



## 42

Healthy elderly subjects  
(no cognitive impairment)



## 20mg daily

Xanamem 30 subjects  
Placebo 12 subjects



## Cognition assessed

Through computerised efficacy tests  
(Cogstate CTB<sup>1</sup>)

**Key objective to expand the Xanamem safety dataset and evaluate potential for higher dosage in future clinical trials**

1. Cogstate Cognitive Test Battery



XanaHES included a cognition endpoint to evaluate the cognitive efficacy of Xanamem using the Cogstate Cognitive Test Battery which evaluated six domains. Cognitive improvement demonstrated in three domains

## XanaHES 20mg Cogstate Cognitive Test Battery: p values and Cohen's d effect size

| Cognitive Evaluation (Test)                        | p value |        |        | Treatment Effect Size: Cohen's d |        |                   |                   |
|--|---------|--------|--------|----------------------------------|--------|-------------------|-------------------|
|  | All     | Male   | Female | Week 2                           | Week 4 | Week 8            | Week 12           |
| Working Memory (One Back Test)                     | <0.01*  | <0.01* | 0.03*  | 0.64#                            | 0.78#  | 0.64#             | 0.83 <sup>Δ</sup> |
| Visual Attention (Identification Test)             | 0.05*   | 0.04*  | 0.60   | 0.19                             | 0.67#  | 0.62#             | 0.67#             |
| Psychomotor Function (Detection Test)              | 0.09    | 0.94   | 0.13   | 0.47                             | 0.65#  | 1.12 <sup>Δ</sup> | 0.76#             |
| Paired Associate Learning (CPAL <sup>1</sup> Test) | 0.21    | 0.34   | 0.49   | 0.87 <sup>Δ</sup>                | 0.01   | 0.66#             | 0.08              |
| Memory (CPAL <sup>1</sup> – Delayed Test)          | 0.50    | 0.55   | 0.21   | 0.34                             | 0.23   | 0.06              | 0.48              |
| Visual Learning (One Card Learning Test)           | 0.92    | 0.41   | 0.64   | 0.11                             | 0.12   | 0.60#             | 0.19              |

*Additional details on slide 5*

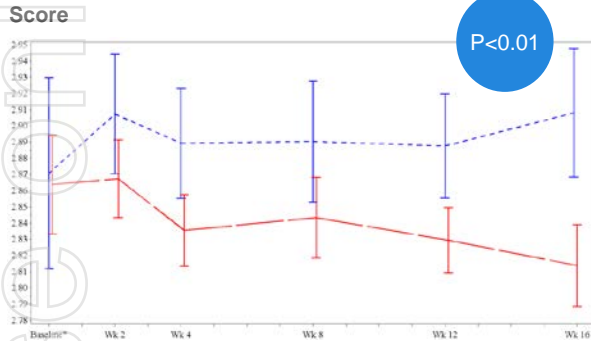
Notes: \* statistical significance achieved; # effect size >0.5 (moderate treatment effect); <sup>Δ</sup> effect size >0.8 (large treatment effect)

1: CPAL – Continuous Paired Associate Learning

Breakthrough results demonstrated statistically significant cognitive efficacy signal in multiple cognition domains – based on Cogstate Cognitive Test Battery

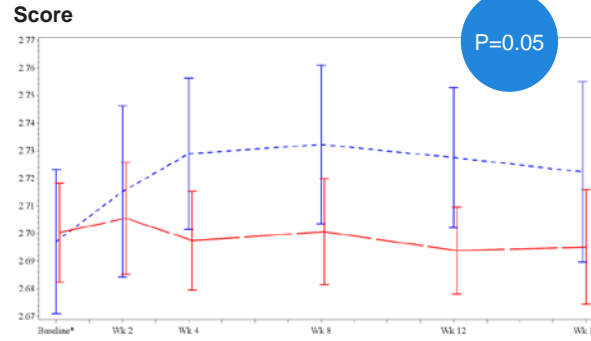
## Working memory (One Back Test)

**Strongly statistically significant result**



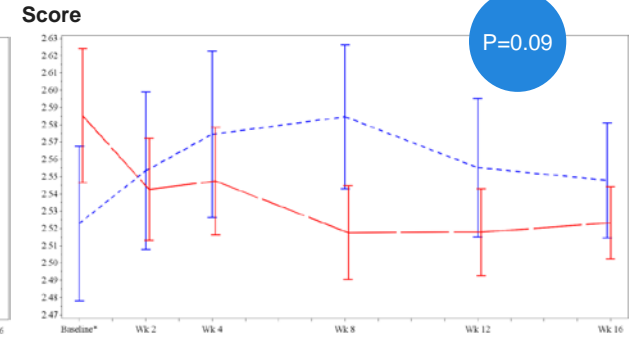
## Visual attention (Identification Test)

**Statistically positive signal**



## Psychomotor function (Detection Test)

**Good trend to a positive result**



**Treatment Group**  
— Xanamem    - - - Placebo

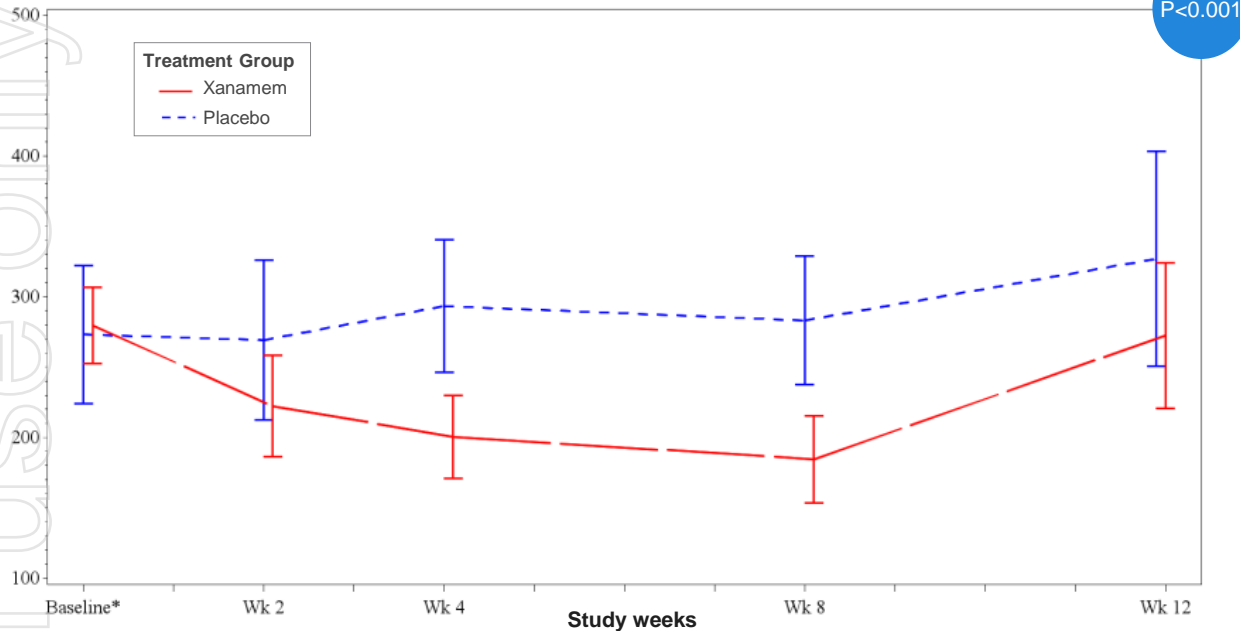
**Efficacy results of particular interest, reflecting high quality and consistent data in a small study population**

Baseline\* Mean of Observed Data

Efficacy results complemented by the statistically significant reduction in serum cortisol observed in the trial

## Significant reduction in cortisol levels (all patients)

Score: Efficacy Measure – Cortisol (nmol/L)



***Xanamem achieved an average decrease of 73.2 vs. placebo ( $p < 0.001$ )***

***These breakthrough results support the cortisol hypothesis that lowering persistently raised cortisol levels in the brain is expected to positively enhance cognition***

Baseline \* Mean of Observed Data

# XanADu: Possible Reasons Behind XanADu results

Likely due to the recurrent challenges seen in Alzheimer's disease drug development



## Conceptual model of the disease

- Causality unknown; cortisol as a target is a hypothesis
- Diagnoses largely based on highly subjective tools



## Outcome/endpoint measures

- Absence of valid biomarkers
- Subjectivity of outcome assessments flawed



## Stage of disease

- Wrong patient population (“too early” or “too late”)
- High heterogeneity as to the real biological drivers behind each individual's disease state



## Patient recruitment and retention

- Overall patient population may have been too heterogeneous to generalise results

## Xanamem

- Dose: too low or too high?
- Dosing regimen: may need bi-daily dosing?
- Treatment duration: may need to treat for longer?



# Xanamem: Phase I Target Occupancy Study & Homogenate Binding Studies

To assist with confirming and optimising Xanamem dosing



## Aim

To accurately demonstrate the effects different doses of Xanamem have on inhibiting the 11 $\beta$ -HSD1 enzyme in the human brain.

### Phase I Target Occupancy studies

- Competitive binding, radio-labelled tracer PET imaging assay
- Subject cohorts tested with Xanamem at 5mg, 10mg, 20mg, and 30mg doses.
- Data available from 10-30mg dosing cohorts

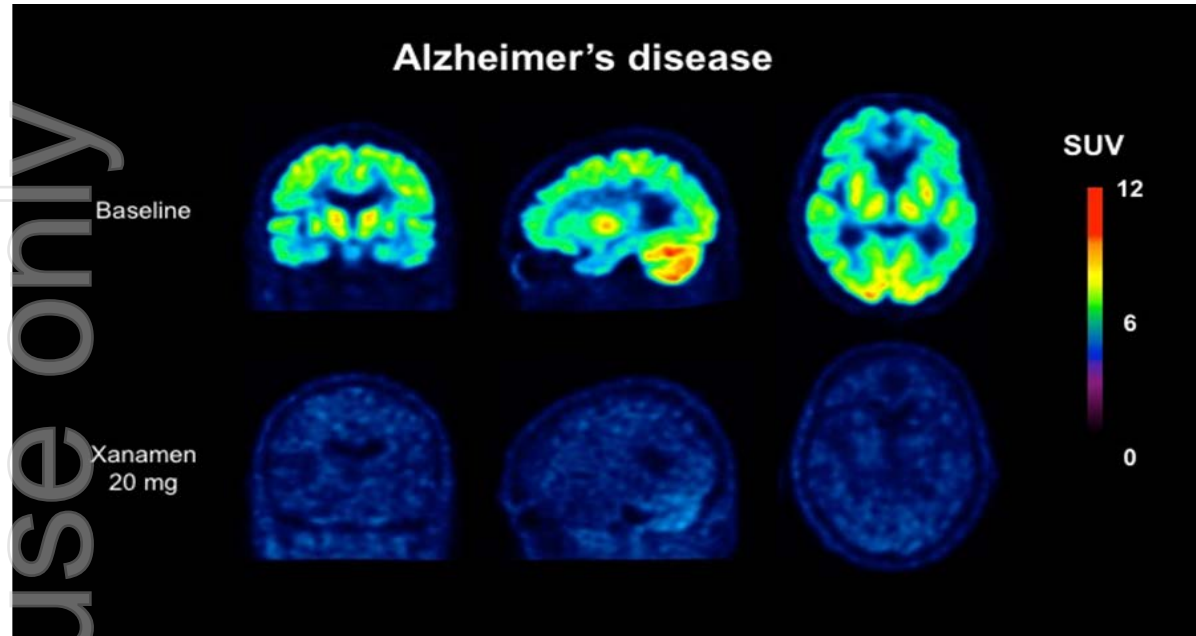
### In vitro Homogenate Binding Studies

- Enzyme occupancy competition studies, saturation binding studies, and enzyme activity assays in rat and human brain sections (ongoing)
- To correlate enzyme occupancy and enzyme activity at incremental doses of Xanamem

Key studies to help interpret XanADu results and support future clinical development strategy

# Target Occupancy Study: Preliminary Results

Phase I target occupancy study demonstrates that 10-30mg Xanamem dosed for seven days significantly occupies neuronal 11 $\beta$ -HSD1 throughout the brain



**50% to 85% occupancy,  
dependent upon brain  
region, dosage and  
study subject**

Further study data available  
in 4Q CY2019

Additional ongoing cohorts at 5mg  
Xanamem and 10mg with delayed  
PET imaging

Phase I Target Occupancy supports Xanamem as a potent, orally bioavailable and brain-penetrant 11 $\beta$ -HSD1 inhibitor



# Long-Term Safety and Toxicology Studies



## Aim

Evaluate safety and toxicology in rodent (six months) and dog (nine months) studies in preparation for longer term clinical studies

- Studies required by all regulators - FDA
- Will allow future **clinical studies beyond 12 weeks**
- Studies **ongoing**
- **No substantive safety issues** observed to date

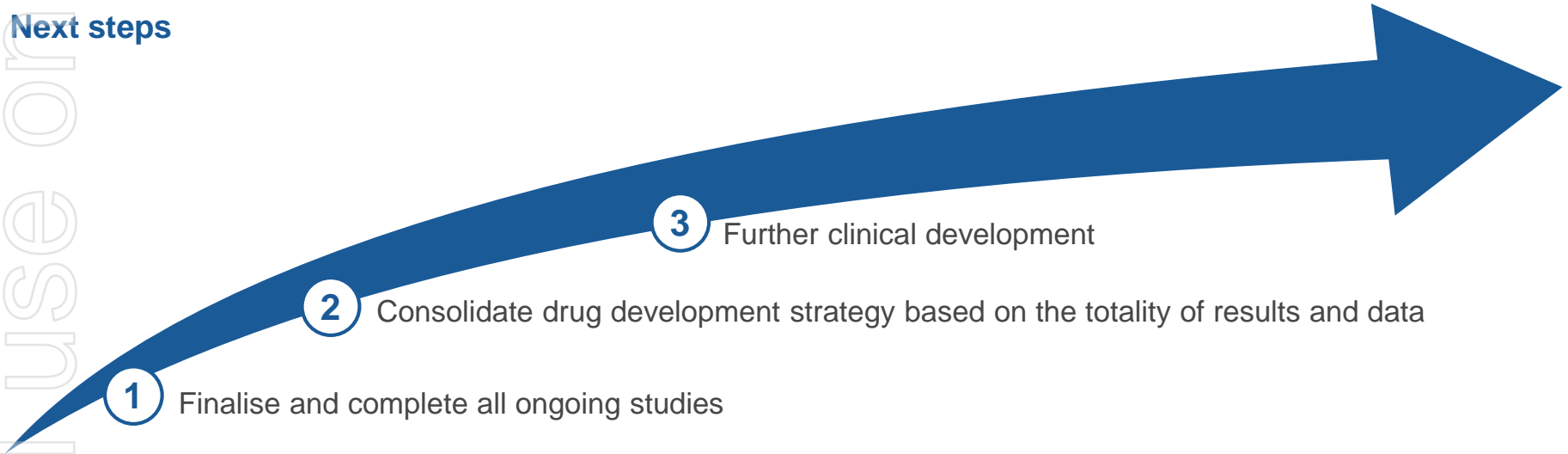
Key study to support future clinical development strategy

# Strategic direction

Key ongoing Xanamem studies are providing data and results in the near term, with the totality of the information from all studies to inform Actinogen's strategic review for future clinical development

Xanamem has demonstrated to be an **efficacious, safe, brain penetrant, orally available, selective 11 $\beta$  -HSD1 inhibitor** with significant pharmacodynamic effects on cortisol

## Next steps

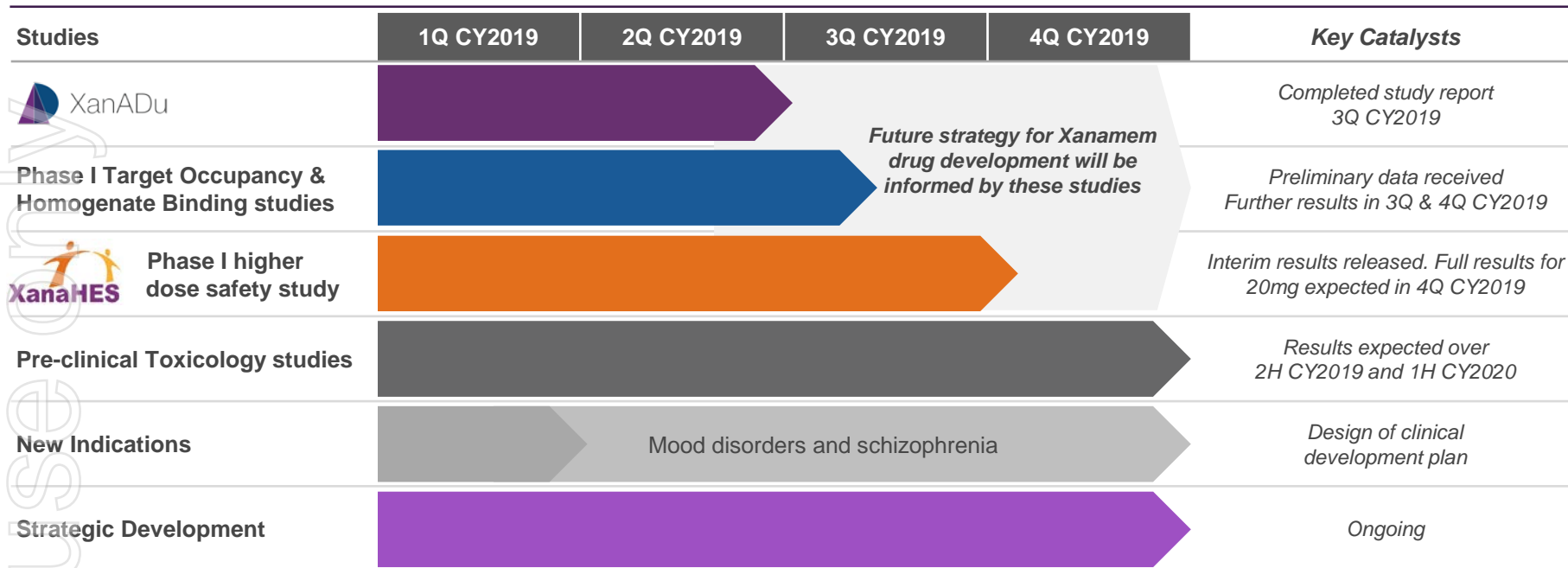




# Development Pipeline and Upcoming Catalysts



Multiple studies currently underway with significant upcoming milestones in the near term



**Actinogen is fully funded to complete all current studies**

Internal use only

# Q&A Session



# Appendix: Background information

Internal use only

# Summary

Actinogen is developing innovative treatments for cognitive impairment associated with neurological and metabolic diseases with an initial focus on Alzheimer's disease



## Xanamem - lead compound

Differentiated with a novel mechanism of action

First-in-class, brain penetrant, orally active, small molecule, inhibitor of 11 $\beta$ -HSD1 enzyme  
Xanamem mechanism of action validated by independent research on the cortisol hypothesis



## Targeted strategic market focus

Initially focused on developing a treatment for Alzheimer's disease  
Addressable market worth >US\$7.5bn with unmet needs and potential upside.  
Target indication underpinned by efficacy results from animal model studies.  
Mood disorders and schizophrenia identified as additional opportunities



## Clinical stage asset

Advanced clinical stage program assessing Xanamem in Alzheimer's disease and cognitive impairment in other neurological conditions. Complementary higher dose and target occupancy phase I studies will inform future development



## Potential value upside

Totality of existing studies will inform further development and commercial potential of Xanamem



## De-risked opportunity

Fully funded programs  
Initial data from additional studies indicate brain penetration, good target occupancy and safety profile



## Experienced leadership

Board and Management with significant drug development and corporate experience, supported by key opinion leaders and Xanamem discovery team

A novel drug designed to inhibit cortisol production in the brain, with the potential to treat cognitive impairment



## Well researched

>15 years of R&D completed



## Well tolerated

Dosed >200 patients with acceptable clinical safety, toxicity & PK / PD<sup>1</sup> profile



## Well protected

Composition of matter IP coverage, patents granted in all major markets



## Validated in Alzheimer's disease

Symptomatic and disease modifying effects (in vivo) and demonstrated effect of cortisol hypothesis (in humans)

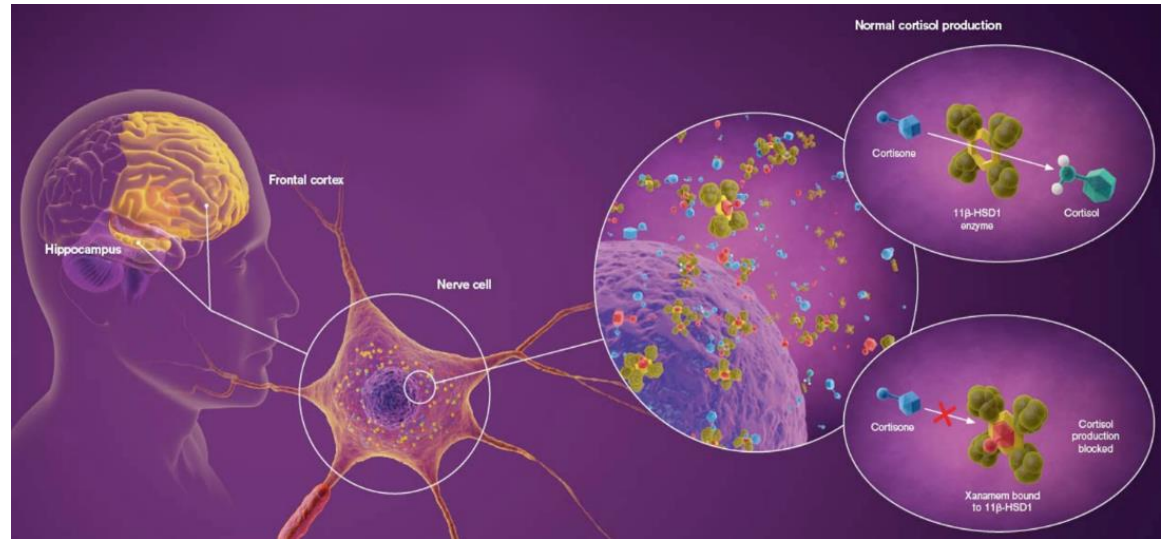


## Potential in other diseases

Secondary focus on cognitive impairment in mood disorders and schizophrenia

## Differentiated mechanism of action:

Highly selective 11 $\beta$ HSD1 inhibitor in the brain which reduces excess cortisol production



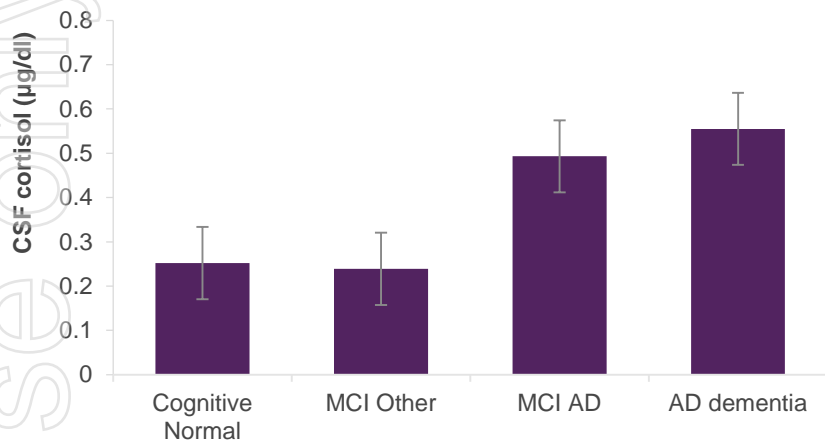
**Xanamem is a novel, first-in-class, potent, orally bioavailable and brain-penetrant 11 $\beta$ -HSD1 inhibitor**

1. PK / PD: pharmacokinetic / pharmacodynamic

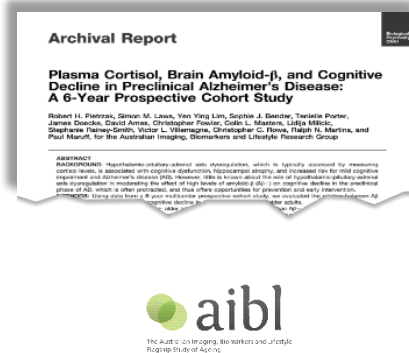
# Alzheimer's strategic focus underpinned by medical research

A growing body of medical literature supports the association between cortisol and Alzheimer's disease

## Raised cortisol associated with Alzheimer's disease<sup>1</sup>



## Supported by growing body of medical literature



Many studies support the association between **cortisol** and **Alzheimer's disease** development and progression<sup>2</sup>

A recent AIBL<sup>3</sup> study provided compelling evidence that elderly subjects with **higher plasma cortisol levels** are at much greater risk of developing Alzheimer's disease

This study<sup>3</sup> also demonstrated that **50% of those aged 65+ have raised cortisol levels**

Research suggests that lowering cortisol levels may prevent the development / progression of Alzheimer's disease

1. MCI: mild cognitive impairment; AD: Alzheimer's Disease
2. Recent studies also support the association between cortisol and cognitive impairment associated with neuroendocrine dysfunction
3. Plasma Cortisol, Brain Amyloid- $\beta$ , and Cognitive Decline in Preclinical Alzheimer's Disease: a 6-Year Prospective Cohort Study. Pietrzak et al., 2017. Biological Psychiatry: Cognitive Neuroscience and Neuroimaging 2:45-52

# Corporate overview ASX:ACW

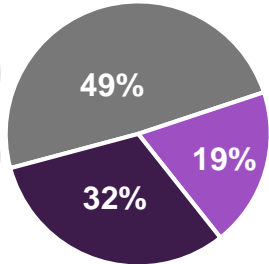


Actinogen is an ASX-listed biotech company focused on innovative approaches to treating cognitive impairment associated with neurological and metabolic diseases

## Overview

- Actinogen is developing Xanamem, a novel therapy for Alzheimer's disease, mood disorders and schizophrenia, with significant market potential
- Xanamem - lead drug, designed to inhibit cortisol production in the brain, with the potential to treat cognitive impairment
- Actinogen has completed a Phase II double-blind, 12 week, randomised, placebo-controlled study of Xanamem in Alzheimer's disease (XanADu)

## Key shareholding metrics



- BVF Partners**
- Top 20 (excl. BVF Partners)**
- 

## 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 Venture Partners



**Dr. Bill Ketelbey**

**CEO & MD**

MBBCh; FFPM; MBA; GAICD

- 30+ years experience** in healthcare, biotech and pharmaceutical industries
- Formerly senior international roles at Pfizer and Director at Westmead Institute of Medical Research



**Dr. George Morstyn**

**Non-executive director**

MBBS; PhD; FRACP; MAICD

- 25+ years experience** in biotech investment and drug development
- Board member of Biomedivc, Cancer Therapeutics and Symbio; Former Senior VP and SMO at Amgen



**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; formerly senior leadership roles in investment banking



# Advisory Boards

World's premier academics involved in the development of Xanamem and as a novel treatment for Alzheimer's disease

## Clinical Advisory Board (Alzheimer's disease)

*Positions Xanamem at the forefront of Alzheimer's drug development*

## Scientific Advisory Board

*Combining deep understanding of cortisol, 11β-HSD1 and drug discovery*



**Prof. Craig Ritchie**  
*Chair*



THE UNIVERSITY  
of EDINBURGH



**Prof. Colin Masters**  
*AO*



THE UNIVERSITY OF  
MELBOURNE



The Royal  
Melbourne Hospital



THE  
FLOREY  
INSTITUTE OF NEUROSCIENCE & MENTAL HEALTH



**Prof. Jeffrey Cummings**




Cleveland  
Clinic




**Prof. Jonathan Seckl**



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**Prof. Brian Walker**



Newcastle  
University



**Prof. Scott Webster**



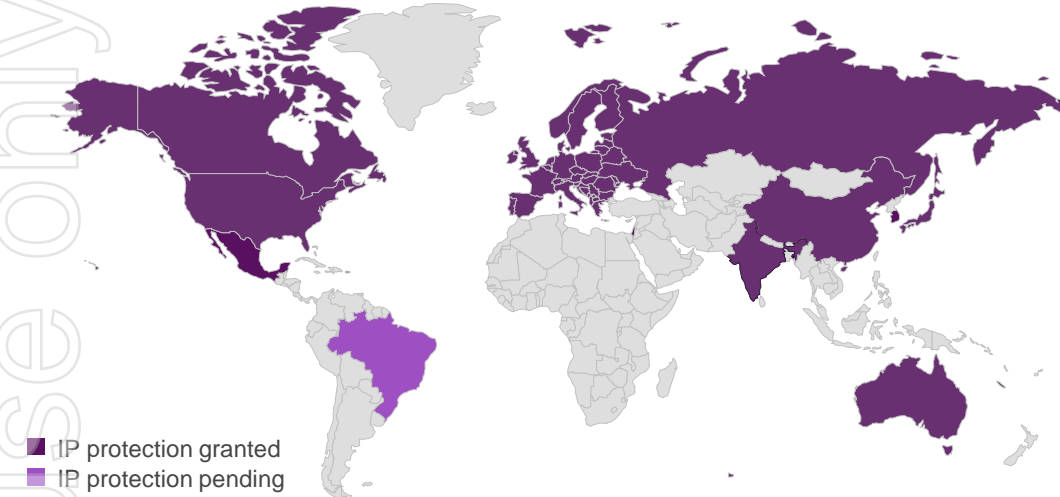
THE UNIVERSITY  
of EDINBURGH



# IP protection

Actinogen maintains a broad granted composition of matter patent estate, with key patents granted in all major target markets

## Geographic patent overview



- Actinogen's patent portfolio **covers a broad range of neurological and metabolic diseases** including Alzheimer's disease
- Xanamem **patents granted in key markets** that account for over 90% of the global Alzheimer's market
- Additional patents and patent extension being actively prosecuted**

**>90%** of the global Alzheimer's disease market

# Market dynamics of Alzheimer's disease

Presents a compelling commercial opportunity for Actinogen to target initially

## Substantial target market with significant upside<sup>1</sup>

| Cortisol-high, cognition normal | Subjective memory decline | Cognitive and functional decline fulfilling dementia |          |        |
|---------------------------------|---------------------------|--|----------|--------|
| At-risk                         | Prodromal                 | Mild   | Moderate | Severe |
| ~25.0m<br>(50% over 65 yrs)     | ~4.0m                     | ~1.5m  | ~1.7m    | ~2.5m  |

Upside potential for earlier use      Key focus

USA

**>US\$7.5bn**

Target annual peak sales (mild AD)<sup>2</sup>

Source: Drugs.com, Biogen, Roche, Datamonitor, Alzheimer's Association

1. Target market statistics based on the current US treatment landscape

2. Base case annual peak sales assumes: (1) Launch: US 2024, EU5, JP and ROW 2025; (2) Penetration: 30% of mild AD market in 5 years (i.e. ~470,000 in the US); (3) Pricing: US – US\$19/day gross (US\$12/day net), ROW: 50% of US price

## Underpinned by favourable market dynamics

- ✓ Targeting **large addressable** markets (US, EU5, JP)
- ✓ All **currently approved drugs are symptomatic treatments** (that do not affect disease progression) **providing limited benefit**
- ✓ Treatment **prices are robust** (despite generic competition) – with users paying for modest clinical efficacy

## US branded products (gross price)



US\$10/day



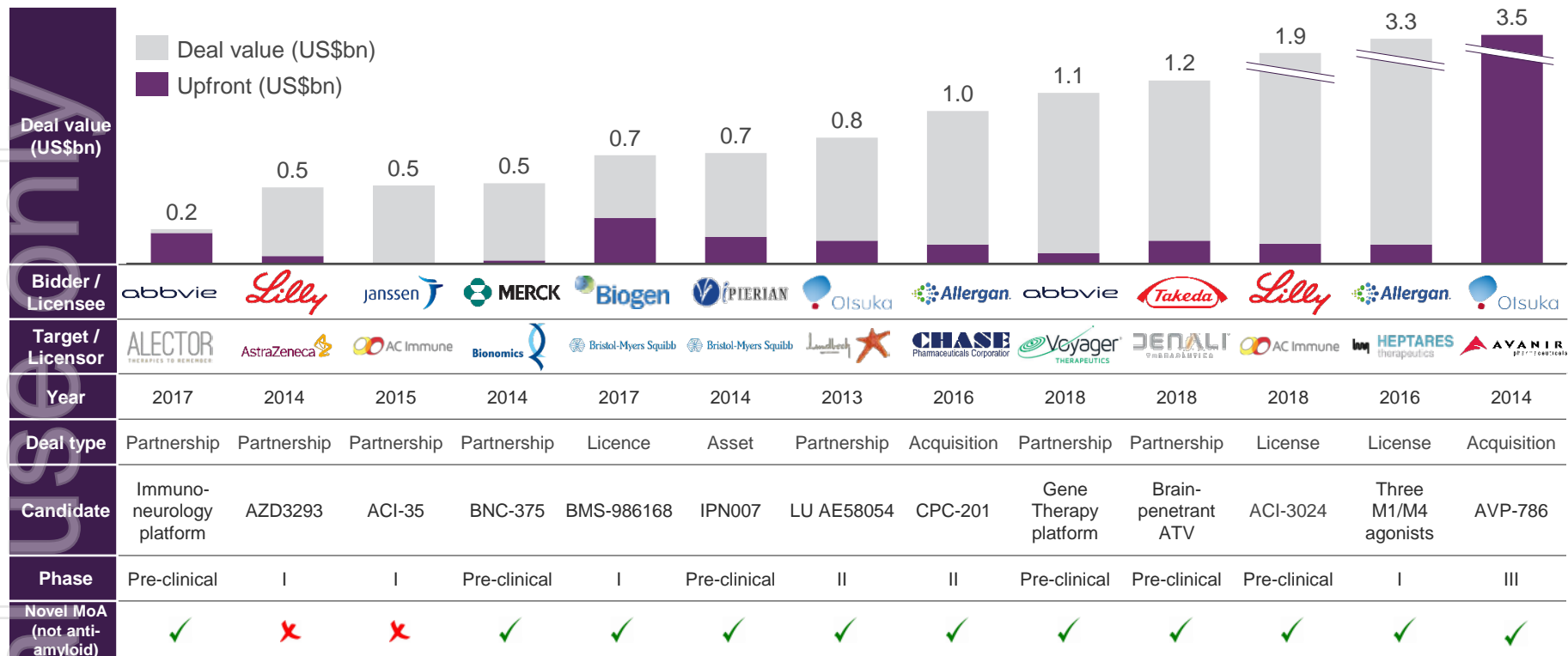
US\$8/day



US\$18/day

# Big Pharma interest

Global Big Pharma demonstrating strong M&A interest in acquiring or partnering with companies and licensing novel mechanism of action assets with Alzheimer's disease as the lead/key indication



# XanADu Phase II clinical trial

Double-blind, randomised, placebo-controlled study to assess the efficacy and safety of Xanamem in subjects with mild Alzheimer's disease<sup>1</sup>



Xanamem treatment course  
**12 weeks**



**186** patients with mild Alzheimer's  
disease (enrolment complete)<sup>2</sup>



**10mg daily**  
Xanamem for 12 weeks (vs. placebo)



Trial conducted at 25 sites in  
**AUS, USA and UK**

Largest AD global clinical trial run by an Australian biotech

1. Study registered on Clinicaltrials.gov: NCT02727699  
2. Fully enrolled 26 November 2018

# XanADu: Phase II Clinical Trial Completed

Double-blind, randomised, placebo-controlled study to assess the efficacy and safety of Xanamem in subjects with mild Alzheimer's disease<sup>1</sup>, with initial results announced 7th May 2019

## XanADu initial results

- Efficacy end points were not achieved
- Potent pharmacodynamic modulation of cortisol-related hormones achieved
- Xanamem is well-tolerated with no safety concerns
- Sub-analyses of results currently underway

## Possible reasons behind XanADu results

- Recurrent challenges seen in AD drug development
- Xanamem dose / study duration

## Ongoing development

- Phase I **target occupancy** studies
- **XanaHES** dose escalation study
- Long-term animal **toxicology** studies
- New indications for future focus selected: mood disorders (such as **bipolar disorder**) and **schizophrenia**

1. ADAS-COG14: Alzheimer's Disease Assessment Scales – Cognitive Subscale Score (version 14); ADCOMs: AD COMposite Scores (composite data derived from ADAS-COG14, CDR-SOB and MMSE); CDR-SOB: Clinical Dementia Rating Scale – Sum of Boxes; RAVLT: Rey Auditory Verbal Learning Test; MMSE: Mini-Mental Status Examination; NTB: Neuropsychological Test Batteries; NPI: Neuropsychiatric Inventory

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