

ANNUAL GENERAL MEETING

Nov 30th 2016

Dr. Bill Ketelbey CEO & Managing Director



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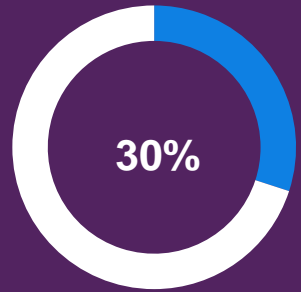
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Focusing on an innovative approach, through the inhibition of cortisol production, for treating *Alzheimer's disease and cognitive impairment* in chronic neurodegenerative and metabolic diseases.

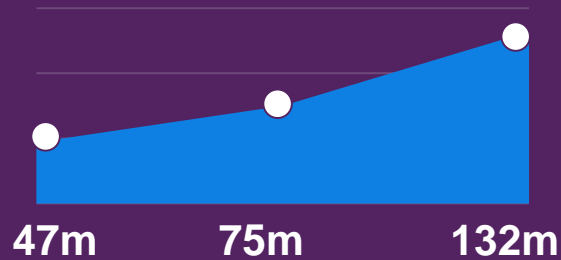
ALZHEIMER'S DISEASE IS EMERGING AS THE MOST SIGNIFICANT HEALTH CHALLENGE OF OUR TIME

- Leading cause of death in the UK and Europe
- Second only to heart disease in Australia
- Of the top ten leading fatal illnesses, Alzheimer's remains the only one that cannot be prevented, treated or cured



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



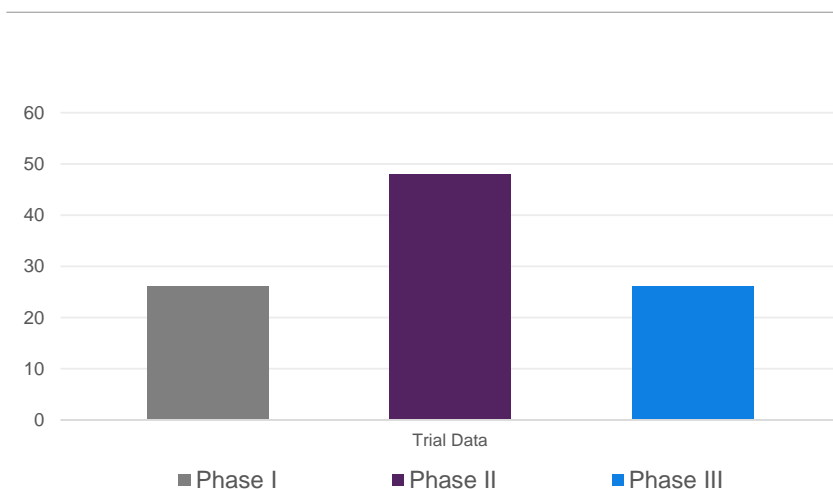
TOTAL COST RISES TO US\$2 TRILLION BY 2030

Dementia will become a trillion dollar disease by 2018

ALZHEIMER'S DRUG-DEVELOPMENT PIPELINE: 2016

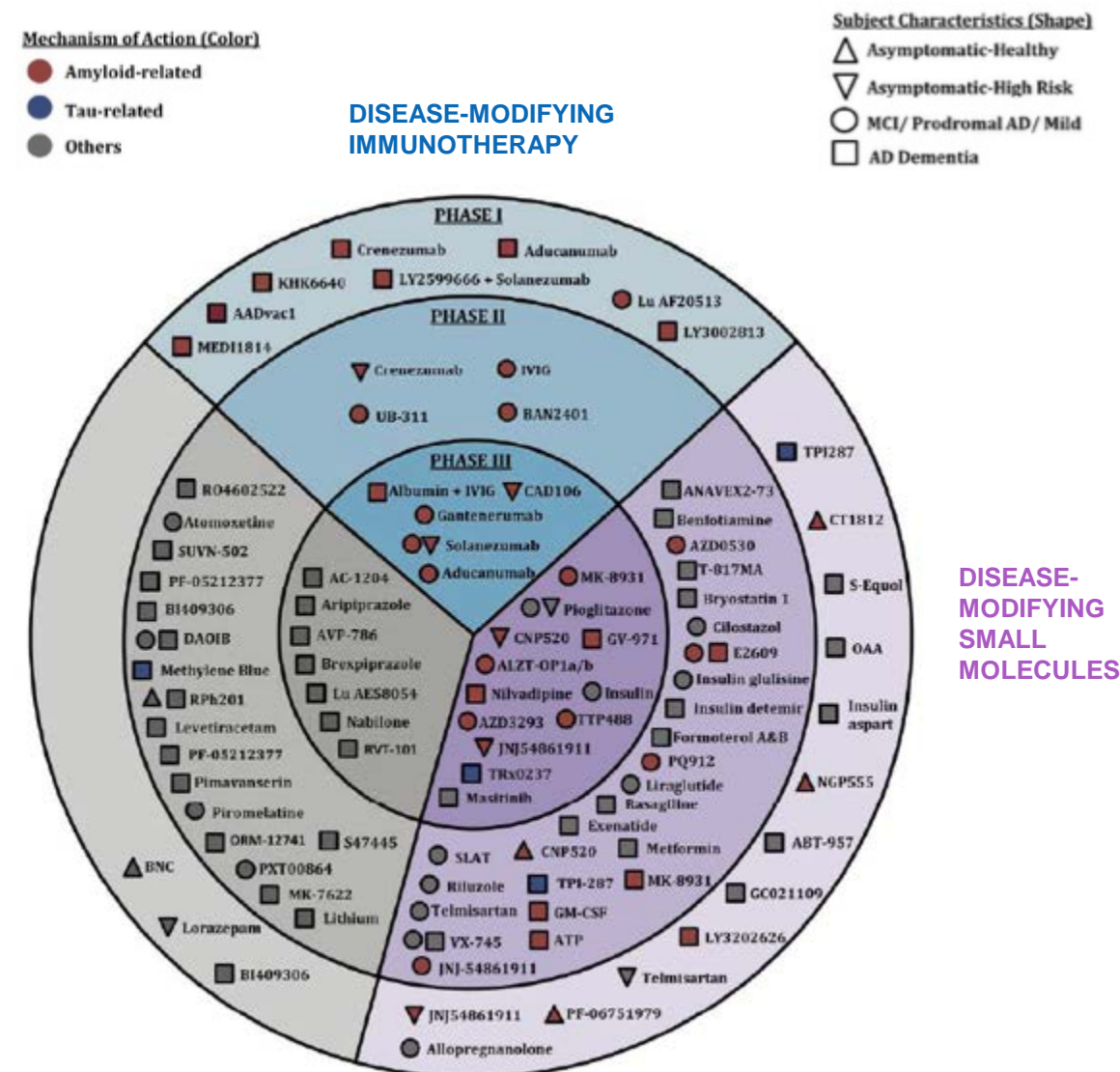
93 DRUGS IN CLINICAL TRIALS

- 74% biopharma sponsored
- 50% amyloid targeted



Source: clinicaltrials.gov as at Jan 4th, 2016

SYMPTOMATIC AGENTS



Source: Cummings, J., Morstorf, T., & Lee, G. (2016)

ALZHEIMER'S DISEASE PIPELINE

TARGETS AND STAGE OF DEVELOPMENT

A D candidates in active clinical development

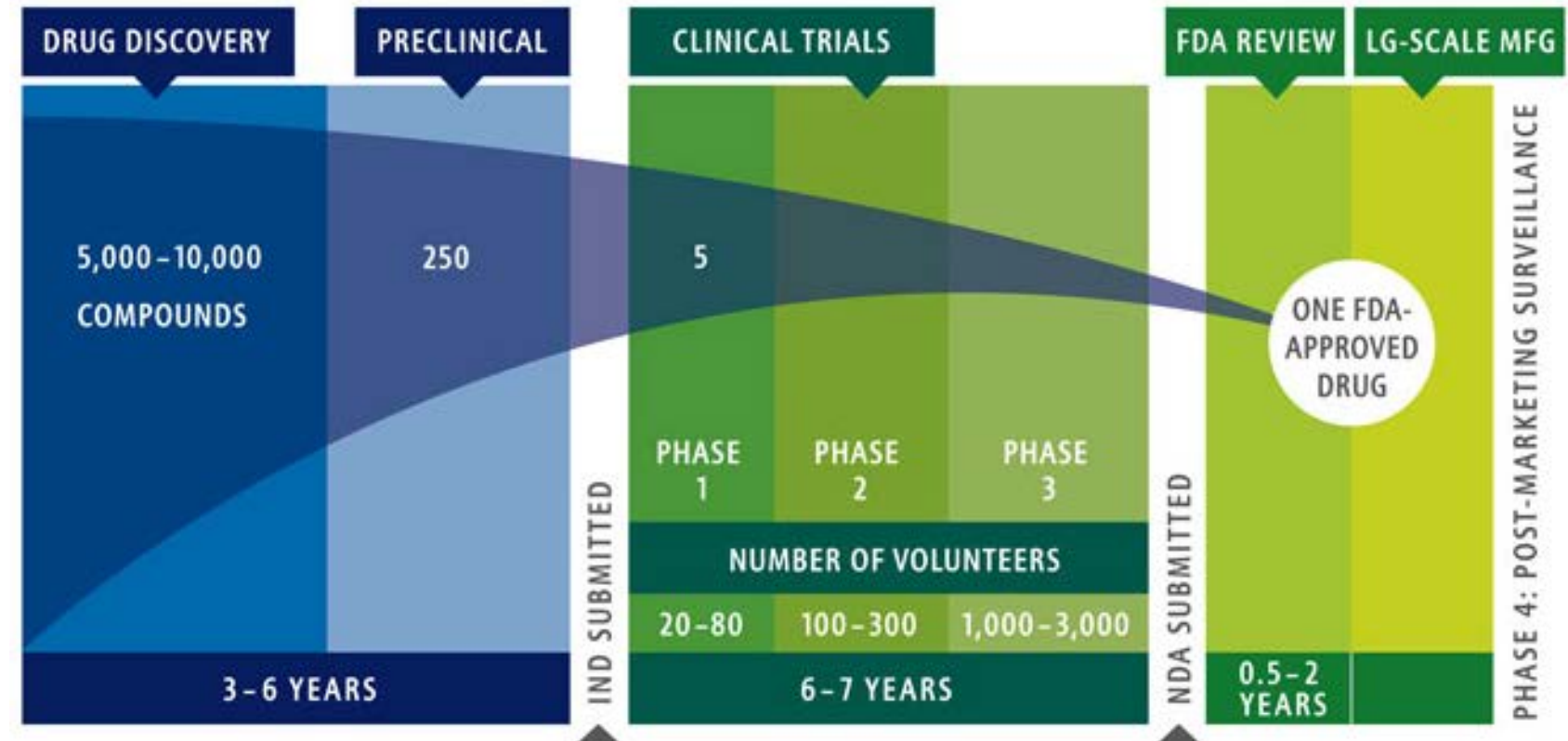
Therapeutic Classes	Mechanism Classes	Phase I	Phase II	Phase III
SYMPTOM RELIEF	11 β -HSD1 inhibitor	1	1	-
	Neuroprotective	5	13	1
	Neurotransmitter based	3	13	6
DISEASE MODIFYING	Anti-amyloid (except BACE inhibitor)	11	9	9
	BACE inhibitor	1	4	4
	Anti-Tau	2	1	1
	Metabolic	2	6	3

DRUG DISCOVERY

15 YEARS AND \$1.5BN

DRUG DISCOVERY & DEVELOPMENT: A LONG, RISKY ROAD

PRE-DISCOVERY



RECENT PUBLICATIONS CONFIRM ASSOCIATION BETWEEN CORTISOL AND ALZHEIMER'S DISEASE



PLASMA CORTISOL, AMYLOID-B, AND COGNITIVE DECLINE IN PRECLINICAL ALZHEIMER'S DISEASE:

A 6-year prospective cohort study

Introduction

Hypothalamic-pituitary-adrenal (HPA) axis dysregulation, which is typically assessed by measuring cortisol levels, is associated with cognitive dysfunction, hippocampal atrophy, and increased risk for mild cognitive impairment and Alzheimer disease (AD). However, little is known about the role of HPA axis dysregulation in predicting cognitive decline or in moderating the effect of high levels of amyloid- β (A β +) on cognitive decline in the preclinical phase of AD, which is often protracted, and thus offers opportunities for prevention and early intervention. We aimed to evaluate the independent and interactive effect of plasma cortisol levels and A β status in predicting cognitive changes in the preclinical phase of AD.

Methods

Cognitively normal older adults ($n=416$) enrolled in the AIBL study underwent A β neuroimaging at a single timepoint. Fasted blood samples were collected at baseline and analysed using a commercial cortisol ELISA, performed according to manufacturer instructions. Because the distribution of raw cortisol values was highly skewed and non-normal, and could not be corrected to normal using \log_{10} transformation, they were dichotomized using a median split procedure.

Five cognitive composites were derived: Episodic Memory, Executive Function, Attention, Language and Global Cognition

Latent growth curve models were conducted to evaluate the relation between baseline plasma cortisol and A β levels, other risk factors, and cognitive composite scores over the 72-month study period.

Results

High plasma cortisol levels were associated with greater decline in global cognition, episodic memory, and attention over a 54-month period. These results suggest that therapies targeted toward lowering plasma cortisol and A β levels may help mitigate cognitive decline in the preclinical phase of AD.

Older adults, high plasma cortisol levels are associated with greater decline in global cognition, and accelerate the effect of A β on decline in global cognition, episodic memory, and attention over a 54-month period.

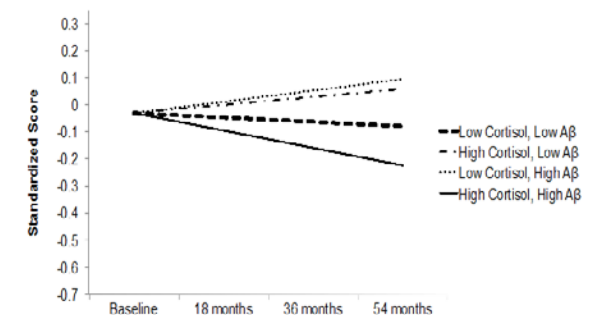
AIBL is a large collaborative study and a complete list of contributors can be found at our website www.aibl.csiro.au.

Simon M Laws^{3,4}, Yen Ying Lim⁵, Sophie J Bender⁶, Tenielle Porter^{3,4}, James Doecke⁷, David Ames^{8,9}, Christopher Fowler⁵, Colin L Masters⁵, Lidija Milicic⁴, Stephanie Rainey-Smith⁴, Victor L Villemagne^{5,10,11}, Christopher C Rowe^{10,11}, Ralph N Martins^{4,12}, & Paul Maruff^{5,13} for the AIBL Research Group

Table 1: Demographic & clinical characteristics

	A β - low cortisol	A β - high cortisol	A β + low cortisol	A β + high cortisol	p
N	158	162	50	46	
Age	69.3 (6.6)	67.9 (6.4)	68.5 (5.5)	73.3 (7.9)	< .001
N (%) Female	86 (54.4%)	92 (56.8%)	24 (48.0%)	28 (60.9%)	.60
N (%) APOE ϵ 4	38 (24.1%)	26 (16.0%)	26 (52.0%)	25 (54.3%)	< .001
Premorbid IQ	107.9 (7.6)	108.5 (6.5)	110.5 (6.6)	109.4 (7.6)	.12
MAC-Q	25.2 (4.3)	25.2 (4.5)	25.5 (5.4)	26.3 (4.8)	.63
HADS depression	2.6 (2.2)	2.6 (2.2)	2.8 (2.9)	2.6 (2.5)	.97
HADS anxiety	4.3 (2.8)	4.3 (2.9)	4.2 (3.0)	4.5 (2.8)	.93
Plasma cortisol	99.2 (25.4)	191.4 (54.2)	91.0 (31.3)	187.8 (47.4)	< .001

for accounting for baseline, for each outcome measure



Summary

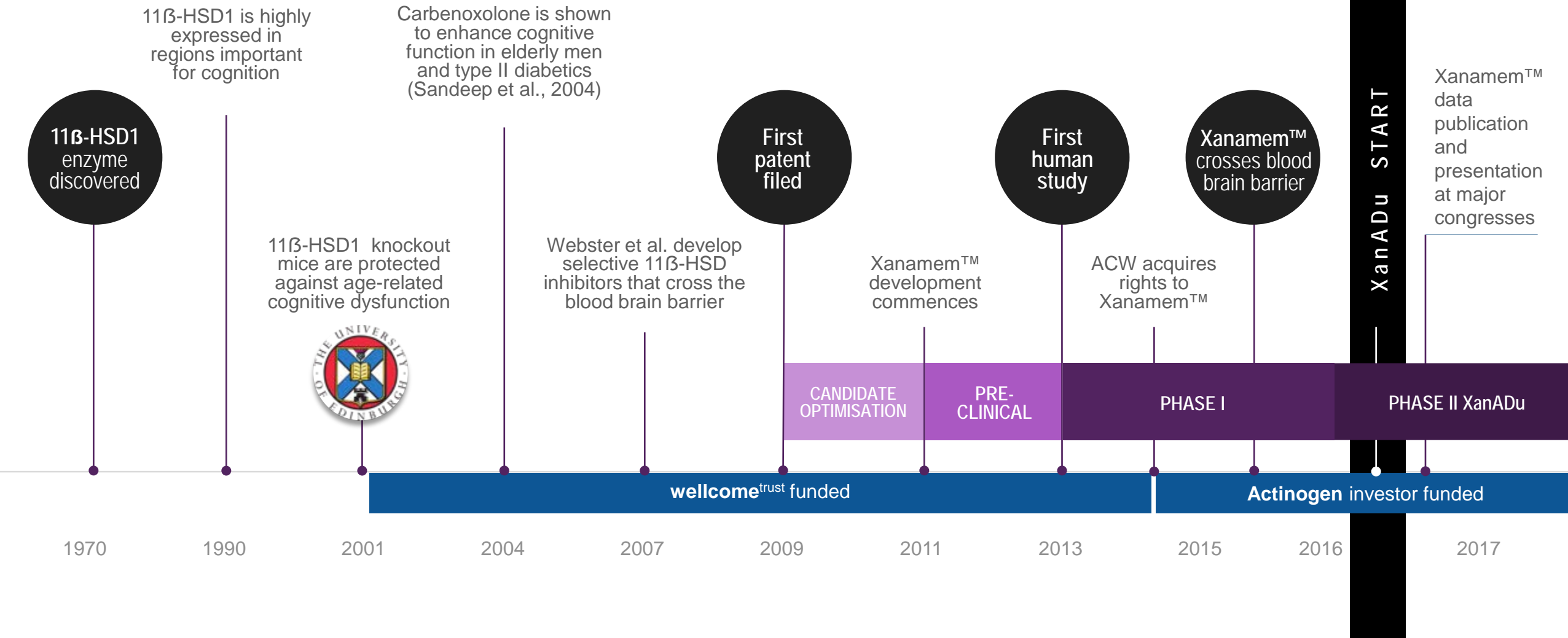
In cognitively healthy older adults, high plasma cortisol levels are associated with greater decline in global cognition, and accelerate the effect of A β on decline in global cognition, episodic memory, and attention over a 54-month period. These results suggest that therapies targeted toward lowering plasma cortisol and A β levels may help mitigate cognitive decline in the preclinical phase of AD.

Acknowledgements AIBL is a large collaborative study and a complete list of contributors can be found at our website www.aibl.csiro.au. We thank all who took part in the study. This research is supported by the Science and Industry Endowment Fund.

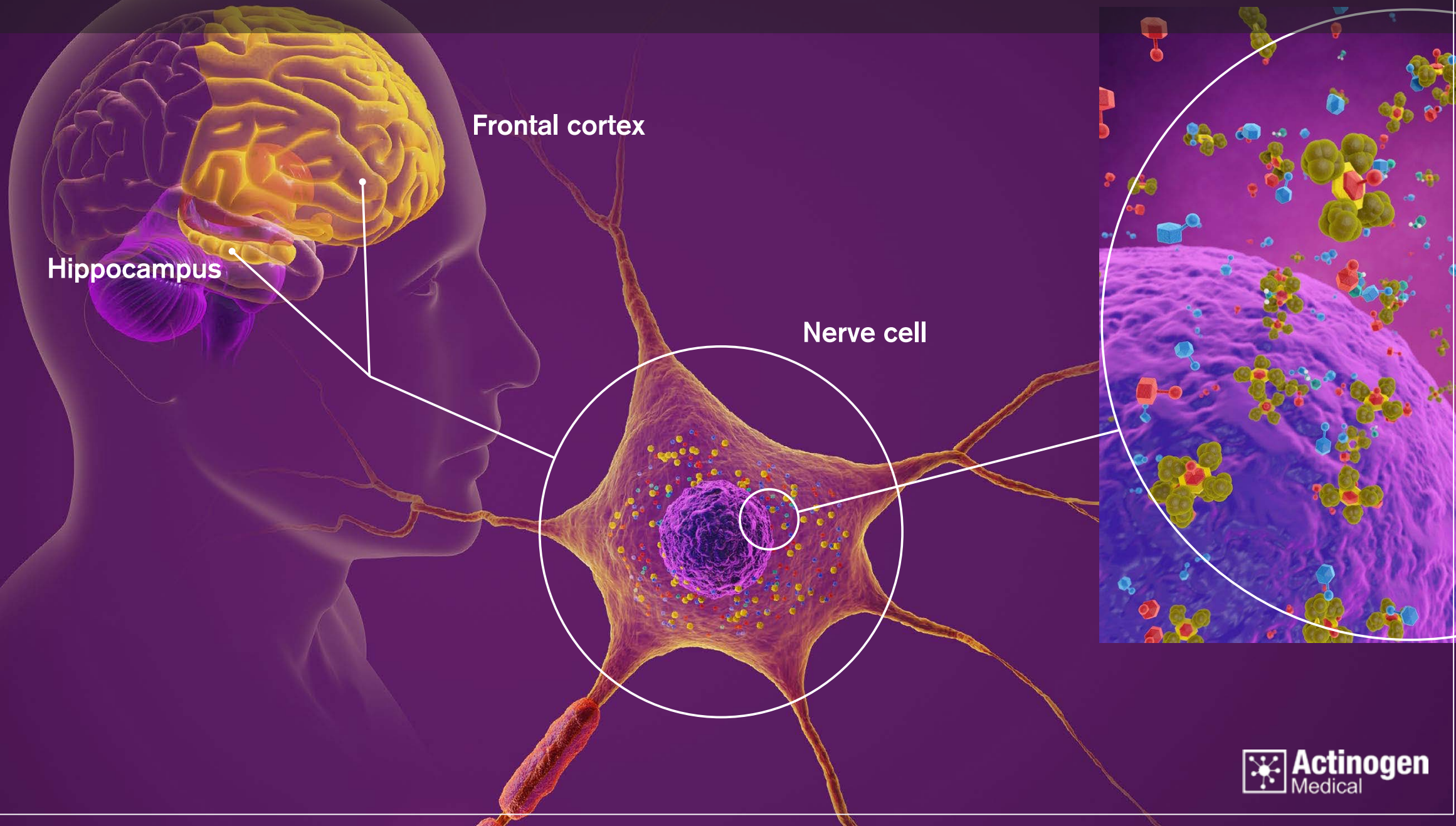
Robert H Pietrzak^{1,2}, Simon M Laws^{3,4}, Yen Ying Lim⁵, Sophie J Bender⁶, Tenielle Porter^{3,4}, James Doecke⁷, David Ames^{8,9}, Christopher Fowler⁵, Colin L Masters⁵, Lidija Milicic⁴, Stephanie Rainey-Smith⁴, Victor L Villemagne^{5,10,11}, Christopher C Rowe^{10,11}, Ralph N Martins^{4,12}, & Paul Maruff^{5,13} for the AIBL Research Group

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ACTINOGEN'S JOURNEY OF DISCOVERY

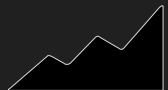
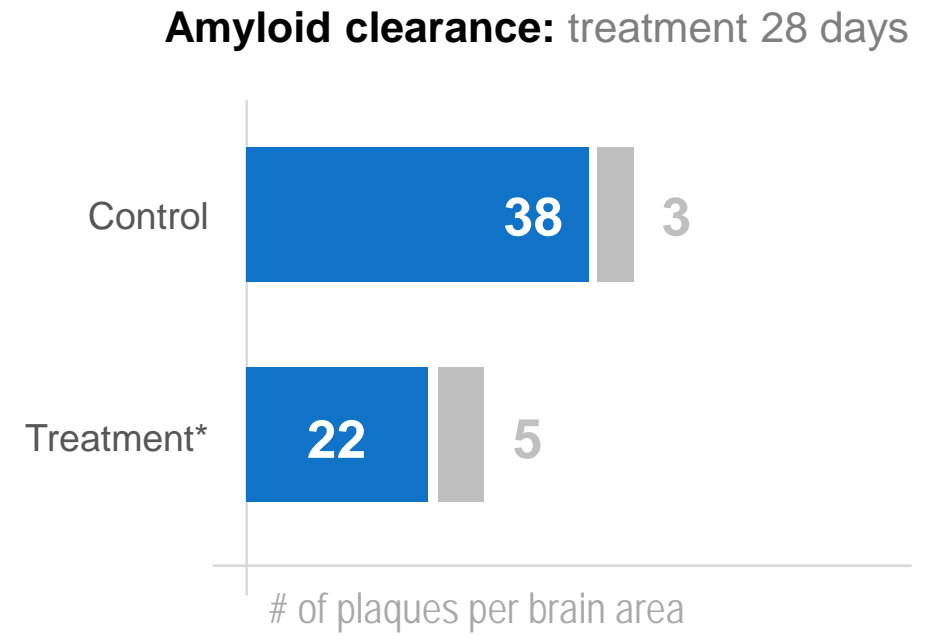
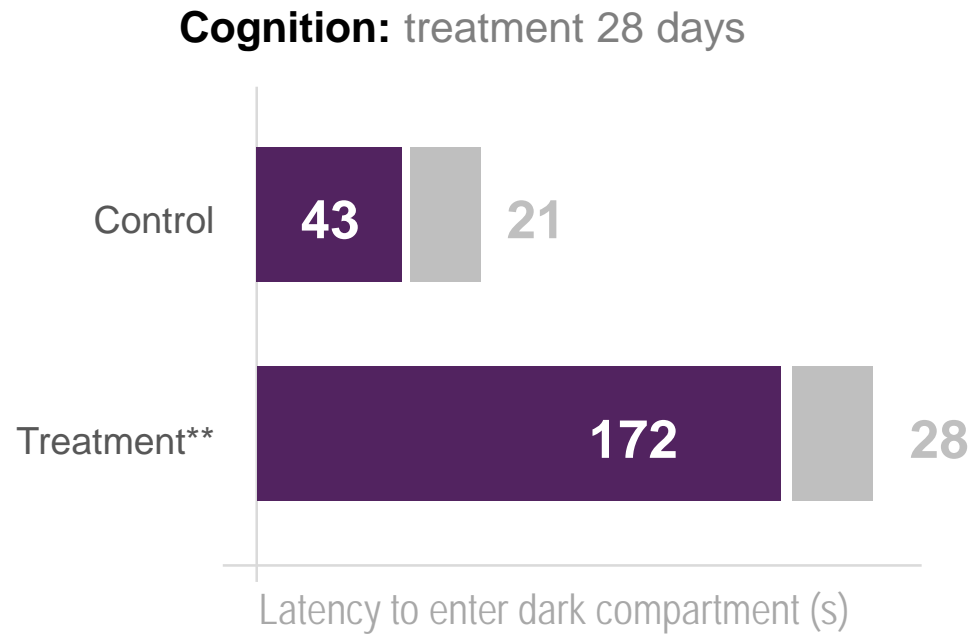


Xanamem™: TARGETING ELEVATED CORTISOL AT THE SITE OF ACTION



Xanamem™

Symptomatic and disease modifying effects in mouse models



Significant improvement in cognition after only 28 days treatment, which continues out to 41 weeks.

Xanamem™ DEVELOPMENT:

proposed study design*

XanADu – Phase II double blind,
randomised, placebo-controlled
study to assess the efficacy of Xanamem™
in participants with mild Alzheimer's disease

The largest global Alzheimer's study ever run by an
Australian biotech company^a

Treatment course
12 weeks

174
Mild Alzheimer's patients

Initiate XanADu at 10mg daily for 12
weeks Vs placebo. Plan to increase
dose to 30mg daily for 12 weeks.

Trial run in
**AUS, USA
and UK**

Co-primary end points
**ADAS-Cog +
ADCOMS**

**Secondary
end-points**
Multiple: MMSE
CDR-sob, RAVLT, NTB, NPI

OUTLOOK



Financial

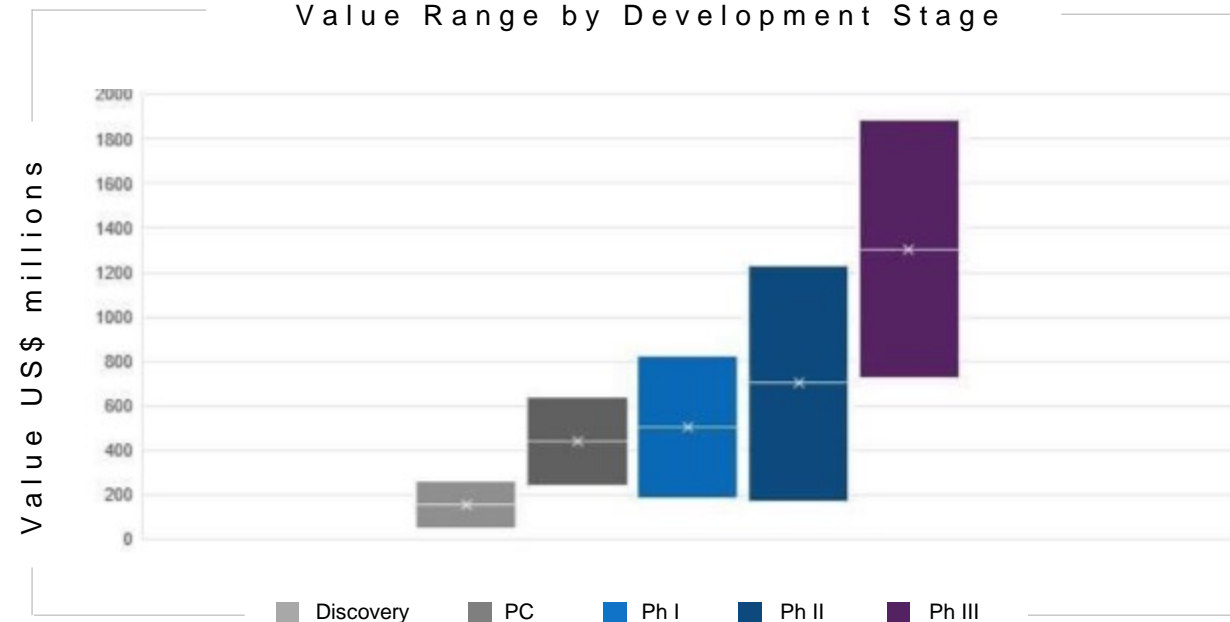
- Cash on hand (4C - Sept 2016): \$6.6m
- Positive cashflow through to 2018
- Additional potential revenue:
 - R&D rebate
 - EMDG
 - Other non-dilutive capital sources
- XanADu budget estimate: TBD
- Current market cap. Vs peers



Strategic Focus

- Research - Phase II
 - XanADu – mild AD
 - Diabetes cognitive impairment
- Business development
 - Being “partner ready”
 - Partnering Actinogen beyond Phase II
 - Publicising Actinogen and Xanamem

Value Range by Development Stage



OUTLOOK

ACTINOGEN and Xanamem™ – on the world stage



AAIC (Alzheimer's Association International Congress)
Xanamem and AIBL posters



ICE (International Congress of Endocrinology)
Oral presentation (Walker)



MMC (Mastering Medicinal Chemistry)
Oral presentation (Webster)



CTAD (Clinical Trials in Alzheimer's disease)
Oral presentation (Ritchie)



British Journal of Pharmacology
Webster publication



Biological Psychiatry: Cognitive Neuroscience and Neuroimaging
AIBL publication

OUTLOOK



Xanamem™'s innovative, differentiated mechanism of action – reinforced by the literature and KOLs



Patent protected to 2031 – composition of matter



Excellent progress with research planning and regulatory approval



XanADu and DCI patient recruitment initiated 2017 with results in 2 years



Actinogens secure financial position



Experienced Board and Management



Alzheimer's - significant unmet medical need in a huge and growing global market

The background of the slide features a detailed illustration of a neural network. A central neuron is prominently displayed, with its cell body and multiple branching dendrites and axons. The axon extends towards the bottom right corner. Other neurons are visible in the background, some with glowing orange tips. A semi-transparent purple rectangular band is positioned horizontally across the middle of the image, containing a white-bordered box with the text "THANK YOU".

THANK YOU