

## **Investor Presentation**

- Updated Investor Presentation and Fact Sheet
- Invitation to Investor Briefings

**19 March 2018: Actinogen Medical (ASX: ACW)** is pleased to announce an updated Investor Presentation and Fact Sheet that will form the basis for the presentations at the open Investor Briefings taking place around the country this week. The Investor Presentation and Fact Sheet are available on the “Investor Centre” section of Actinogen’s website. Investors can also click on the following link to access the newsletter – <http://actinogen.com.au/acw-investor-centre/>

Details of the previously announced Investor Briefings:

### **Invitation to Investor Briefing**

**Actinogen Medical (ASX: ACW)** invites all shareholders and the wider investment community to a series of open Investor Briefings that will take place around Australia, during March.

The Company will provide an overview of the business and an update on XanADu, its Phase II clinical trial of Xanamem for the treatment of Alzheimer’s disease.

The briefings will take place at the following locations and times:

**Perth: Monday 19<sup>th</sup> March, 4:30pm – 5:30pm**

*Steve’s Hotel in the Cellar, 30 The Avenue, Nedlands, Perth*

**Adelaide: Tuesday 20<sup>th</sup> March, 4:30pm – 5:30pm**

*Baker Young Offices, Board Room, Level 6, 121 King William St, Adelaide*

**Melbourne: Wednesday 21<sup>st</sup> March, 4:30pm – 5:30pm**

*Mantra on Russell, Flinders Conference Room, 222 Russell Street, Melbourne*

**Sydney: Thursday 22<sup>nd</sup> March, 5pm – 6pm**

*The Royal Exchange, Main Dining Room and Bar, 1 Gresham Street, Sydney*


The briefings will be followed by a drinks service and the opportunity to talk with Actinogen management.

For registration and catering purposes, ***please RSVP and indicate which location you will be attending to:***

Therese Russell  
Actinogen Medical  
[therese.russell@actinogen.com.au](mailto:therese.russell@actinogen.com.au)

**ENDS**

**Actinogen Medical**

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## **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 Xanamem 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 11 $\beta$ -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, will enrol 174 patients at 20 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.

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

# Alzheimer Treatment Needs a New Approach – Xanamem™

Investor Open Briefing

March 2018



**Actinogen**  
Medical

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# Actinogen Medical (ASX:ACW)

- Developing Xanamem for the treatment of Alzheimer's disease (AD) and cortisol associated cognitive impairment
- Xanamem, a novel differentiated mechanism of action: prevents the production of excess brain cortisol
- Persistently raised cortisol in the brain is associated with the development and progression of AD
- First-in-class, brain penetrant, orally active, inhibitor of 11 $\beta$ HSD1 enzyme, reducing conversion of cortisone to cortisol
- Experienced board and management; expert clinical and scientific advisory board

\* As at 14 March 2018

## STOCK METRICS\*

ASX CODE	ACW
Market Capitalisation	\$37.5m
Enterprise Value	\$30.5m
52-week Share price range	\$0.04-\$0.09
Top 20 Shareholdings	49%

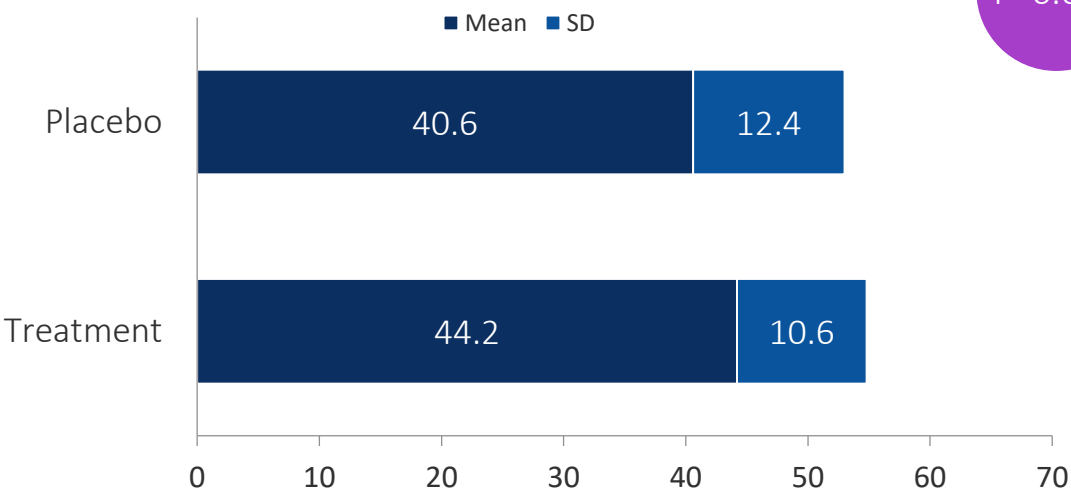
## LARGEST HOLDERS

Rank	Name	A/C designation	%IC
1	Edinburgh Technology Fund Limited		6.81
2	JK Nominees Pty Ltd	<The JK A/C>	5.66
3	Sunset Capital Management Pty Ltd	<Sunset Superfund A/C>	3.37
4	Warambi Sarl		3.10
5	BNP Paribas Nominees Pty Ltd Hub24 Custodial Serv Ltd DRP		3.05
6	Mr Martin Rogers		2.83
7	Webinvest Pty Ltd	<OLSB Unit A/C>	2.82
8	Bannaby Investments Pty Ltd	<Bannaby Super Fund A/C>	2.32
9	Denlin Nominees Pty Ltd		2.16
10	Oaktone Nominees Pty Ltd		2.08
11	David McAuliffe		1.87

# Cortisol inhibition improves cognition – Key Factor in 2014 Acquisition

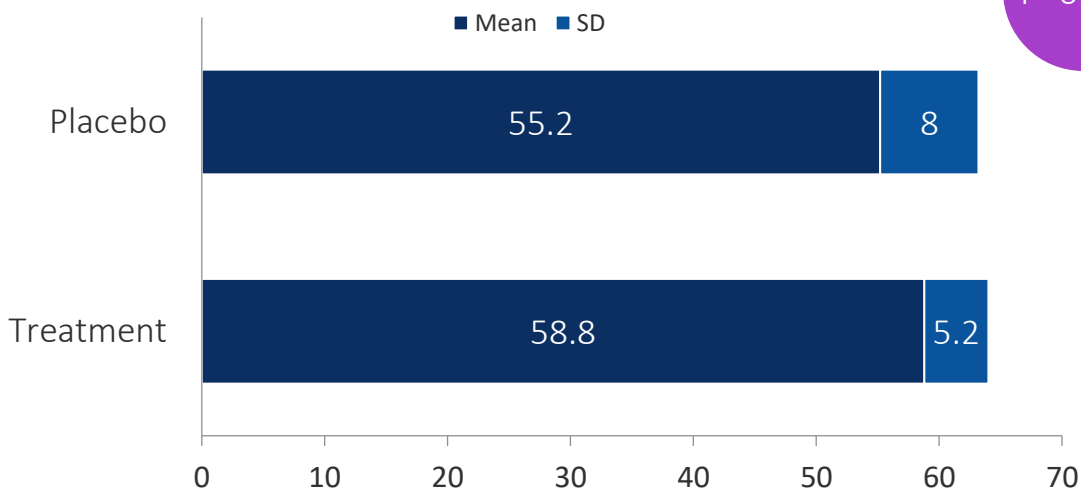
Two 2004 pilot studies concluded that inhibiting cortisol production in the brain with carbenoxolone improves cognitive function in healthy elderly men & type 2 diabetics – this established Edinburgh Uni hypothesis

VERBAL FLUENCY – Study 1\*



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

VERBAL MEMORY – Study 2\*\*



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

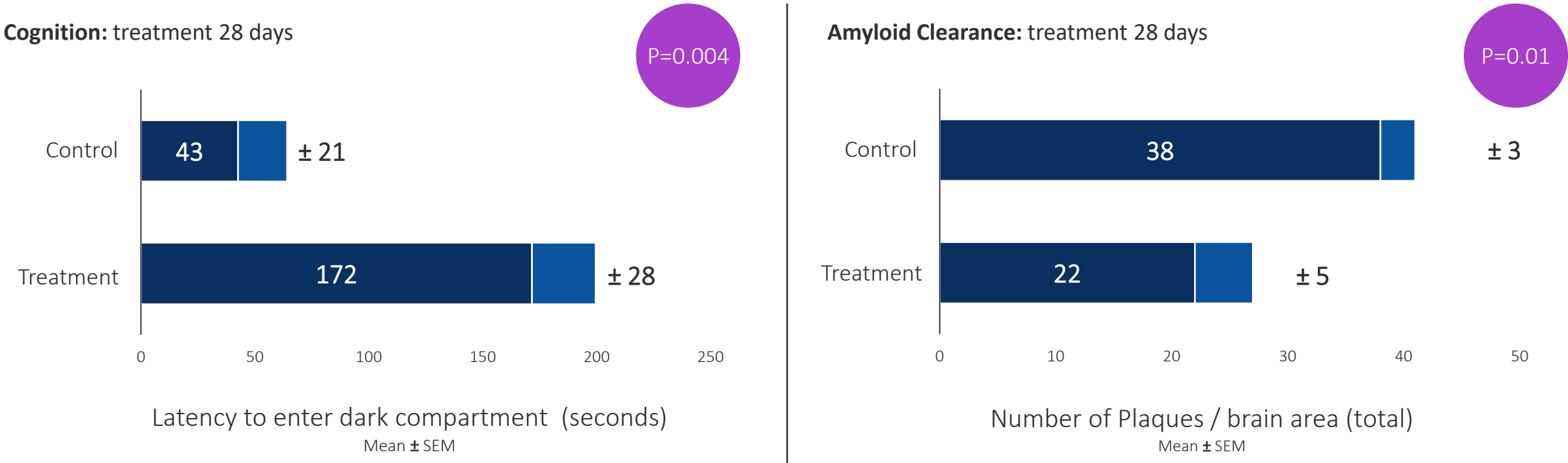


Significant improvement in verbal fluency and verbal memory after only 4 and 6 weeks treatment

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

# Robust Animal Data with new candidate - Key Factor in 2014 Acquisition

Symptomatic and disease modifying effects in mouse models – AUD \$25 million invested pre acquisition



Significant improvement in cognition after only 28 days treatment, continuing out to 41 weeks

UE2316 in Tg2576 rodent model of Alzheimer’s disease.  
Source: Sooy, et al., 2015. Endocrinology 156 (12) 4592-4603

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# Xanamem



# Xanamem

- A novel, first in class, potent, orally bioavailable, brain-penetrant, 11 $\beta$ HSD1 inhibitor
- Differentiated mechanism of action: blocking cortisol production in the brain
- Symptomatic and disease modifying effects *in vivo*
- Well-tolerated – dosed >100 patients/subjects: acceptable clinical safety, toxicity and PK/PD profile
- Effective human brain concentrations demonstrated
- XanADu – phase II clinical study underway, dosing subjects with mild AD dementia in USA, UK, AU
- Planning ongoing for additional clinical indications
- Composition of matter IP coverage  $\geq$  2031, patents granted in all major markets
- **Fully funded** following completion of ~A\$5.3 million capital raise in November 2017



# Cortisol: a validated biomarker and target for AD

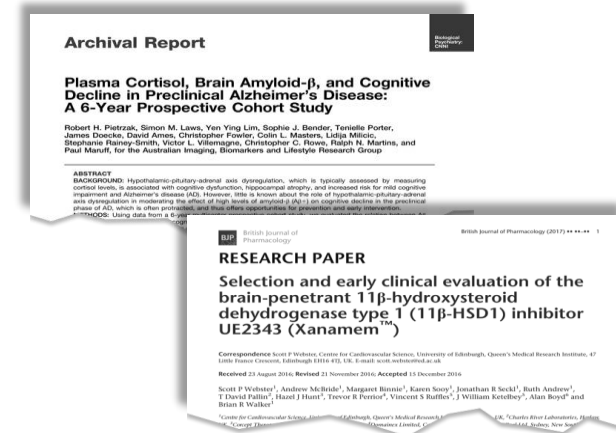
## Cortisol and Alzheimer's

- Recent independent studies support the association between cortisol and AD development and progression<sup>1-5</sup>
- Cognitive impairment in patients with neuroendocrine dysfunction<sup>6-9</sup>
- Compelling evidence provided by the Australian Imaging, Biomarker & Lifestyle Study of Ageing (AIBL) study (2017)<sup>5</sup>
  - Subjects with higher plasma cortisol at much greater risk of developing AD
  - Accelerated effect of A $\beta$ <sup>+</sup> on decline in global cognition, episodic memory and attention

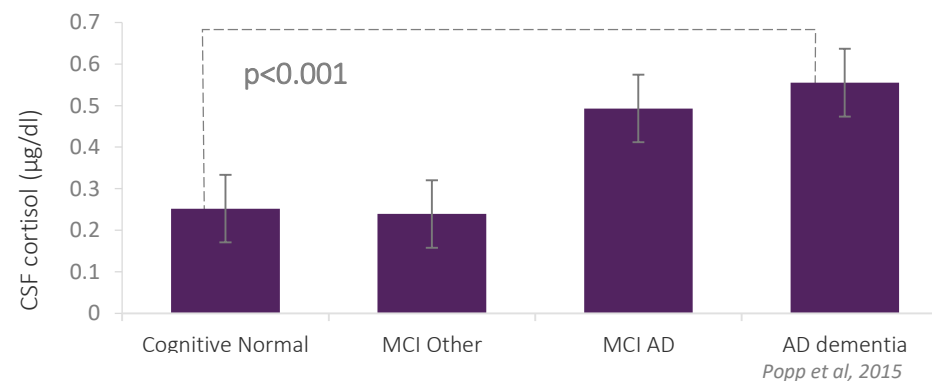
## Xanamem

- Data presented at four major international medical congresses in 2016 – AAIC Toronto; CTAD San Diego; ICE Beijing; MMC Lisbon
- Pre-clinical and Phase I data published<sup>10-11</sup>

[1] Geerlings *et al.*, 2015, *Neurology* 85: 1-8; [2] Lehallier *et al.*, 2016, *JAMA Neurology* 73(2), 203-212; [3] Popp *et al.*, 2015, *Neurobiol. Aging* 36:601–607; [4] Ennis *et al.*, 2017, *Neurology* 88(4):371-378; [5] Pietrzak *et al.*, 2017, *Biol Psychiatry: Cognitive Neuroscience and Neuroimaging*, 2:45-52; [6] Lupien *et al.*, 2009, *Nat Rev Neurosci* 10:434–445; [7] Starkman *et al.*, 1999, *Biol Psychiatry* 46: 1595–1602; [8] Lupien *et al.*, 1998, *Nat Neurosci* 1:69–73; [9] MacLulich *et al.*, 2005, *Psychoneuroendocrinology* 30:505–515; [10] Sooy *et al.*, 2015, *Endocrinology* 156(12):4592-4603; [11] Webster *et al.*, 2017, *British J Pharmacol* 174:396-408.



## MEAN CSF CORTISOL LEVELS

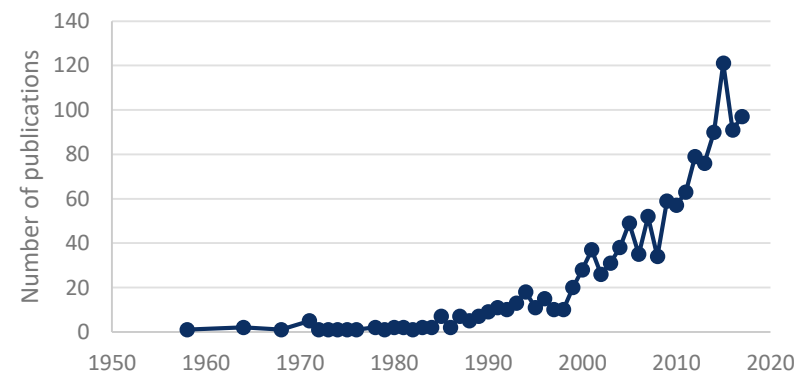


# Cortisol, cognitive decline and AD: a growing body of literature

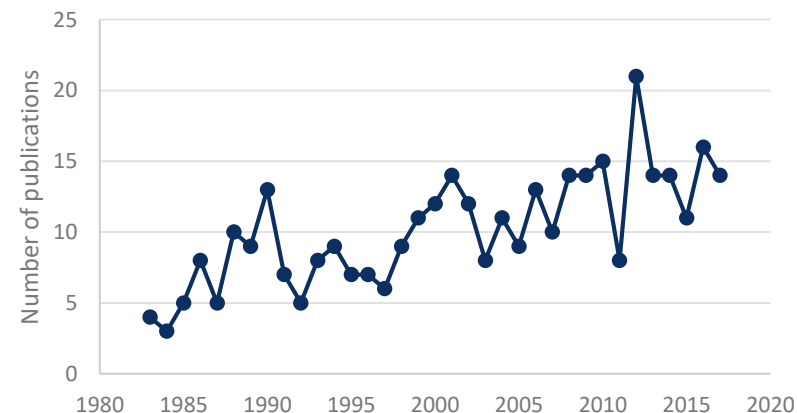
## Recent relevant reviews:

- Cortisol: Mediator of association between Alzheimer's disease and diabetes mellitus? (Notarianni, 2017, *Psychoneuroendocrinology*)
- Unified theory of Alzheimer's disease (UTAD): implications for prevention and curative therapy. (Nehls 2016, *J Mol Psychiatry*)
- Is Dysregulation of the HPA-Axis a Core Pathophysiology Mediating Co-Morbid Depression in Neurodegenerative Diseases? (Du and Pang, 2015; *Front Psychiatry*)
- The impact of stress and glucocorticoids on memory. (Tatomir et al. 2014; *Clujul Med.*)
- Contribution of glucocorticoids and glucocorticoid receptors to the regulation of neurodegenerative processes. (Vyas and Maatouk, 2013; *CNS Neurol Disord Drug Targets*)
- Stress-induced cytokines and neuronal dysfunction in Alzheimer's disease. (Ricci et al., 2012; *J. Alzheimer's Dis.*)
- Local amplification of glucocorticoids in the aging brain and impaired spatial memory (Yau and Seckl, 2012; *Front. Aging Neuroscience*)

## PUBMED: "CORTISOL AND COGNITION"



## PUBMED: "CORTISOL AND ALZHEIMER'S"



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# XanADu – Phase II Trial

# XanADu – Xanamem in Alzheimer's disease

Phase II double blind, randomised, placebo-controlled study to assess the efficacy and safety of Xanamem in participants with mild Alzheimer's disease\*

- 84 patients enrolled (48% of total study cohort) and more than 35 patients already completed study\*\*
- On track for last patient in Q4 2018 and top line results in Q2 2019
- DSMB interim analysis Q2 2018



Xanamem treatment course

**12 weeks**



**174**

Mild Alzheimer's patients



Xanamem 10mg daily  
for 12 weeks vs placebo



Trial conducted at 20 sites in  
**AUS, USA and UK**

Primary and secondary endpoints are standard and experimental cognitive outcome measures used in Alzheimer's research: ADASCog14, ADCOMS, CDR-SOB, MMSE, RAVLT, NTB-ED

\*Registered on Clinicaltrials.gov: NCT02727699

\*\*As at 14 March 2018

# Interim Analysis



## XanADu Interim Analysis



Data Safety Monitoring Board (DSMB) analysis to be performed on first 50 evaluable patients



DSMB opinion available Q2 2018



DSMB analysis may provide early insights into the XanADu study

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# Investment potential

# Commercially experienced, globally recognised

## Board of Directors



Dr. Geoff Brooke  
Chairman



Dr. Bill Ketelbey  
CEO & MD



Dr. Jason Loveridge  
Non-Executive Director



Dr. George Morstyn  
Non-Executive Director

## Xanamem Clinical Advisory Board



Prof. Craig Ritchie  
Chair



Prof. Colin Masters



Prof. Jeffrey Cummings





# Dr Geoff Brooke



Dr. Geoff Brooke  
Chairman of  
Actinogen Medical

Dr Geoff Brooke is the Chairman of Actinogen. He graduated in Medicine and Surgery from the University of Melbourne and worked at St Vincent's Hospital in Melbourne before completing an MBA at IMD in Lausanne in Switzerland. He has spent 30 years in the medical venture capital industry, having been recruited by Johnson & Johnson to establish a seed fund in the US. He later joined Rothschild in London and set up its biotech venture business in Australia. Dr Brooke undertook an MBO of that business and hence established GBS Venture Partners, which grew to become a leader in the Australian venture capital industry. Dr Brooke has been integral in the establishment of and exit from numerous biotech companies.

- Spent years in the US medical venture capital field
- Recruited by Rothschild to establish its Australian biotech investment business. Eventually undertook MBO of that business forming GBS Ventures
- GBS became one of Australia's most successful venture funds
- Founder, investor in and director of numerous successful ventures with exits in excess of \$1.5B

Some of the GBS successes are listed below, which include up-front payments and potential royalties/milestone payments:



AUD \$900 million



AUD \$250 million



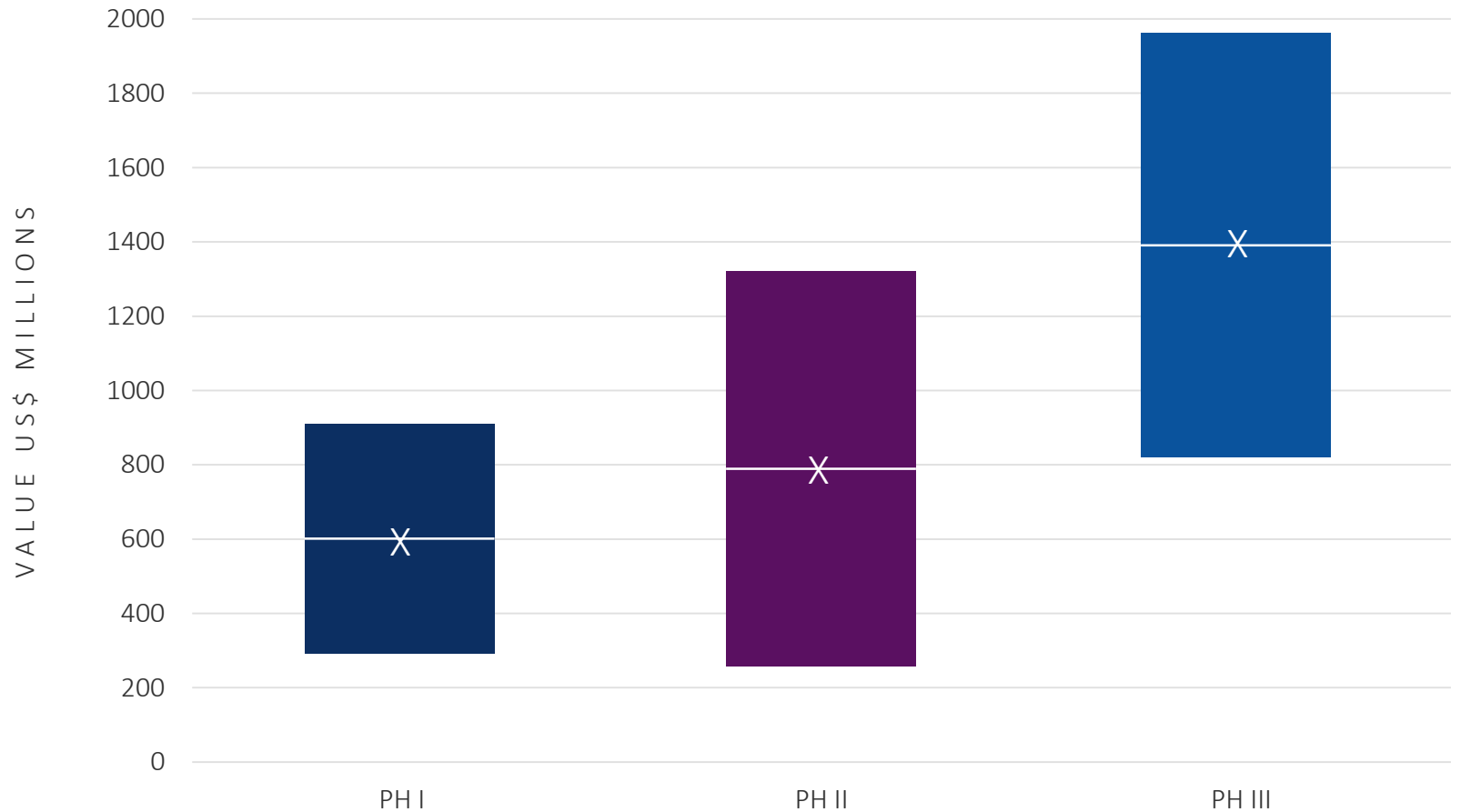
AUD \$300 million



AUD \$250 million

# Peer comparison

What big pharma companies are paying for acquisition of drug developers in the Alzheimer's space



# Recent comparable deals

Assets with Alzheimer's disease as the lead indication or key indication

Licensee/acquirer	Licensor/acquired	Year	Candidate(s)	Phase	Deal Value (US\$M)	Upfront (US\$M)
Takeda	Denali	2018	ATV platform, three programs	Pre-clinical	<u>~\$1,000</u>	\$150
Biogen	BMS	2017	BMS-986168	Ph 1	<u>\$710</u>	\$300
Allergan	Heptares	2016	Three M1/M4 agonists	Ph I	<u>\$3,340</u>	\$125
Janssen	AC immune	2015	ACI-35	Ph Ib	<u>\$509</u>	Undisclosed
Merck	Bionomics	2014	BNC-375	pre-clinical	<u>\$526</u>	\$20
Eli Lilly	AstraZeneca	2014	AZD3293	Ph I	<u>\$500</u>	\$50
Iperian	BMS	2014	IPN007	pre-clinical	<u>\$725</u>	\$175
Otsuka	Lundbeck	2013	Idalopirdine	Ph II	<u>\$825</u>	\$150
Janssen	Orion	2013	ORM-12741	Ph IIa	<u>Undisclosed</u>	\$31

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Xanamem™ in closing .....

# Summary



A huge market with a significant unmet medical need

## Xanamem

- Differentiated, with a novel mechanism of action
- Small molecule - oral
- High quality development plan and regulatory review
- Solid IP out to at least 2031
- Potential utility in other neurological indications

## XanADu

- Fully funded to completion
- DSMB interim analysis Q2 2018
- On track for last patient enrolled before end 2018
- 84 patients enrolled (48% of total); 35 already completed



Substantial independent support for cortisol/Alzheimer's hypothesis



Highly experienced Board



Growing interest in Xanamem from pharma partners



A compelling investment opportunity

Dr. Bill Ketelbey

CEO & Managing Director

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[www.actinogen.com.au](http://www.actinogen.com.au)



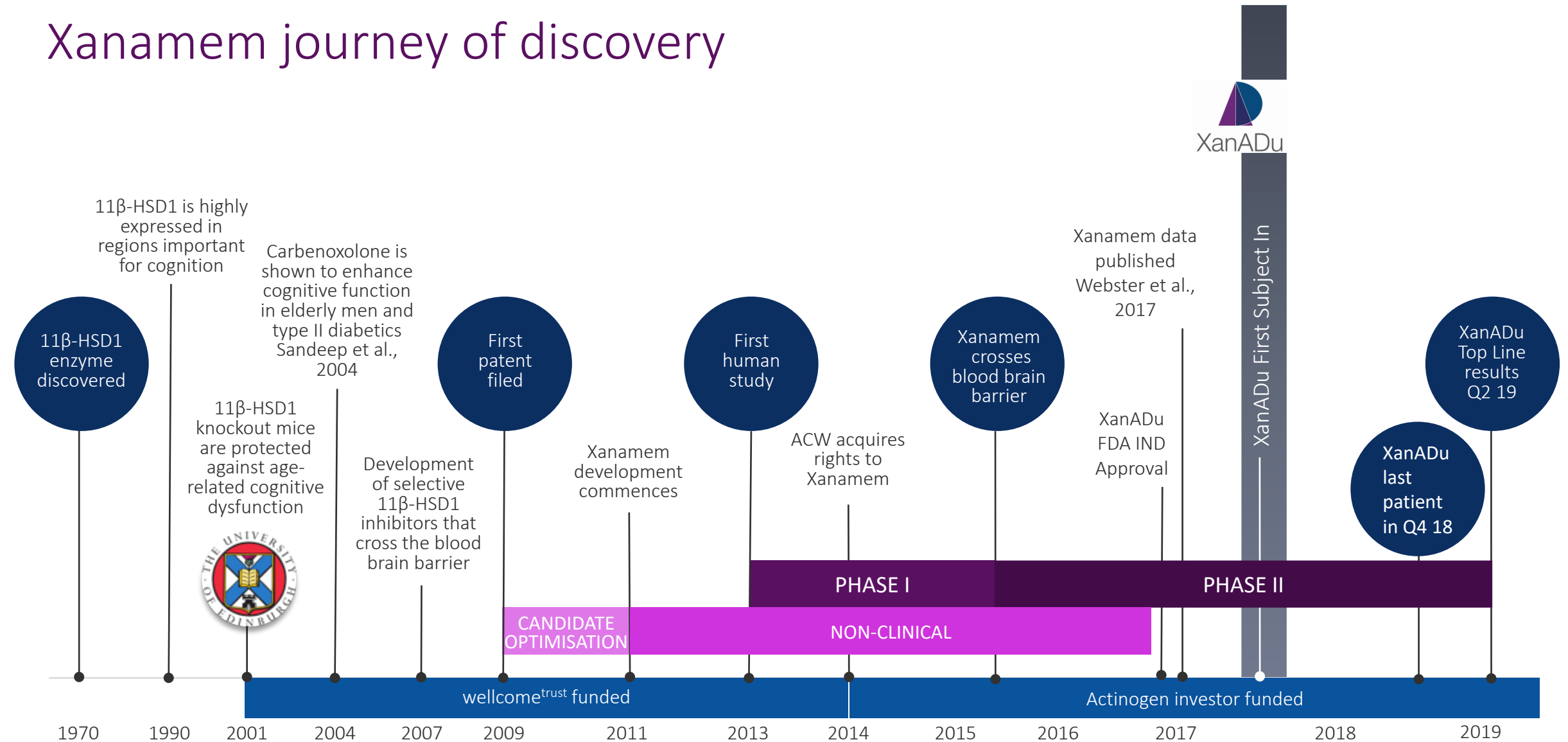
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Appendix



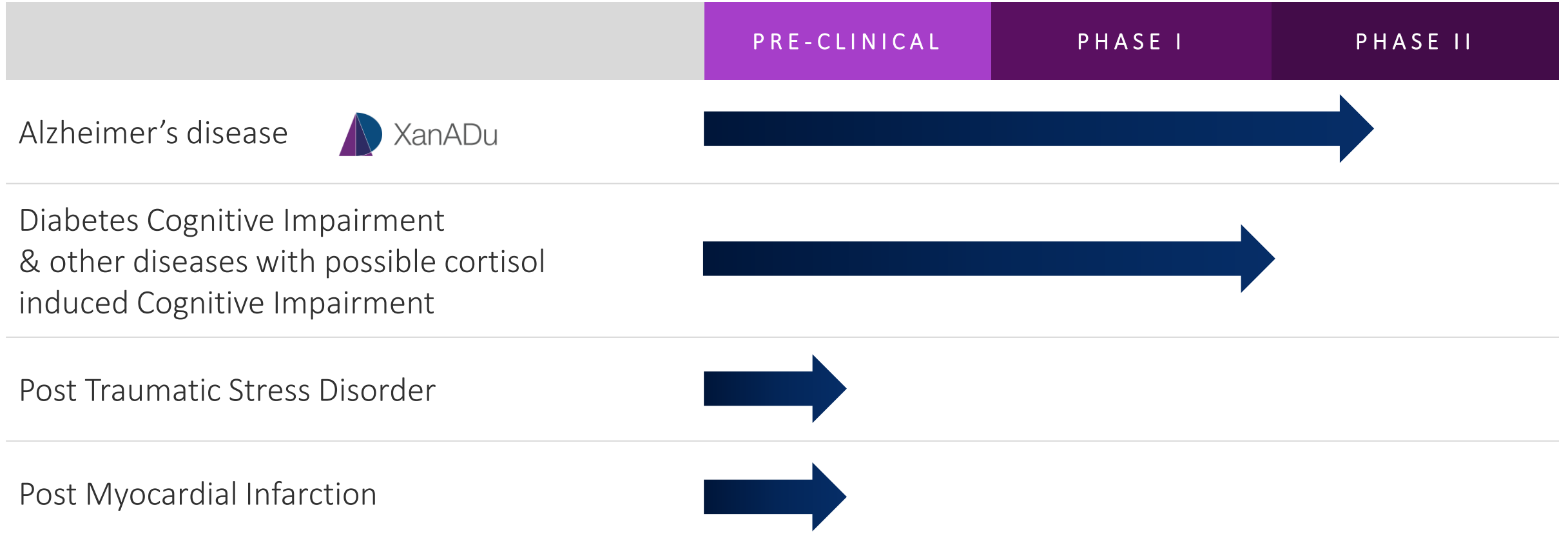
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# Xanamem journey of discovery





# Xanamem pipeline of indications, back-up compounds\*



\* Back-up compounds to Xanamem, licenced from Edinburgh University