



## ASX ANNOUNCEMENT

### Actinogen to be showcased at key conferences

- **Actinogen to present update at Microcap Investment Conference in Melbourne**
- **XanADu Alzheimer's study 95% enrolled – only 8 more patients required**

**Sydney, 17 October 2018: Actinogen Medical (ASX: ACW, 'the Company')** is pleased to advise that the Company's CEO and Managing Director, Dr. Bill Ketelbey will be presenting at the **9<sup>th</sup> Annual Australian Microcap Investment Conference** in Melbourne on 18<sup>th</sup> October 2018. Dr. Ketelbey will be providing an update on Actinogen's recent progress and outlook.


The latest investor presentation, containing the key information that will be presented, is available below.

### Key Investment Highlights

- **Novel compound:** Xanamem, Actinogen's lead compound, is validated by independent research and differentiated with a novel mechanism of action
- **Targeted strategic market focus:** Alzheimer's disease addressable market worth >US\$5bn with unmet needs and potential upside
- **Advanced clinical stage asset:** Fully funded advanced clinical stage program with reported positive interim analysis. Completion of patient enrolment into XanADu Alzheimer's study imminent with only 8 patients still required (>95% enrolled). On track to release results in Q2 2019
- **Potential value upside:** Well positioned to unlock further value in Alzheimer's and other indications, supported by significant big pharma interest.
- **De-risked opportunity:** Initiated additional XanADu-related studies and pipeline development opportunities
- **Experienced leadership and advisors:** Significant drug development and investment experience guided by leading clinicians and discovery teams

## ENDS

### **Actinogen Medical**

Dr. Bill Ketelbey  
CEO & Managing Director  
P: +61 2 8964 7401  
E: bill.ketelbey@actinogen.com.au  
 @BillKetelbey

### **Investor and Media Enquiries**

Ben Walsh  
WE Buchan  
M: +61 411 520 012  
E: bwalsh@we-buchan.com

### **About Actinogen Medical**

Actinogen Medical (ASX: ACW) is an ASX-listed biotech company focused on innovative approaches to treating cognitive decline that occurs in chronic neurodegenerative and metabolic diseases. Actinogen Medical is developing its lead compound Xanamem, as a promising new therapy for Alzheimer's disease, a condition with a multibillion-dollar market potential. In the US alone, the cost of managing Alzheimer's disease is estimated to be US\$250bn, and is set 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.

### **About Xanamem™**

Xanamem's novel mechanism of action sets it apart from other Alzheimer's treatments. It works by blocking the excess production of cortisol - the stress hormone – through the inhibition of the 11β-HSD1 enzyme in the brain. This enzyme is highly concentrated in the hippocampus and frontal cortex, the areas of the brain most affected by Alzheimer's disease. There is a strong association between chronic stress and excess cortisol that leads to changes in the brain affecting memory, and to the development of amyloid plaques and neural death – all hallmarks of Alzheimer's disease.

### **About XanADu**

XanADu is a Phase II double-blind, 12-week, randomised, placebo-controlled study to assess the safety, tolerability and efficacy of Xanamem in subjects with mild dementia due to Alzheimer's disease. XanADu, is enrolling 174 patients at 25 research sites across Australia, the UK and the USA. Enrolment is expected to complete in Q4 2018, with top-line results expected in Q2 2019. 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.

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

# Australian Microcap Investment Conference

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

Dr. Bill Ketelbey: CEO & Managing Director

October 2018



**Actinogen**  
Medical

# Key investment highlights

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



## Novel compound

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



## Targeted strategic market focus

Initially focused on developing a treatment for Alzheimer's disease  
Addressable market of >US\$5bn with unmet needs and potential upside  
Target indication underpinned by efficacy results from animal model studies



## Clinical stage asset

Fully funded advanced clinical stage program  
Reported positive interim analysis  
Enrolment >95% complete and top line results available by mid CY2019



## Potential value upside

Well positioned to unlock further value  
Significant big pharma interest



## De-risked opportunity

Additional Xanamem studies initiated  
Pipeline development opportunities under evaluation



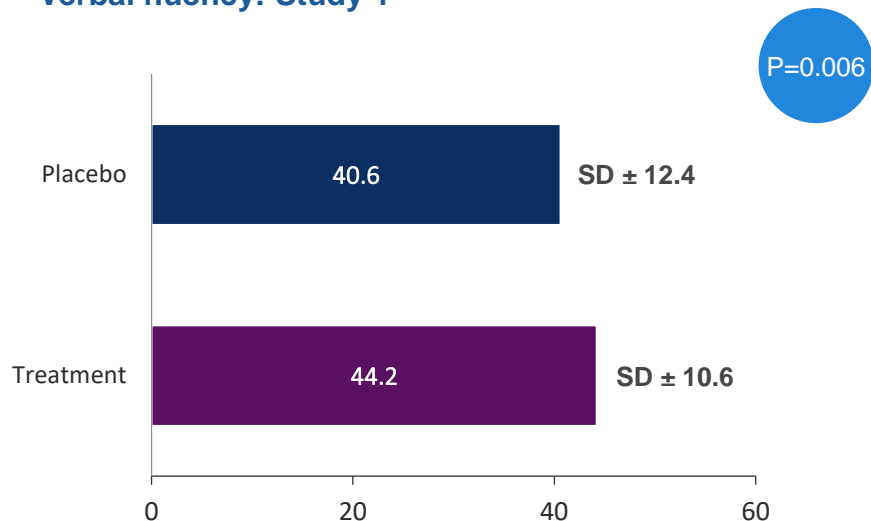
## Experienced leadership/advisors

Significant drug development and investment experience  
Leading AD clinicians and Xanamem discovery team

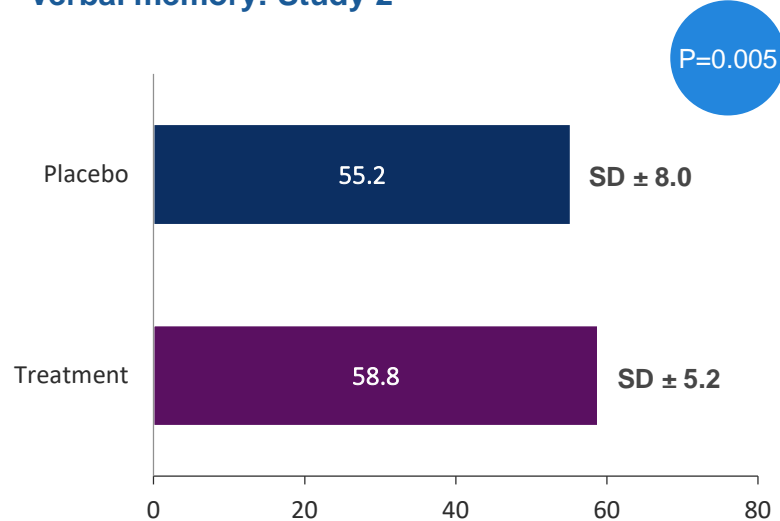
# Human pilot studies validate the cortisol hypothesis

Two completed pilot studies that indicated inhibiting cortisol production in the brain improves cognitive function in healthy elderly men and subjects with Type 2 diabetes

## Verbal fluency: Study 1<sup>1</sup>



## Verbal memory: Study 2<sup>2</sup>



**Significant improvement in verbal fluency and verbal memory after only 4 and 6 weeks of treatment**

Source: 11 $\beta$ -Hydroxysteroid dehydrogenase inhibition improves cognition function in healthy elderly men and type 2 diabetics Sandeep et al., 2004 PNAS (vol. 101, no. 17) 6734-6739

1. Study 1: 10 healthy subjects Age 55-75 (Mean Age = 65.5  $\pm$  5.5) receiving 100mg carbenoxolone 3 times daily compared to placebo for 4 weeks, in a double-blind randomised crossover study

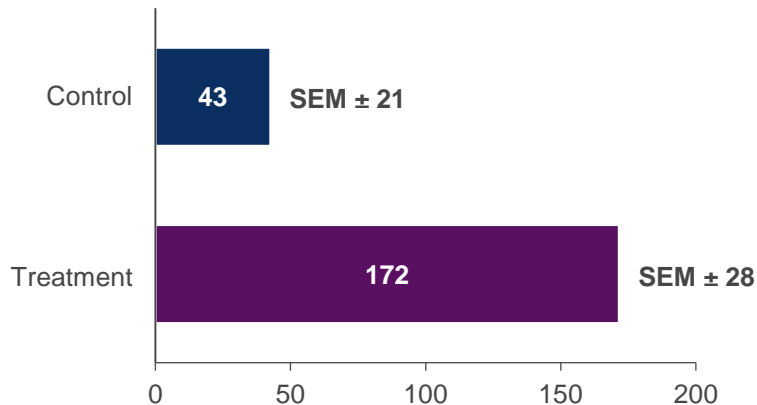
2. Study 2: 12 type 2 diabetics (m=9; f=3) Age 52-70 (Mean Age = 60  $\pm$  4.9) receiving 100mg carbenoxolone 3 times daily compared to placebo for 6 weeks, in a double-blind randomised crossover study.

# Efficacy underpinned by animal model

Significant and rapid symptomatic and disease modifying effects demonstrated with significant improvement in cognition within one month, continuing out to 41 weeks

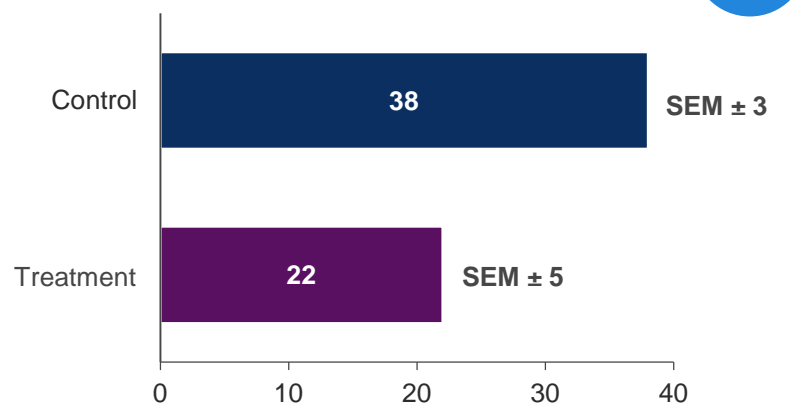
## Cognition: 28 days treatment

Latency to enter dark compartment (seconds)



## Amyloid clearance: 28 days treatment

Number of Plaques / brain area (total)



Results from the animal model study underpins the significant promise of the XanADu study

# What is Xanamem

Actinogen's lead compound, Xanamem, is a novel drug designed to inhibit the production of cortisol in the brain, with the potential to treat cognitive impairment and Alzheimer's disease



## Well researched

Over 15 years of R&D completed, with A\$40m invested to date



## Well tolerated

Dosed >150 patients with acceptable clinical safety, toxicity and PK / PD<sup>1</sup> profile



## Differentiated mechanism of action

Highly selective inhibitor of the 11 $\beta$ HSD1 enzyme in the brain preventing excess cortisol production



## Validated

Symptomatic and disease modifying effects (in vivo) and effective demonstration of cortisol hypothesis (in humans)



## Well protected

Composition of matter IP coverage  $\geq$  2031, patents granted in all major markets



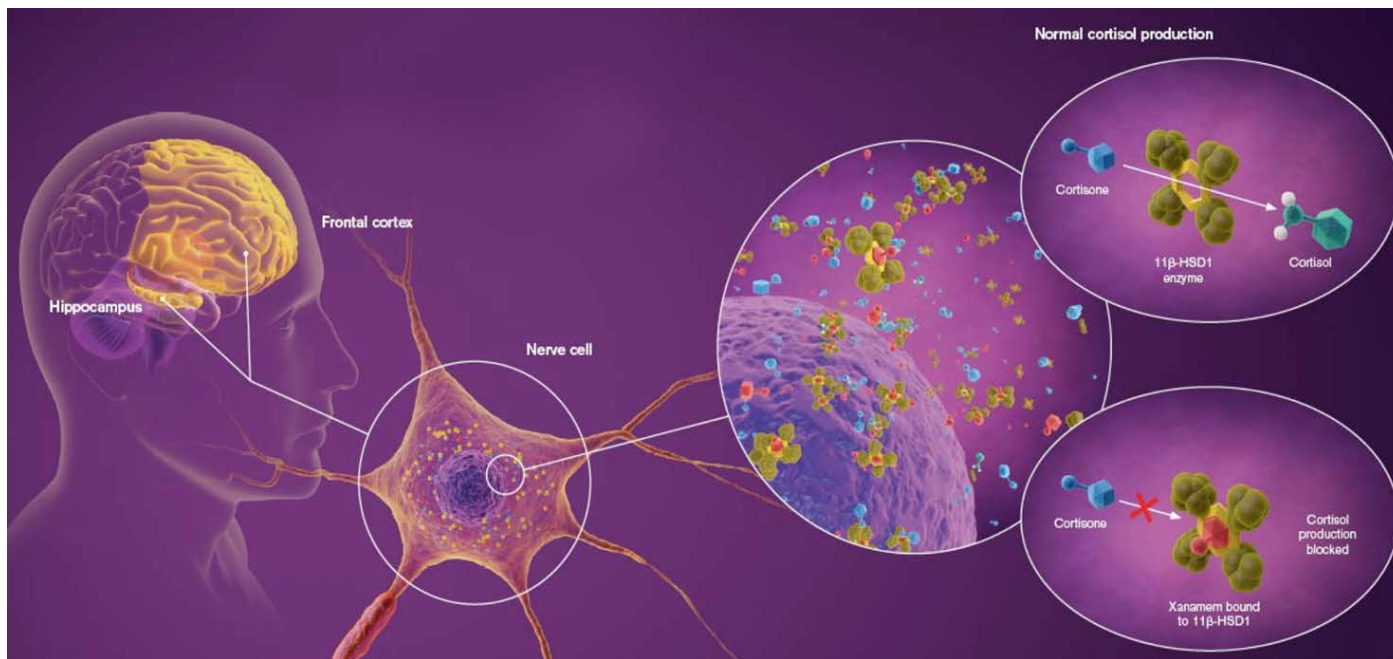
**Xanamem is a novel, first-in-class, potent, orally bioavailable and brain-penetrant 11 $\beta$ -HSD1 inhibitor**

1. PK / PD: pharmacokinetic / pharmacodynamic

# Mechanism of action

Xanamem inhibits the activity of the 11 $\beta$ -HSD1 enzyme, reducing the production of cortisol in the brain

## Overview



**Xanamem is targeting diseases with possible cortisol induced cognitive impairment**

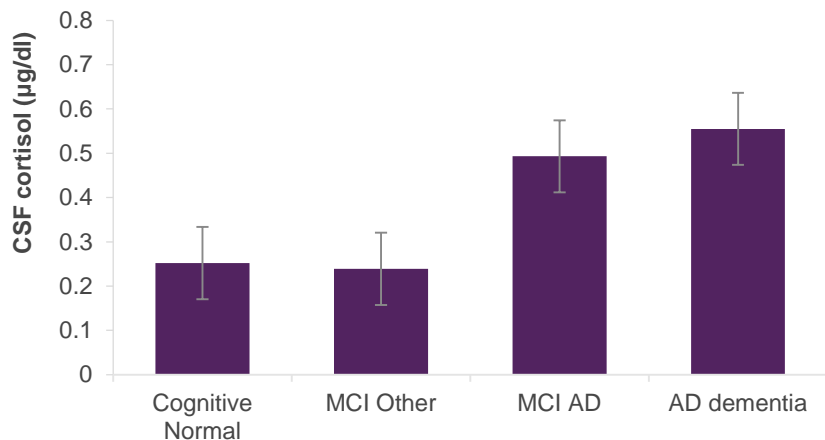
- **Alzheimer's disease (key focus)**
- Diabetes
- Depression
- Parkinson's disease
- Schizophrenia
- and more....



# Initial 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. AIBL (Australian Imaging, Biomarker & Lifestyle Study of Ageing) study published in 2017

# 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**



**174** patients with mild Alzheimer's disease (**166 enrolled; >111 completed**)<sup>2</sup>



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



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

**Fully funded study on track to complete enrolment in 4Q CY2018 with top line results in 2Q CY2019**

1. Study registered on Clinicaltrials.gov: NCT02727699  
2. As at 17<sup>th</sup> October 2018

# Interim analysis

Positive recommendations from the DSMB<sup>1</sup> reflect confidence in the safety of the drug and the design of the XanADu study. Supports the broader development of Xanamem



## First DSMB review (23 May 2018)

- Evaluation of 50 patients' safety and efficacy data reviewed by an independent DSMB<sup>2</sup>
- **Recommendation by DSMB to continue XanADu without modification**

## Second DSMB review (22 August 2018)

- Evaluation of 125 patients' safety data
- **Reaffirmed continuation of XanADu without modification**

## Third DSMB review

- Expected to be completed before the end of CY2018



**Positive DSMB recommendations underpin the XanADu study and further development of Xanamem in other indications**

1. DSMB: Data Safety Monitoring Board

2. Evaluable patients to have completed the study – note: an additional 37 patients' safety data was also included in the analysis (data was from patients still ongoing in the study)

# Additional Xanamem studies

Actinogen is focused on completing key additional studies to enhance the Xanamem data set



## Target occupancy study

Aims to accurately demonstrate the effect different doses of Xanamem has on the 11 $\beta$ -HSD1 enzyme in the human brain

Currently underway with **results expected in 2Q CY2019**



## Higher dose safety study

To expand the safety data-set for Xanamem and allow for higher doses of the drug to be used (including in non-Alzheimer's applications)

Study is expected to **initiate in 4Q CY2018**



## Further safety / toxicology studies

To allow for longer treatment periods, as normally required by global regulatory authorities in the development of any drug

Studies are expected to **initiate in 4Q CY2018**

**Actinogen is fully funded to complete these key Xanamem studies**

# Other potential indications

Secondary focus is on developing the use of Xanamem in other indications to optimise shareholder value

## Overview



Multiple potential target indications beyond Alzheimer's represent significant market expansion opportunities



Growing literature on cortisol-induced cognitive impairment associated with many conditions



Actinogen intends to follow a rapid development pathway to identify suitable target indications



Development program leverages existing data from earlier clinical programs

## Possible target indications

Diabetes

Depression

Parkinson's disease

Schizophrenia

Post-traumatic  
stress disorder

And more..

**Preliminary assessment currently underway to identify high priority indications for development**

# 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 (50% over 65 yrs)	~4.0m	~1.5m	~1.7m	~2.5m

Upside potential for earlier use      Key focus

  
**>US\$5bn**

Target annual peak sales<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 and JP 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), 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



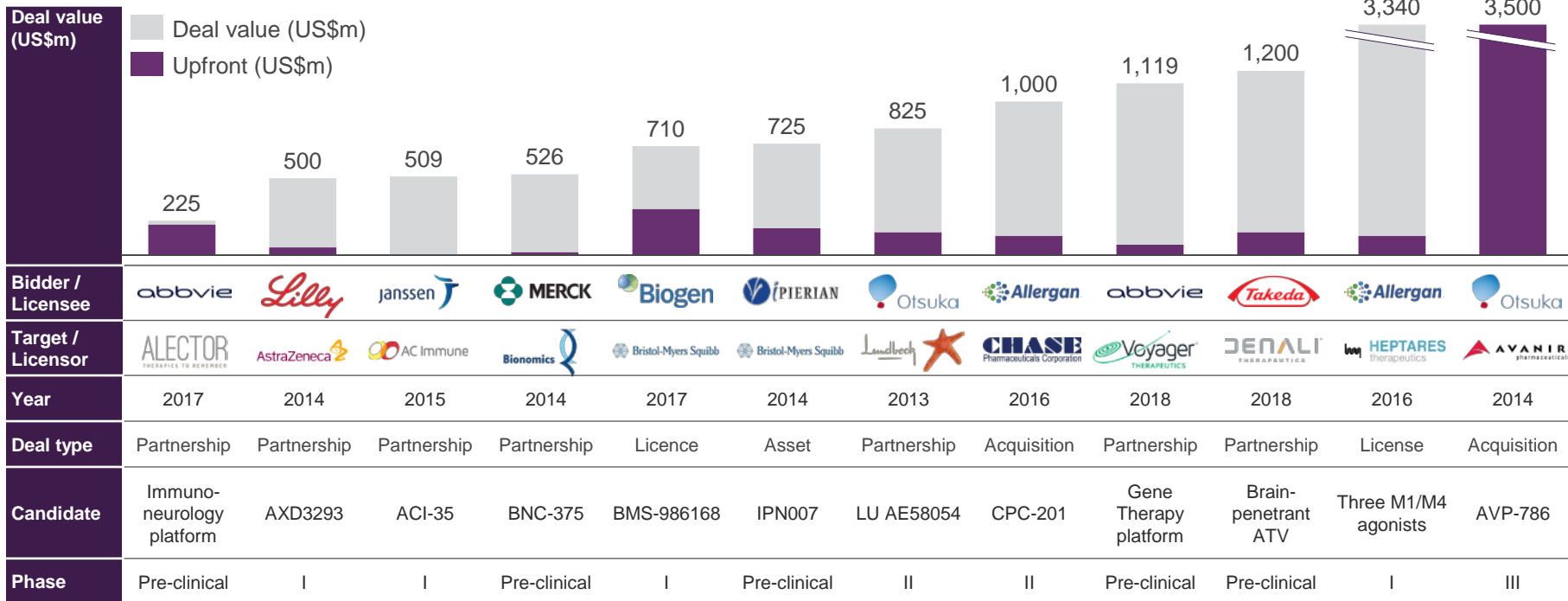
US\$8/day



US\$18/day

# Big Pharma interest

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



# Board of Directors

Commercially experienced and globally recognised leadership team with decades of experience in drug development and biotech investment



**Dr. Geoff  
Brooke**

*Chairman*

- **30+ years experience** in the healthcare investment industry
- Founder and MD of Medvest Inc and GBS Venture Partners
- MBBS (University of Melbourne); MBA (IMEDE, Switzerland)



**Dr. Bill  
Ketelbey**

*CEO & MD*

- **30+ years experience** in the healthcare, biotech and pharmaceutical industries
- Formerly senior international roles at Pfizer; Director at the Westmead Institute of Medical Research
- MBBCH (University of the Witwatersrand); FFPM; MBA (Macquarie); GAICD



**Dr. Jason  
Loveridge**

*Non-executive  
director*

- **20+ years experience** in biomedical technology industry
- Venture investor with JAFCO Nomura; Non-Executive Director of Resonance Health (ASX: RHT); CEO of 4SC AG
- B.Sc (UNSW), PhD (University of Adelaide) FRSM



**Dr. George  
Morstyn**

*Non-executive  
director*

- **25+ years experience** in biotechnology investment
- Board member of Cancer Therapeutics, Symbio and Biomedvic; Former Senior VP and SMO at Amgen
- MBBS (Monash University); PhD (Walter and Eliza Hall Institute); FRACP; MAICD





# Advisory Boards

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

## Xanamem™ Clinical Advisory Board

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



**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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of EDINBURGH



**Prof. Brian  
Walker**



**Newcastle  
University**



**Prof. Scott  
Webster**



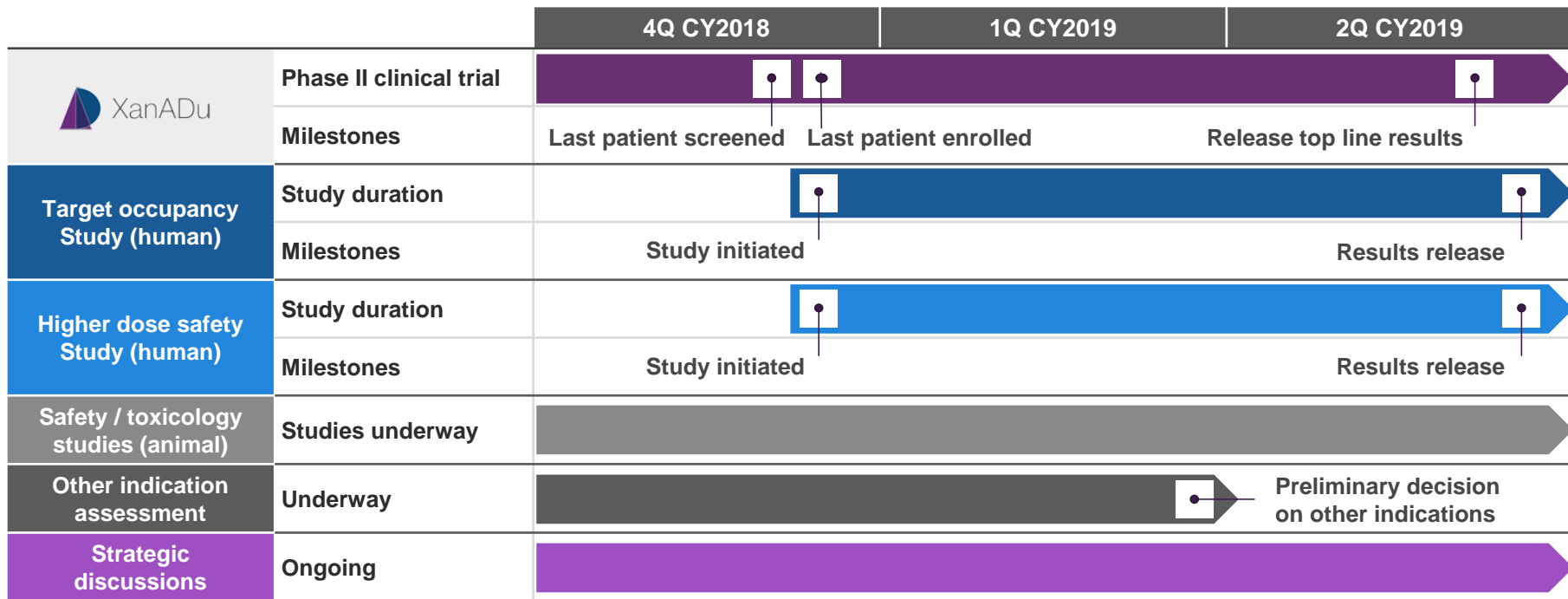
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of EDINBURGH

## Scientific Advisory Board

*Combining deep understanding of cortisol,  
11 $\beta$ -HSD1 and drug discovery*

# Upcoming catalysts

Significant upcoming milestones across 2018/19



# Key investment highlights

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## Experienced leadership/advisors

Significant drug development and investment experience  
Leading AD clinicians and Xanamem discovery team

Dr. Bill Ketelbey: CEO & Managing Director

P: +61 2 8694 7401

E: [bill.ketelbey@actinogen.com.au](mailto:bill.ketelbey@actinogen.com.au)



**Actinogen**  
Medical

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