

## Actinogen to be showcased at key conferences

- Actinogen CEO to present at multiple Investor, Alzheimer's and Biotech conferences, during the second half of October
- Opportunity to showcase Actinogen's novel, potential breakthrough treatment for Alzheimer's disease and other conditions presenting with cognitive decline
- An update on the progress made with Actinogen's Alzheimer's trial, XanADu, will be presented: 35 patients, representing 20% of the total trial cohort, have already been enrolled
- Alzheimer's disease is now the leading cause of death in Australian women and second only to heart disease in Australian men
- Of the top-ten leading fatal illnesses globally, Alzheimer's remains **the only one** that cannot be prevented, treated or cured, underscoring the urgency to develop effective new therapies

**Sydney, 17 October 2017: Actinogen Medical (ASX: ACW)** is pleased to advise that the CEO, Dr. Bill Ketelbey will be presenting at, and participating in, a number of conferences in Melbourne and Adelaide during the second half of October.

### **AC4R Annual Scientific Meeting**

On the 17<sup>th</sup> October, Dr. Ketelbey is presenting an update on the promising progress made with XanADu, Actinogen's international trial of Xanamem in mild Alzheimer's disease, at the **AC4R Annual Scientific Meeting** in Melbourne. The Australasian Consortium of Centres for Clinical Cognitive Research (AC4R) is the peak body representing Dementia Research Centres in Australasia. Many AC4R members have enrolled patients into XanADu, making it a key operational conference for Actinogen.

### **8<sup>th</sup> Australian Microcap Investment Conference**

On the 18<sup>th</sup> October, Dr. Ketelbey is presenting at the **8<sup>th</sup> Australian Microcap Investment Conference** in Melbourne. This conference, the largest in Australia focused on the microcap sector, provides an opportunity for the investment community to understand the potential for significant returns on an investment in Actinogen. Additionally, the audience will be updated on the progress being made with XanADu, Actinogen's international trial of Xanamem in mild Alzheimer's disease and the development of Xanamem in other conditions presenting with cognitive decline.

### **17<sup>th</sup> Alzheimer's Australia Biennial National Dementia Conference**

On the 19<sup>th</sup> October, Dr. Ketelbey is presenting at the **17<sup>th</sup> Alzheimer's Australia Biennial National Dementia Conference** in Melbourne. This conference brings together a diverse range of voices and expertise with an interest in dementia, including people living with dementia, carers and service providers, and the Alzheimer's research community. Dr. Ketelbey will present on Xanamem, with its novel mechanism of action, and its strengths as a potential treatment for Alzheimer's disease. The progress being made with XanADu, Actinogen's international trial of Xanamem in mild Alzheimer's, will also be presented.

## **Australia Biotech Invest**

On the 24<sup>th</sup> October, Dr. Ketelbey will present at **Australia Biotech Invest**, also in Melbourne. This is Australia's premier life science investment conference and provides the opportunity to showcase Actinogen to, and engage directly with, an anticipated 200 investors and prospective partners from around the world.

## **Ausbiotech 2017**

Finally, from the 25<sup>th</sup>-27<sup>th</sup> October in Adelaide, Dr. Ketelbey will attend **Ausbiotech 2017** – the Ausbiotech National Conference. The focus for Actinogen at this meeting is the potential partnership opportunities presented by over 800 delegates from across the global biotechnology and pharmaceutical industries. Actinogen will be meeting with many of these biotech and pharmaceutical companies.

Key updates will be presented on XanADu, Actinogen's international trial of Xanamem in Alzheimer's disease, and will include:

- Patients are being actively recruited at all 20 research sites in Australia, the USA and UK.
- 35 patients, representing 20% of the total patient cohort, have already been enrolled into the trial.
- The first patients in Australia and the USA recently completed the trial.

The urgency to develop effective new therapies for Alzheimer's disease is underscored by the recent ABS data showing that Alzheimer's disease has now become the leading cause of death in Australian women and is second only to heart disease in Australian men. The number of Australians with Alzheimer's disease is expected to double ever 20 years with the cost of managing these patients likely to swamp available health budgets. 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.

Investing in Actinogen could provide the breakthrough needed in the development of a new treatment for Alzheimer's disease.

While each presentation will be tailored to the particular meeting and audience, the latest Investor Presentation deck contains the key information that will be presented over the next 2 weeks, and is available at: <http://actinogen.com.au/wp-content/uploads/2017/10/20171011-Investor-Presentation-Oct-2017.pdf>

**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 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, 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.**

# Xanamem™ for Alzheimer's disease

Dr Bill Ketelbey CEO

October 2017



**Actinogen**  
Medical

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# Actinogen Medical

- Headquartered in Sydney, Australia. ASX:ACW
- Developing Xanamem for the treatment of Alzheimer's disease (AD) and cognitive impairment in chronic neurodegenerative diseases.
- Xanamem, a novel first-in-class, brain penetrant, orally active, inhibitor of the 11 $\beta$ HSD1 enzyme – prevents the production of excess cortisol in the brain.
- Persistently raised cortisol in the brain is associated with the development and progression of Alzheimer's disease.
- Experienced board and management; expert clinical and scientific advisory board.

## STOCK METRICS \*

ASX CODE	ACW
Market Capitalisation	\$35m
Enterprise Value	\$32.0m
52-week High/Low	\$0.04-\$0.09
Top 20 Shareholdings	56%

## TOP 10 HOLDERS

Rank	Name	A/C designation	%IC
1	EDINBURGH TECHNOLOGY FUND LIMITED		7.76
2	JK NOMINEES PTY LTD	<THE JK FUND A/C>	6.45
3	WEBINVEST PTY LTD	<OLSB UNIT A/C>	4.24
4	WARAMBI SARL		3.53
5	SUNSET CAPITAL MANAGEMENT PTY LTD	<SUNSET SUPERFUND A/C>	3.22
6	MR MARTIN ROGERS		3.22
7	MR BENJAMIN CRANSTOUN DARK	<THE BEN DARK HOLDINGS A/C>	2.54
8	DENLIN NOMINEES PTY LTD		2.46
9	OAKTONE NOMINEES PTY LTD		2.37
9	TISIA NOMINEES PTY LTD	<HENDERSON FAMILY A/C>	2.37
10	BNP PARIBAS NOMINEES PTY LTD HUB24 CUSTODIAL SERV LTD DRP		2.20




# Commercially experienced, globally recognised

## Board of Directors



Dr. Geoff Brooke  
Chairman



Dr. Bill Ketelbey  
CEO & MD



Dr. Jason Loveridge  
Non-Executive Director

## Xanamem Clinical Advisory Board



Prof. Craig Ritchie  
Chair



Prof. Colin Masters

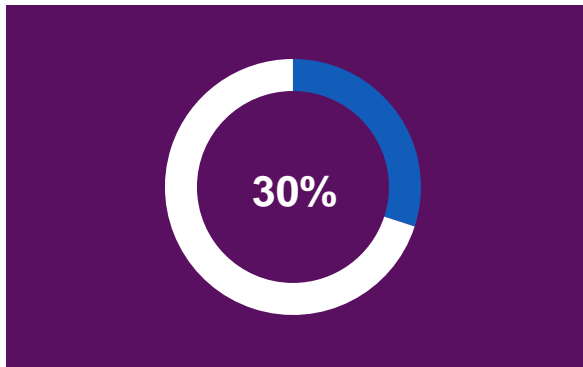


Prof. Jeffrey Cummings



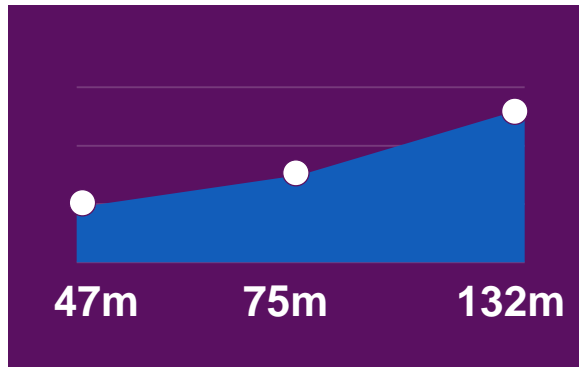
# Alzheimer's disease: a vast unmet medical need

- There are nearly 50 million Alzheimer's disease sufferers world-wide and the number is set to double every 20 years
- It's the leading cause of death in Australian women and second only to heart disease in Australia, overall
- Of the top-ten leading fatal illnesses, Alzheimer's remains the only one that cannot be prevented, treated or cured
- There are only 4 drugs available to treat Alzheimer's disease (donepezil, rivastigmine, galantamine, memantine), however they all provide only limited symptomatic benefit – generally around 6 months. Once the patient fails on one of these, there are no alternatives

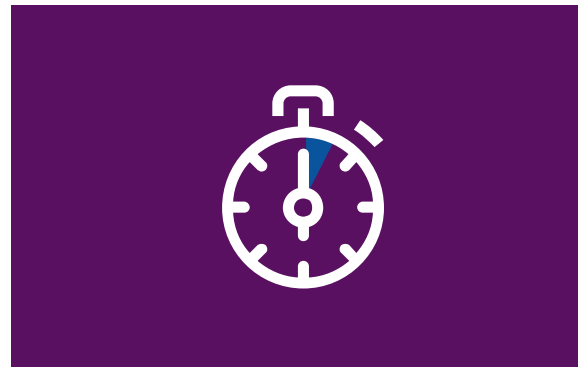


**30% OF 85 YEAR OLDS  
HAVE ALZHEIMER'S DISEASE**

1 in 3 seniors will die with Alzheimer's disease or other dementia



**NUMBERS WILL DOUBLE  
EVERY 20 YEARS**



**ONE PERSON EVERY 3  
SECONDS**

Globally there were ~10m new cases of dementia in 2015



**TOTAL COST RISES TO  
US\$2 TRILLION BY 2030**

Dementia will become a trillion dollar disease by 2018

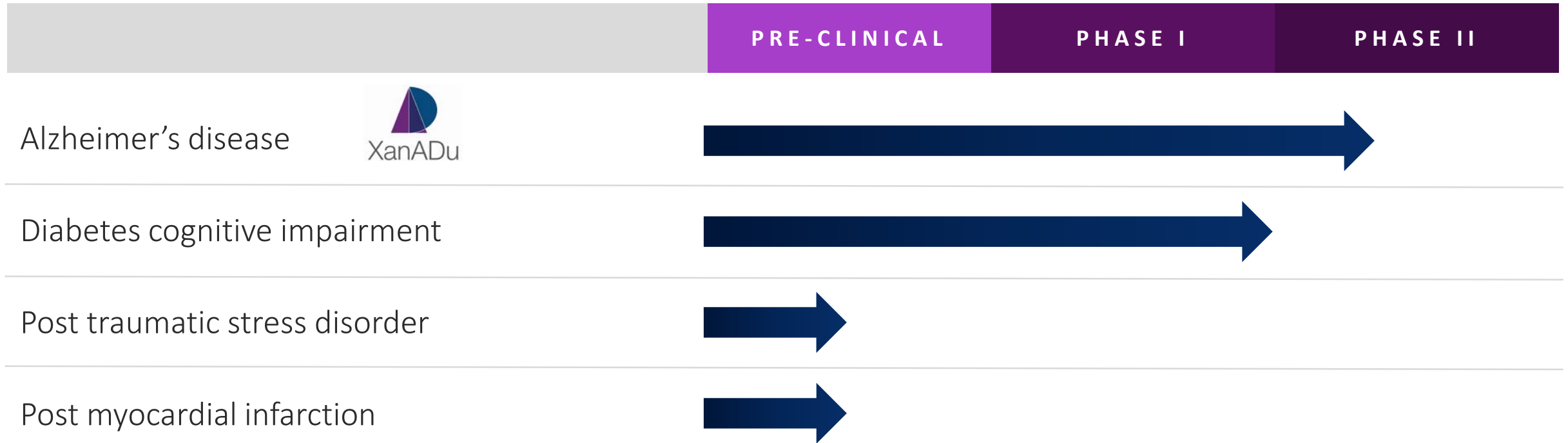


# Xanamem

- 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: acceptable clinical safety, toxicity and PK/PD profile
- Efficacious human brain concentrations
- Compelling data package: clinical safety, in vitro and in vivo mechanistic and efficacy data
- 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 most major markets



# Xanamem development indications



Alzheimer's disease



Diabetes cognitive impairment

Post traumatic stress disorder

Post myocardial infarction

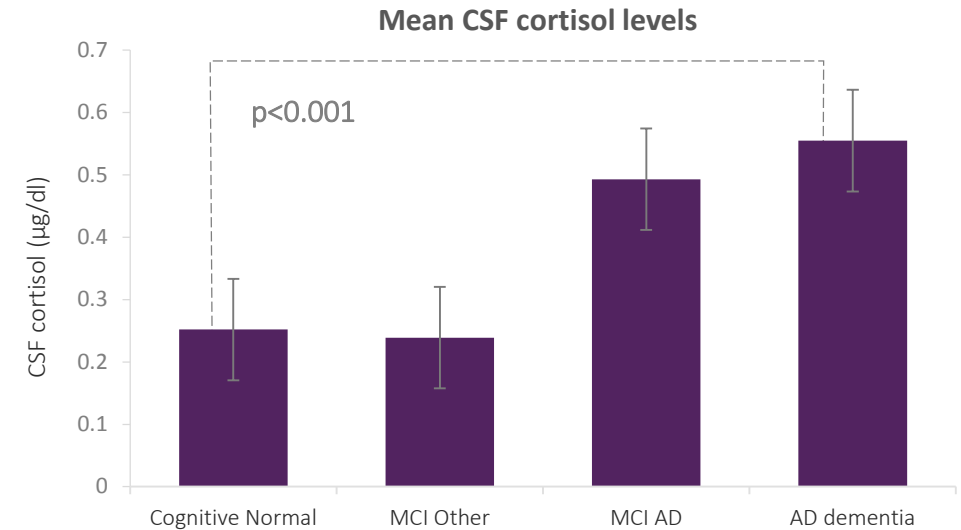
# Cortisol: a validated biomarker and target for AD

## Cortisol and Alzheimer's

- Recent independent studies support the association between cortisol and development and progression of Alzheimer's disease <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 $\beta$ + on decline in global cognition, episodic memory, and attention

## Xanamem

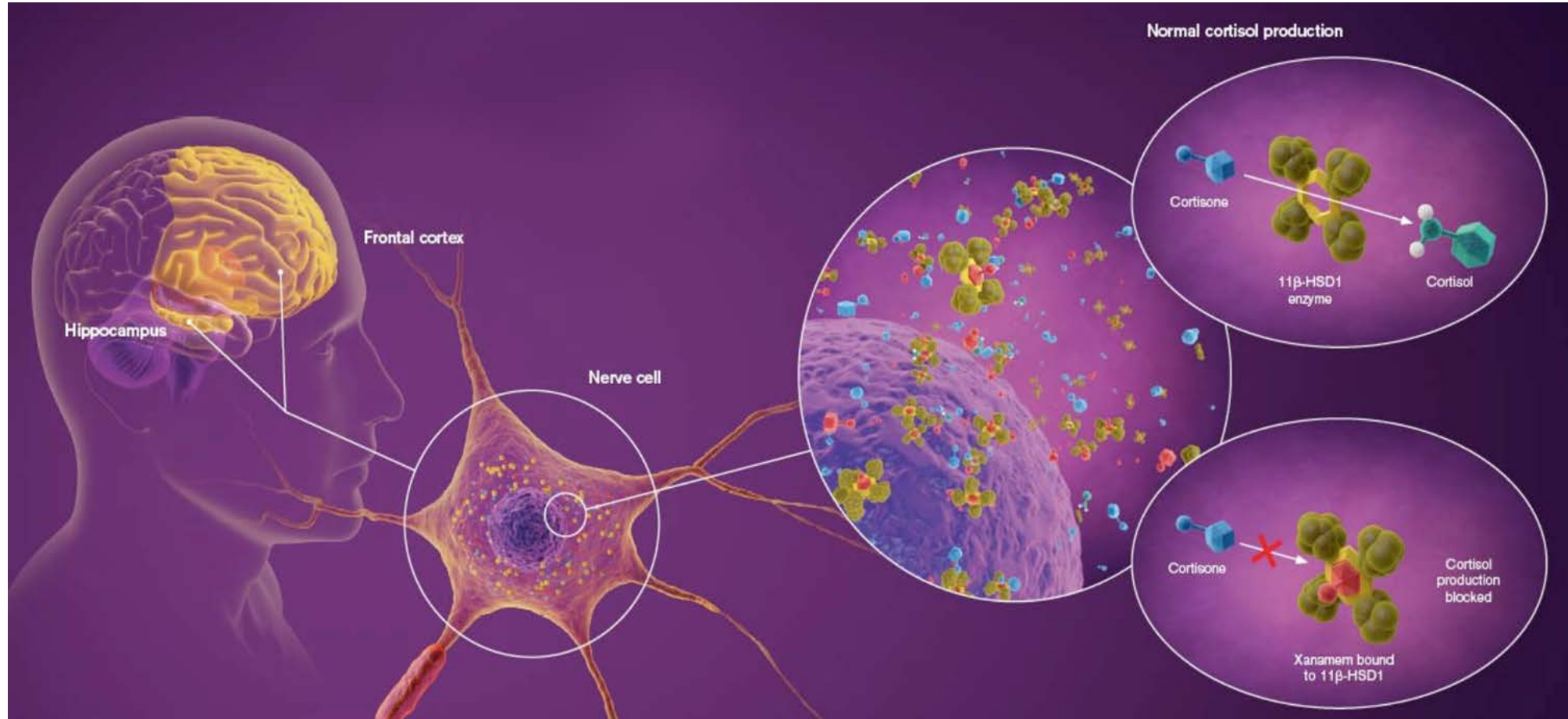
- Data presented at four major international medical congresses in 2016 – AAIC Toronto; CTAD San Diego; ICE Beijing; MMC Lisbon
- Pre-clinical and Phase I data published <sup>10-11</sup>



Popp et al, 2015

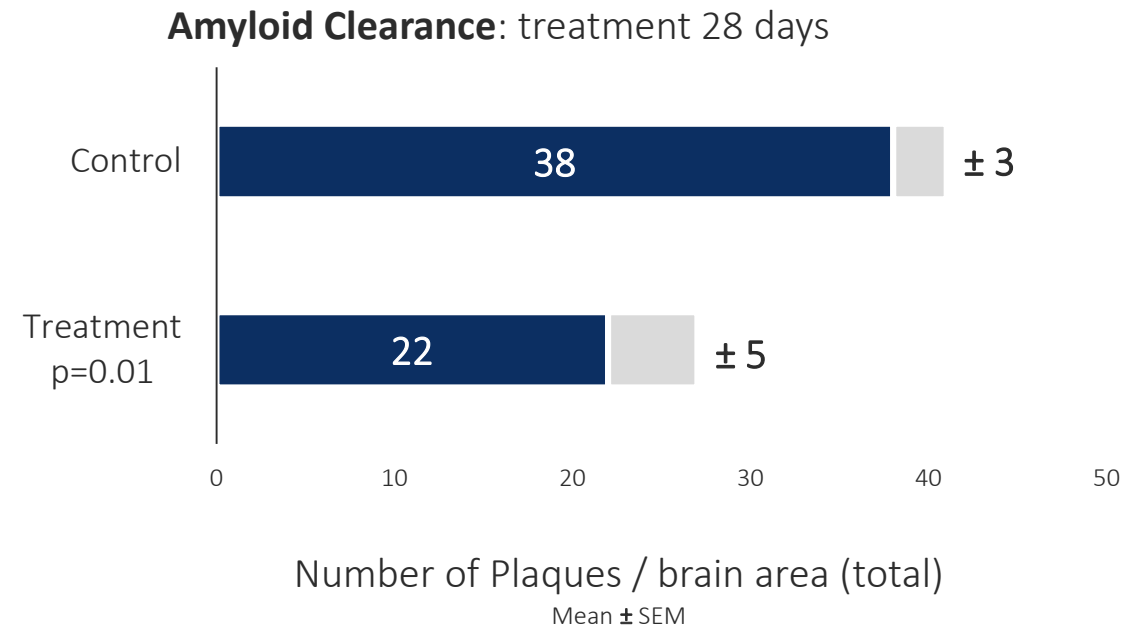
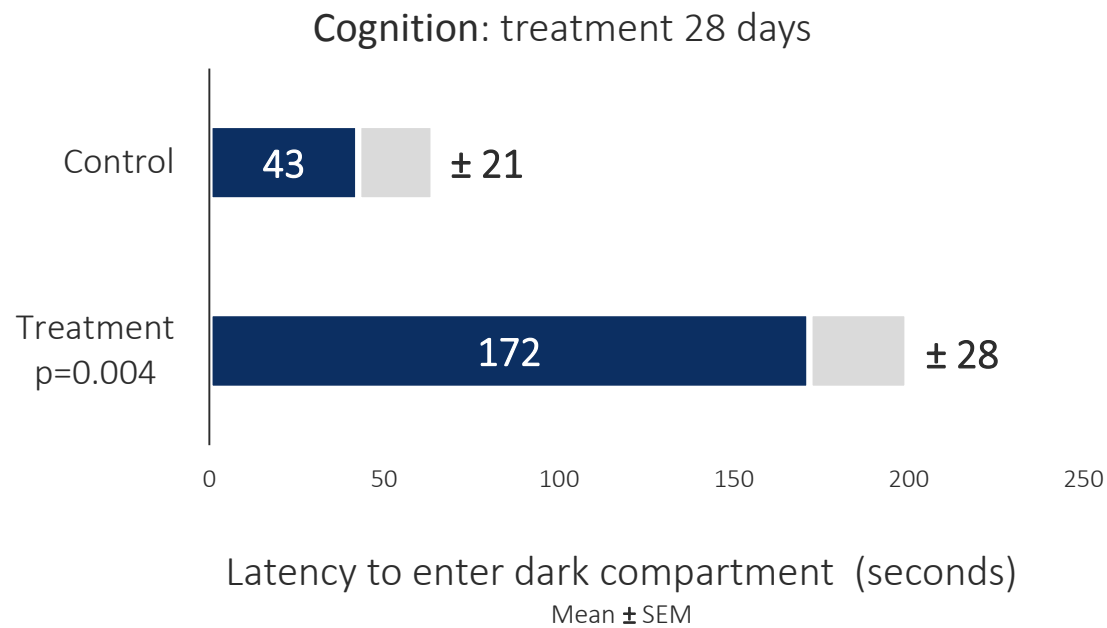
# Mechanism of action

Xanamem binds to 11 $\beta$ HSD1, reducing brain cortisol production



# Xanamem

## Symptomatic and disease modifying effects in mouse models



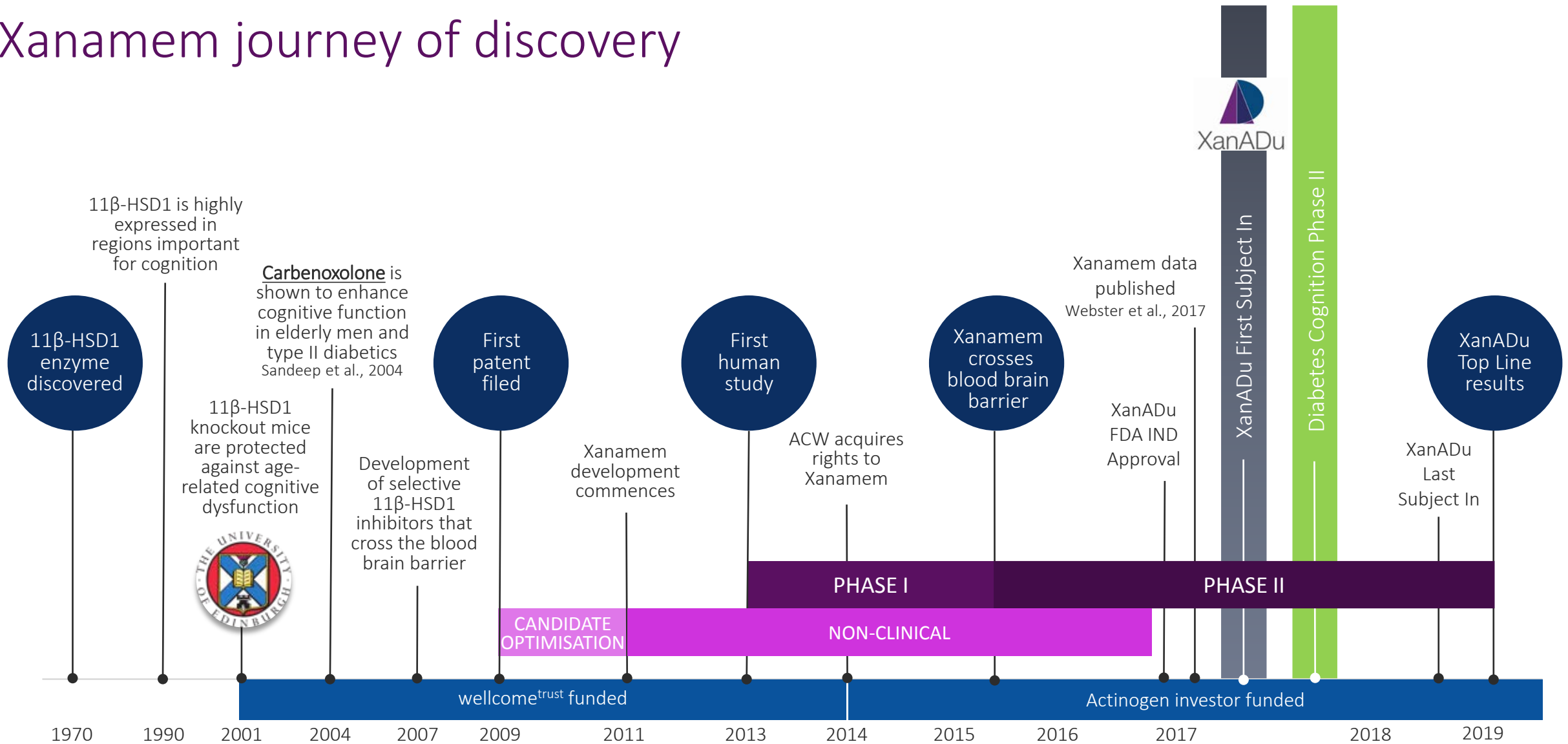
Significant improvement in cognition after only 28 days treatment, continuing out to 41 weeks



# Clinical Development



# Xanamem journey of discovery



# Xanamem completed clinical studies

(Building on extensive historic 11 $\beta$ HSD1 class safety data from metabolic disease research)

## A phase I **single ascending dose** (SAD) study<sup>1</sup>

- Surrogate peripheral pharmacodynamic markers support **potent target engagement** (48 healthy males and females)
- Low number of clinically insignificant treatment-emergent adverse events (TEAEs)

## A phase I **multiple ascending dose** (MAD) study<sup>1</sup>

- TEAEs mild to moderate in intensity (24 healthy males)

## A phase I **single-dose fed-fasted crossover** study

- TEAEs mild to moderate in intensity (12 healthy males)

## A phase I **CSF/plasma pharmacokinetic** study<sup>1</sup>

- Xanamem readily achieves CSF concentrations higher than its IC<sub>50</sub> (4 healthy males)
- TEAEs mild to moderate in intensity

# Xanadu Phase II trial

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

- 34 patients enrolled (end-Sept) and first patient has already completed study.
- All 20 study sites open and patients enrolled in USA, UK and Aus.



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

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# Xanamem secondary indication – DCI

## Diabetes-related mild Cognitive Impairment

- Several potential secondary indications considered
- DCI selected due to a strategic mix of scientific, clinical, and commercial factors
  - Type 2 Diabetes Mellitus (T2DM) is a significant risk factor for cognitive impairment and dementia <sup>1-4</sup>
  - T2DM patients more likely to show abnormalities in hypothalamic-pituitary-adrenal (HPA) axis regulation <sup>5</sup>
  - Non-selective 11 $\beta$ HSD1 inhibitor carbenoxolone demonstrated cognitive improvements in cognitively normal patients with T2DM <sup>6</sup>
- Large potential patient population, >15M diabetes patients with dementia
- Expert clinical development partner (University of Edinburgh, UK)



# Commercial

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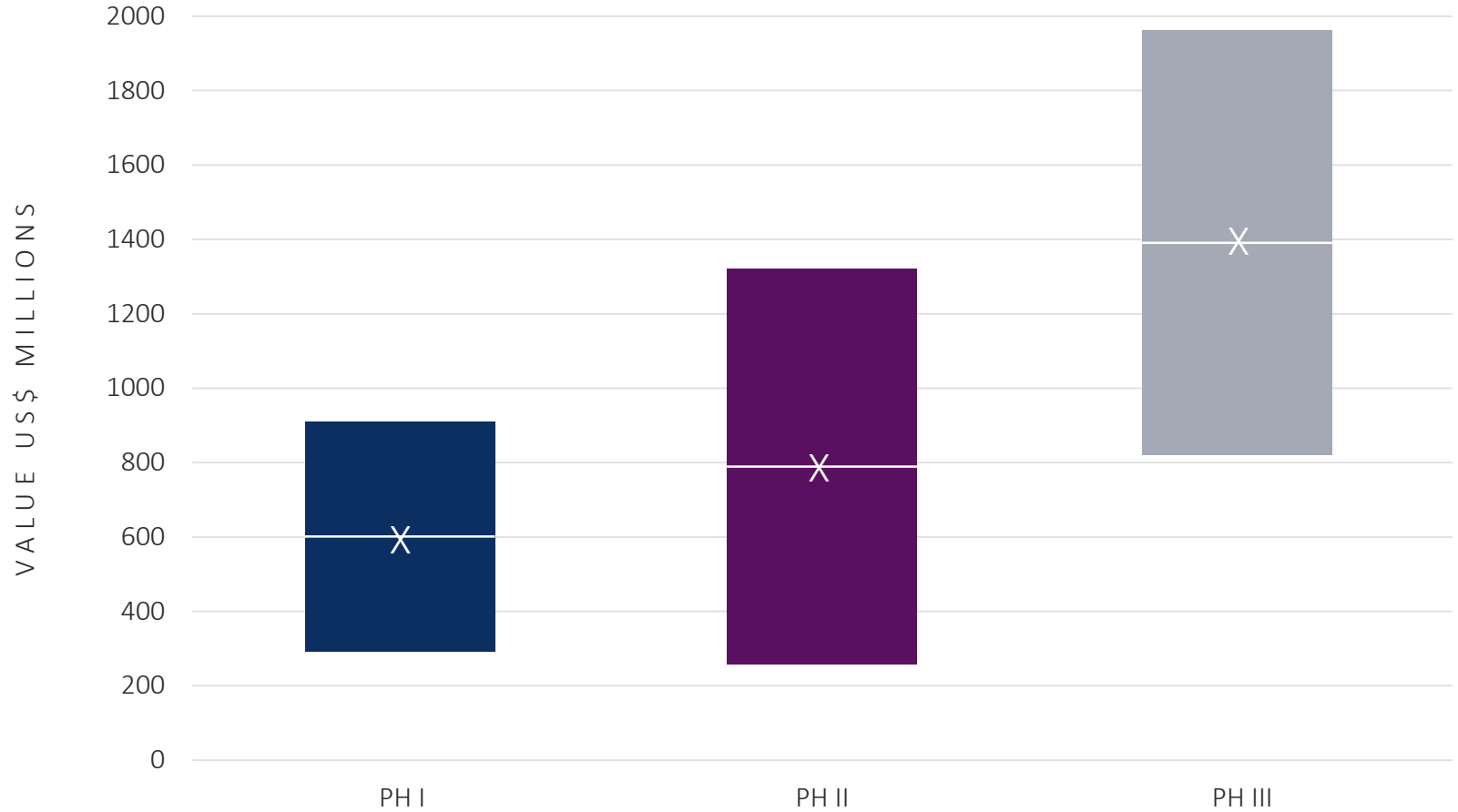
# Value proposition

- Strong therapeutic rationale, differentiated mechanism of action
- Differentiated from, but complementary to anti-A $\beta$ , anti-Tau and other AD therapeutic strategies
- Solid non-clinical and clinical data set
- First in class compound, designed for brain penetration
- 11 $\beta$ HSD1 class safety data
- Significant opportunities for additional clinical indications
- Composition of matter IP coverage  $\geq$  2031, patents granted in most major markets
- Deep commercial, scientific and clinical expertise
- Strong commercial and clinical interest



# Peer comparison

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



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# Summary

- A novel, first in class, potent, orally bioavailable, brain-penetrant, 11 $\beta$ HSD1 inhibitor
- Strong therapeutic rationale, differentiated mechanism of action: blocking cortisol production in the brain
- Symptomatic and disease modifying effects *in vivo*
- Well-tolerated: acceptable clinical safety, toxicity and PK/PD profile
- Efficacious human brain concentrations
- Compelling data package: clinical safety, in vitro and in vivo mechanistic and efficacy data
- XanADu – phase II clinical study underway, dosing subjects with mild AD dementia in USA, UK, AU
- Planning ongoing for additional clinical indications
- Differentiated from, but complementary to anti-A $\beta$ , anti-Tau and other AD therapeutic strategies
- Significant investment upside potential on peer comparison
- Composition of matter IP coverage  $\geq$  2031, patents granted in most major markets
- Experienced board and management; expert scientific advisory board

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