

Xanamem™ for Alzheimer's disease

Dr Bill Ketelbey CEO



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 β 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

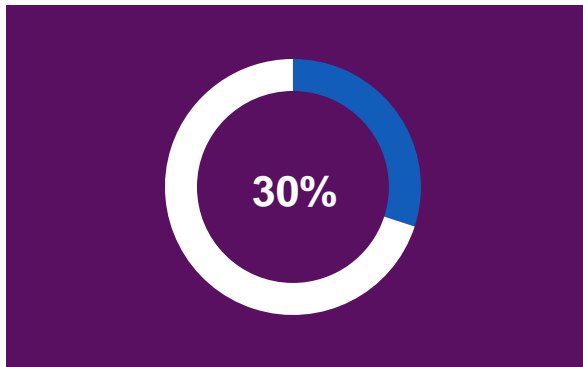


Prof. Jeffrey Cummings



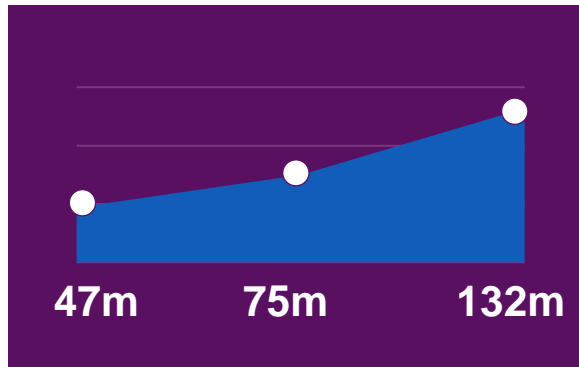
Alzheimer's disease: a vast unmet medical need

- 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

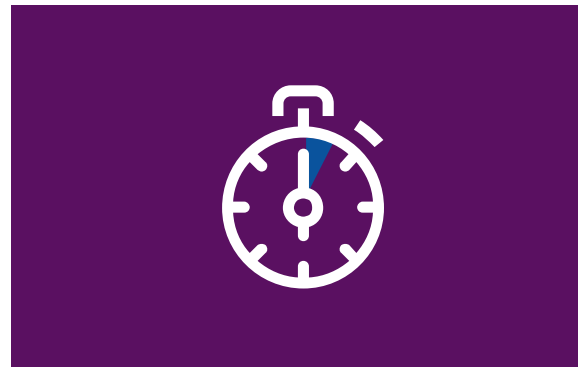


**30% OF 85 YEAR OLDS
HAVE ALZHEIMER'S DISEASE**

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**

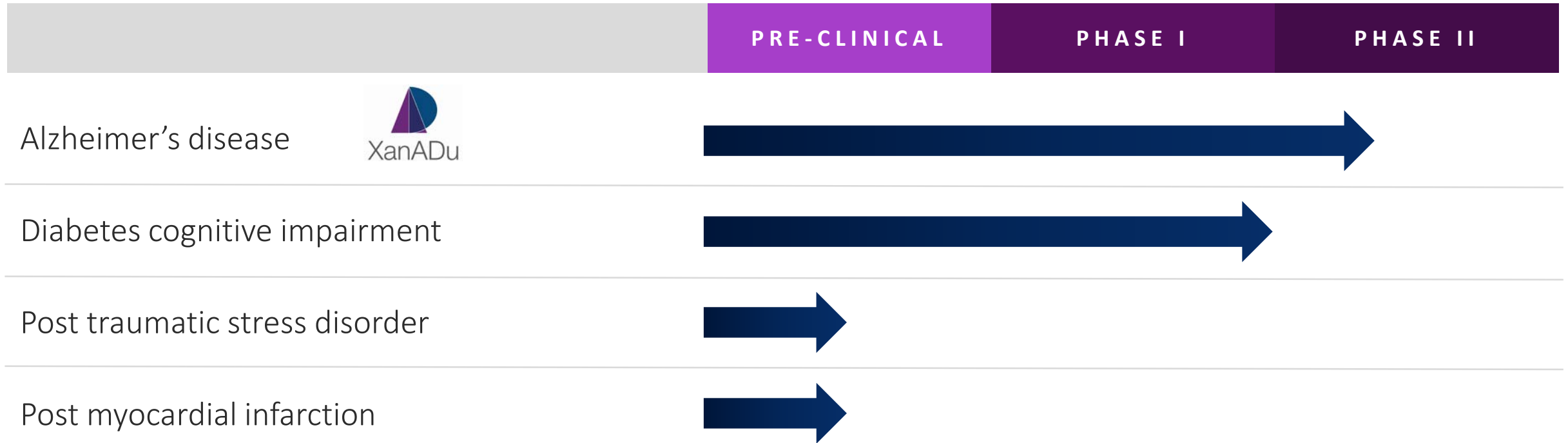
Dementia will become a trillion dollar disease by 2018

Xanamem

- A novel, first in class, potent, orally bioavailable, brain-penetrant, 11 β 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

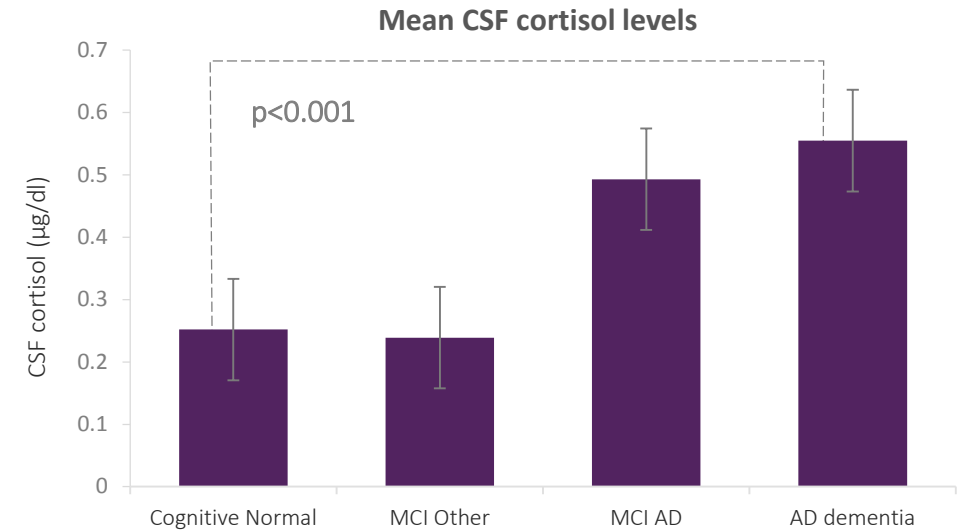
Cortisol: a validated biomarker and target for AD

Cortisol and Alzheimer's

- Recent independent studies support the association between cortisol and development and progression of Alzheimer's disease ¹⁻⁵
- Cognitive impairment in patients with neuroendocrine dysfunction ⁶⁻⁹
- Compelling evidence provided by the Australian Imaging, Biomarker & Lifestyle Study of Ageing (AIBL) study (2017) ⁵
 - subjects with higher plasma cortisol at much greater risk of developing AD
 - accelerated effect of A β + on decline in global cognition, episodic memory, and attention

Xanamem

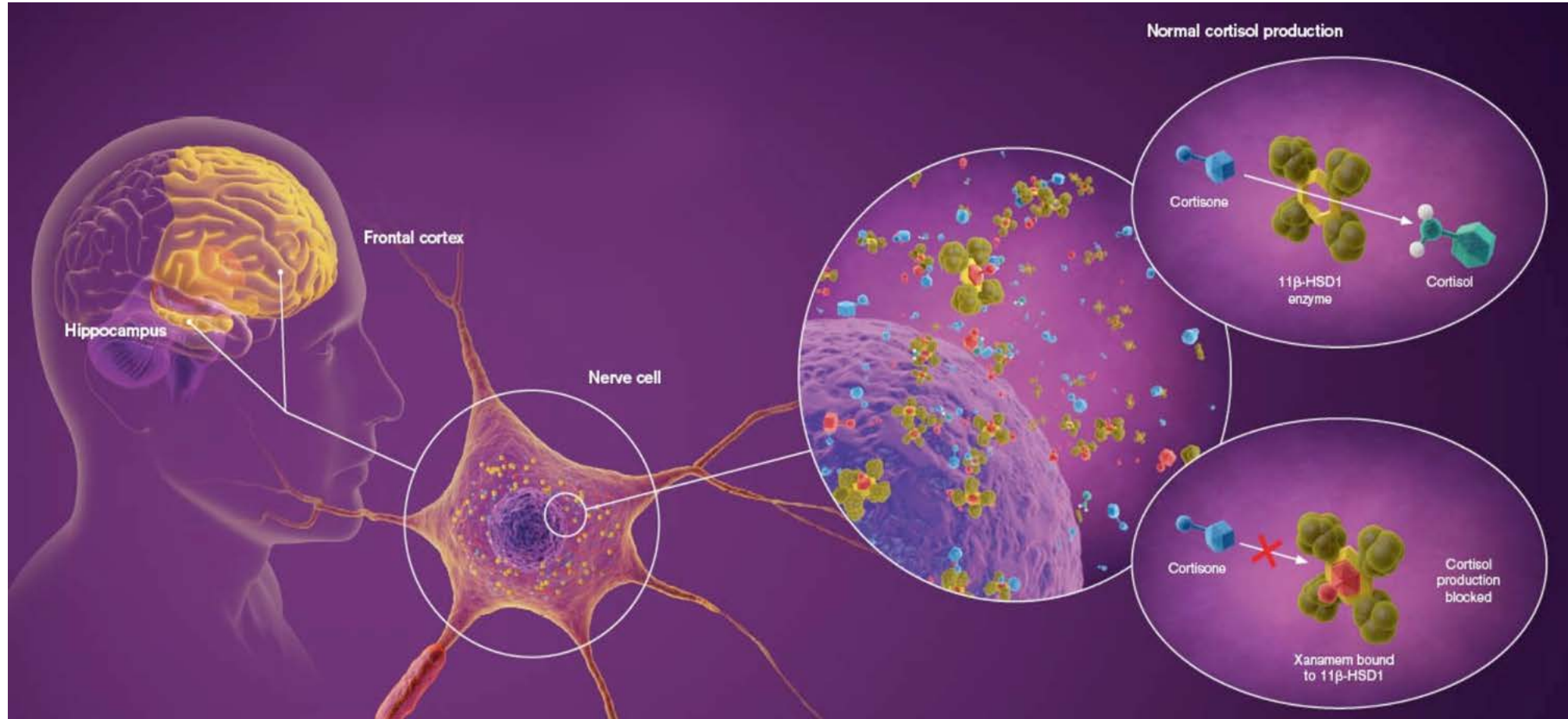
- Data presented at four major international medical congresses in 2016 – AAIC Toronto; CTAD San Diego; ICE Beijing; MMC Lisbon
- Pre-clinical and Phase I data published ¹⁰⁻¹¹



Popp et al, 2015

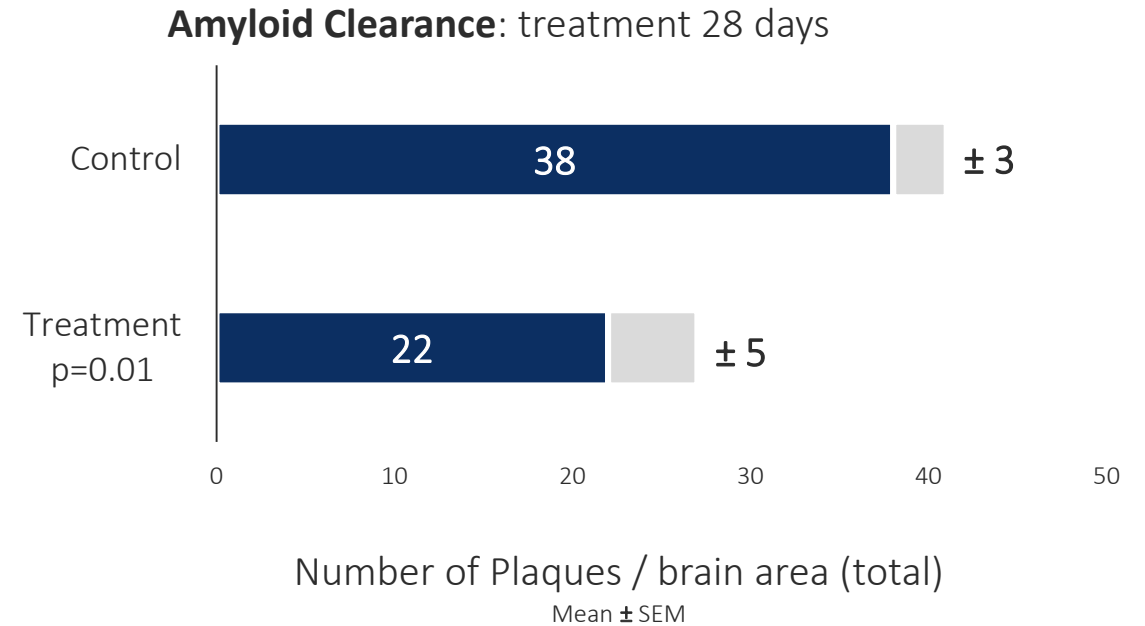
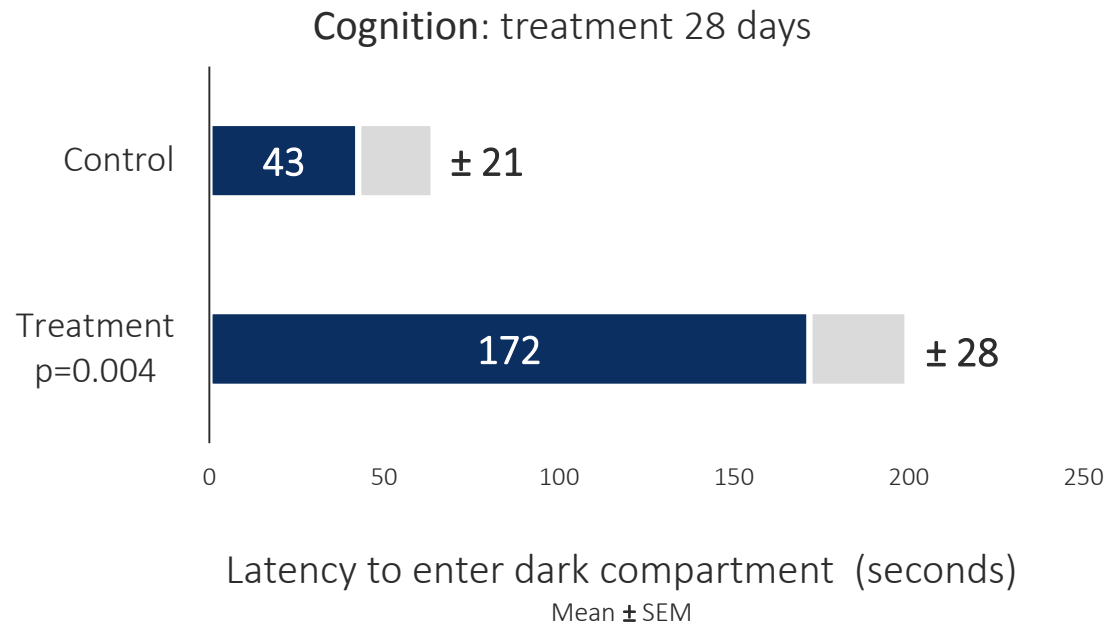
Mechanism of action

Xanamem binds to 11 β 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

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



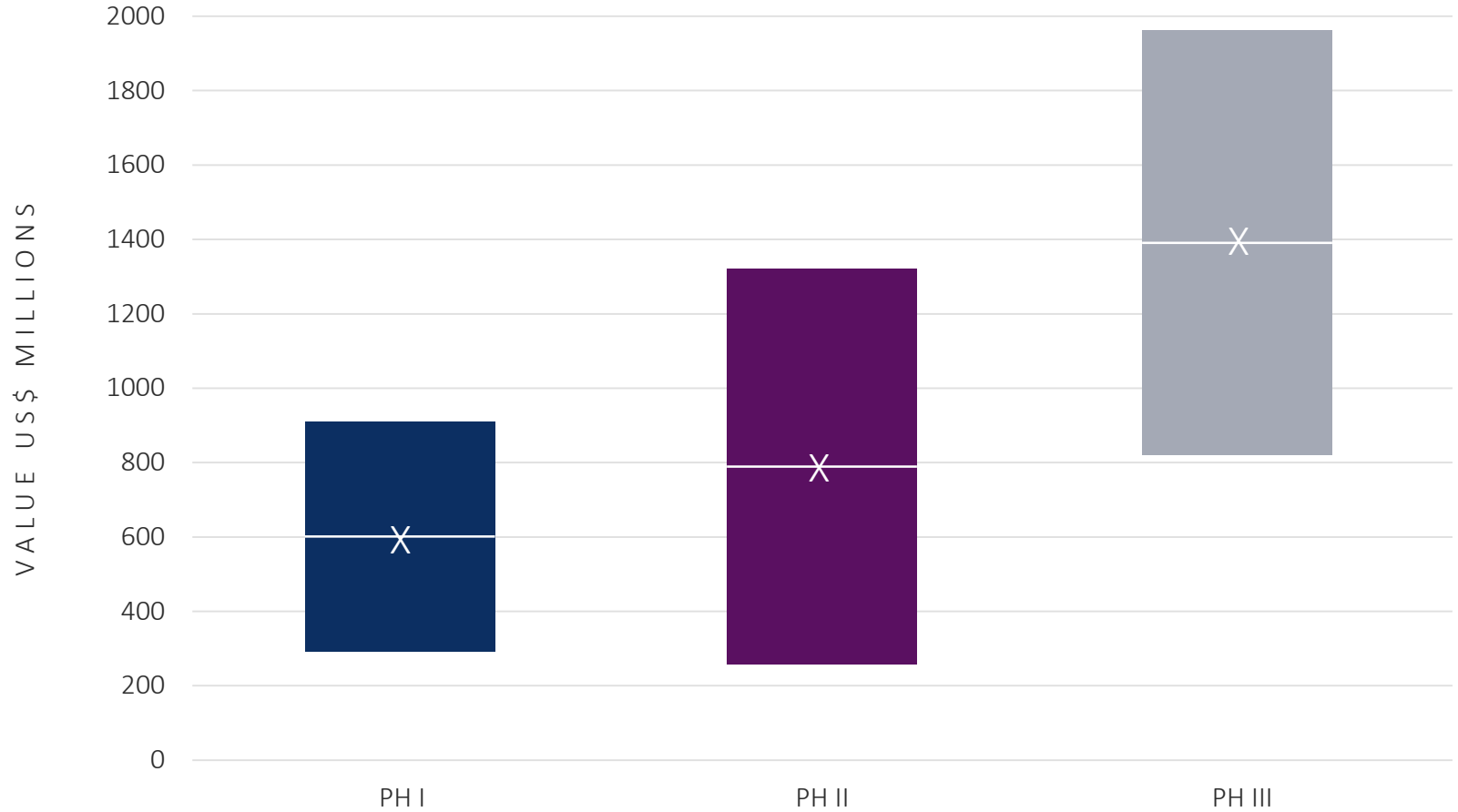
Commercial

Value proposition

- Strong therapeutic rationale, differentiated mechanism of action
- Differentiated from, but complementary to anti-A β , anti-Tau and other AD therapeutic strategies
- Solid non-clinical and clinical data set
- First in class compound, designed for brain penetration
- 11 β 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



Summary

- A novel, first in class, potent, orally bioavailable, brain-penetrant, 11 β 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 β , 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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