Actinogen Medical attending BIO 2017

- Actinogen Medical presenting at BIO International Convention, the world's largest and most prestigious biotechnology convention in San Diego, this month.
- BIO International attracts the global biotech industry to network on new opportunities and partnerships.
- Ideal forum to showcase Actinogen Medical and Xanamem, including the successful initiation of our XanADu Alzheimer's Disease trial and plans to initiate a second Phase II trial of Xanamem in Diabetes Cognitive Impairment.

Sydney 19 June 2017. Actinogen Medical (ASX: ACW) is pleased to announce that the Company's CEO, Dr. Bill Ketelbey, is leading the Actinogen team and presenting at the BIO International Convention in San Diego in June 2017. This follows the successful initiation of XanADu, its Phase II trial of Xanamem in Alzheimer's Disease, and the progress made towards the commencement of a second Phase II trial of Xanamem in Diabetes Cognitive Impairment.

The BIO International Convention, hosted by the Biotechnology Innovation Organisation (BIO), is the largest global convention for the biotechnology industry and attracts the biggest and best organisations in biotech to network on new opportunities and potential partnerships. Participation at BIO offers Actinogen Medical unparalleled networking opportunities to showcase Xanamem and the quality research that supports its development.

The BIO presentation is attached.

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$2 trillion 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 with the identifier: NCT02727699.

Xanamem™ for Alzheimer's Disease

Dr Bill Ketelbey, CEO, Actinogen Medical

BIO International Convention, June 2017

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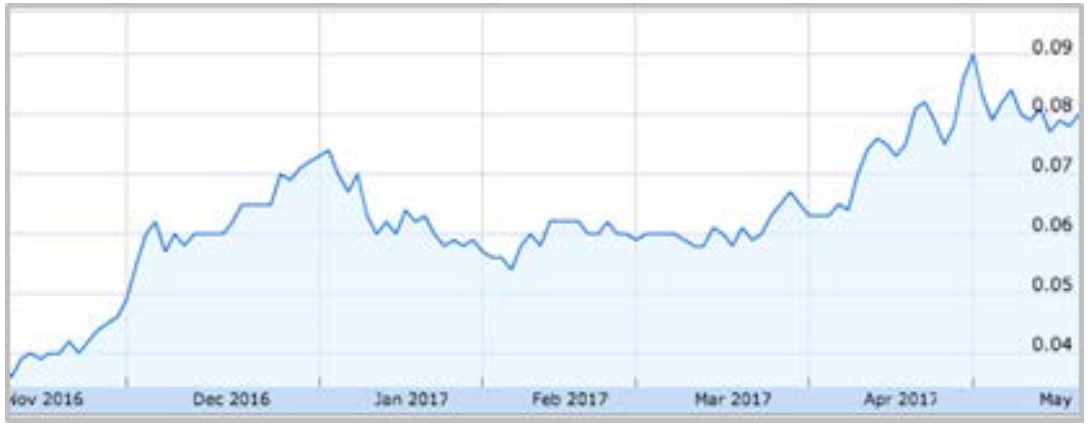
ACTINOGEN MEDICAL

- Headquartered in Sydney, Australia
- Globally focused development and commercial strategy
- Dedicated board and management; expert scientific advisory board
- Targeting Alzheimer's disease (AD) and cognitive impairment in chronic neurodegenerative diseases
- Xanamem™, a first in class, brain penetrant 11βHSD1 inhibitor:
  - ➢ for AD, diabetes cognitive impairment (DCI) and other indications associated with cognitive decline

STOCK METRICS*



ASX CODE	ACW
Market Capitalisation	$49.6m
Enterprise Value	$44.4m
52-week High/Low	$0.04-$0.10
Top 20 Shareholdings	55%

*Data as at 15 May 2017

COMMERCIALLY EXPERIENCED, GLOBALLY RECOGNISED

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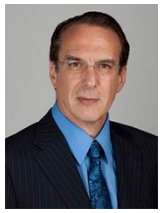


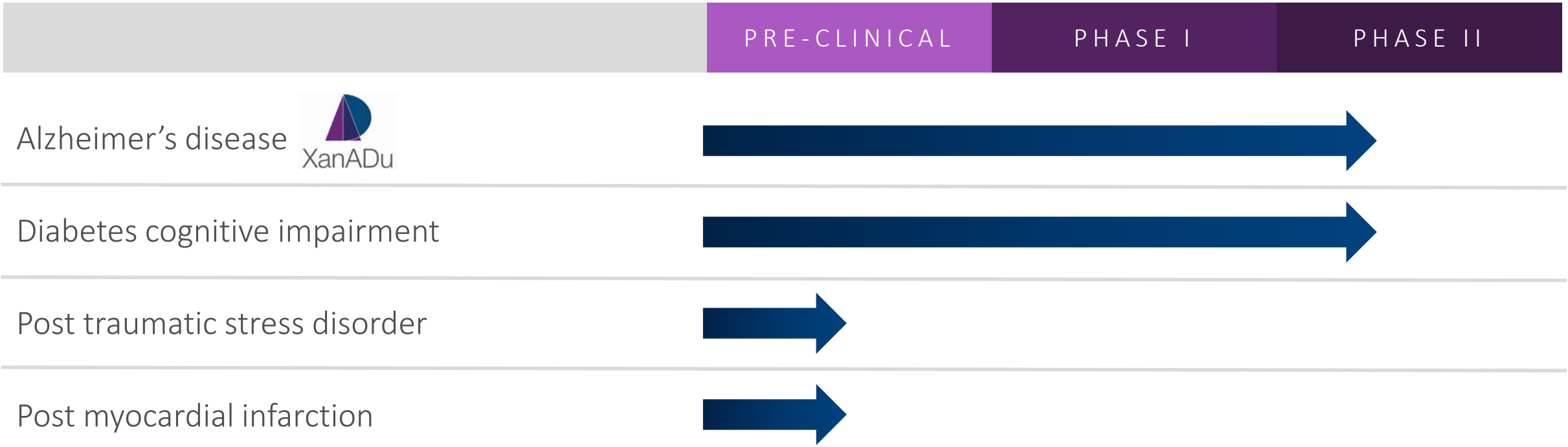
Professor Jeffrey Cummings

Cleveland Clinic

XANAMEM™

- **A novel, first in class, potent, orally bioavailable, brain-penetrant, 11βHSD1 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
- Phase II study commencing soon in **Diabetes Cognitive Impairment**
- **Composition of matter IP coverage ≥ 2031**

XANAMEM™ DEVELOPMENT INDICATIONS



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CORTISOL: A VALIDATED BIOMARKER AND TARGET FOR AD

Elevated plasma cortisol levels are associated with:

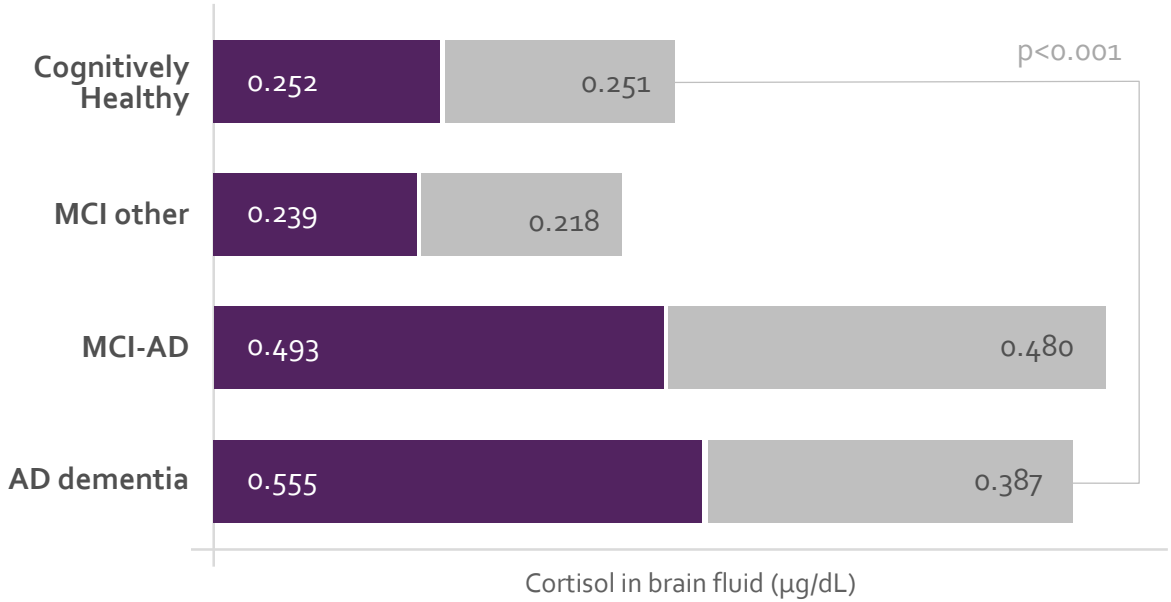
- Greater decline in global cognition
- **Accelerated effect of Aβ+** on decline in global cognition, episodic memory, and attention

(>1100 healthy elderly subjects prospectively followed for 54 months [1])

aibl
The Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing

- **Cognitive impairment** in patients with neuroendocrine dysfunction [2-5]
- **Accelerated disease progression** in AD patients [6]

Brain cortisol and Alzheimer's disease [6]



MCI-AD = MCI of Alzheimer's type
MCI-Oother = MCI of other type

[1] Pietrzak *et al.*, 2017, Biol Psychiatry: Cognitive Neuroscience and Neuroimagery, 2:45-52; [2] Lupien *et al.*, 2009, Nat Rev Neurosci 10:434–445; [3] Starkman *et al.*, 1999, Biol Psychiatry 46:1595–1602; [4] Lupien *et al.*, 1998, Nat Neurosci 1:69–73; [5] MacLullich *et al.*, 2005, Psychoneuroendocrinology 30:505–515; [6] Popp *et al.*, 2015, Neurobiol Aging 36:601–607.

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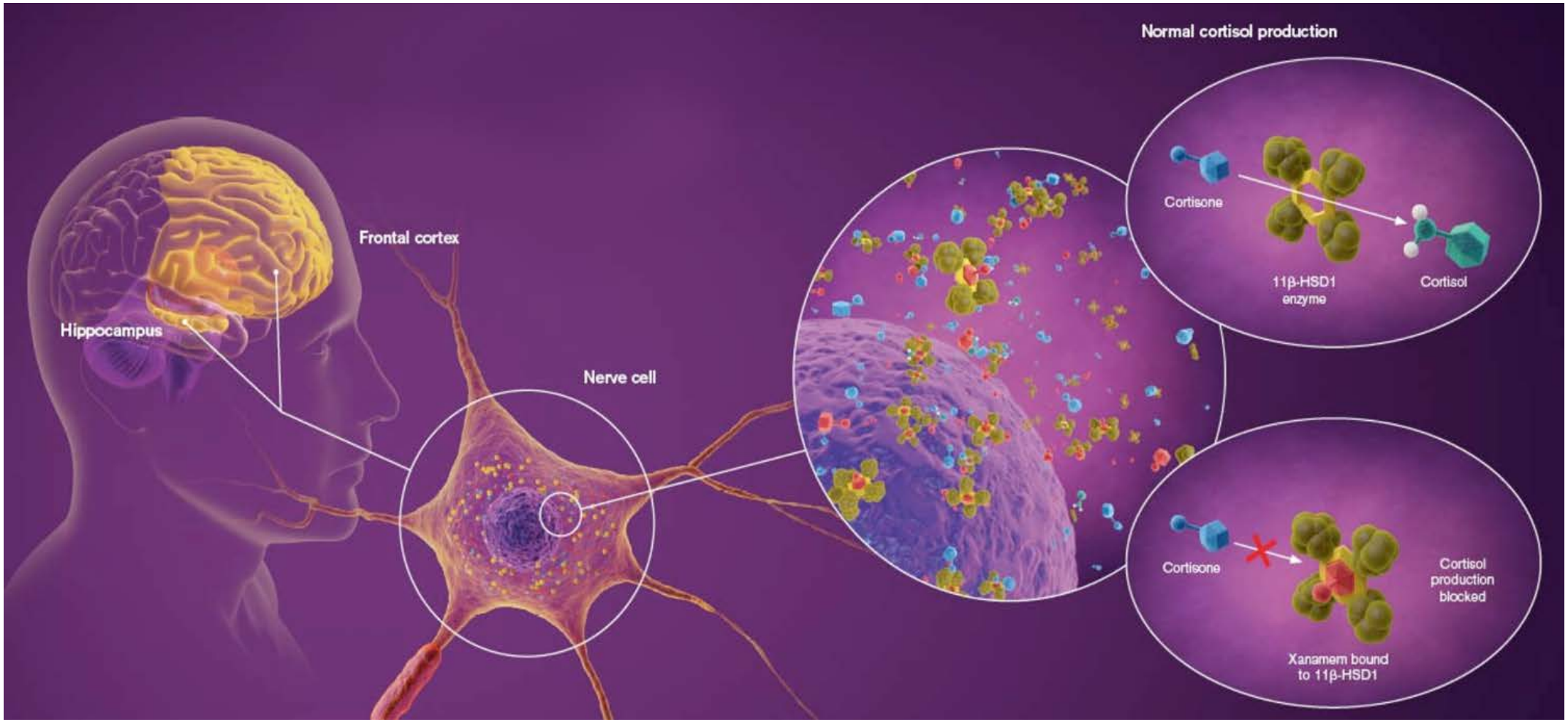
MECHANISM OF ACTION

Xanamem™ binds to 11βHSD1, reducing brain cortisol production



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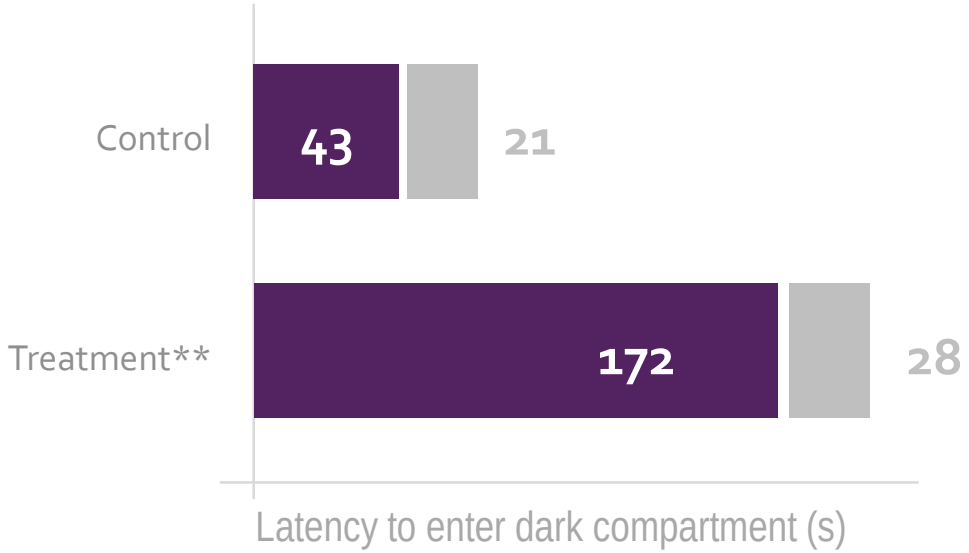
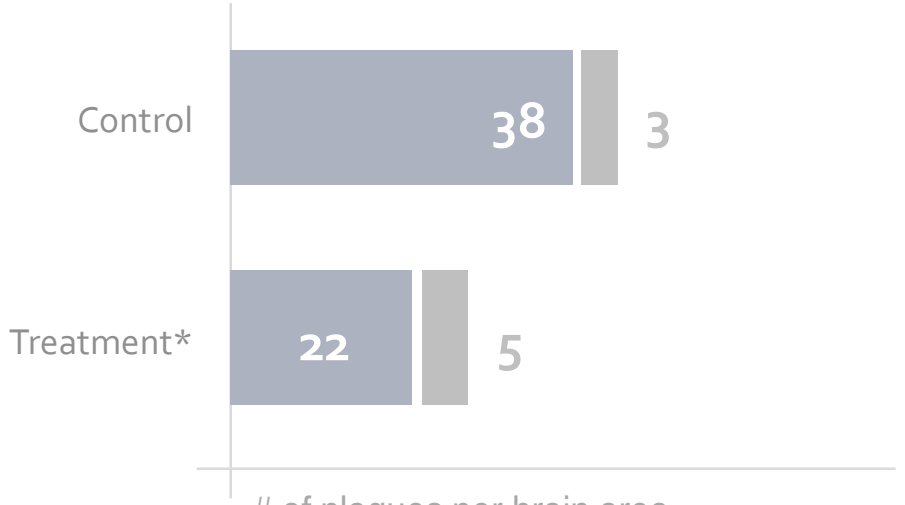
Symptomatic and disease modifying effects in mouse models

Cognition: treatment 28 days



Amyloid clearance: treatment 28 days



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

UE 2316 The mean plus the SEM. ** = P< 0.004, * = P<0.01 Tg2576 rodent model of Alzheimer's disease.
Source: Sooy *et al.*, 2015. Endocrinology 156(12):4592-4603.

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CLINICAL DEVELOPMENT

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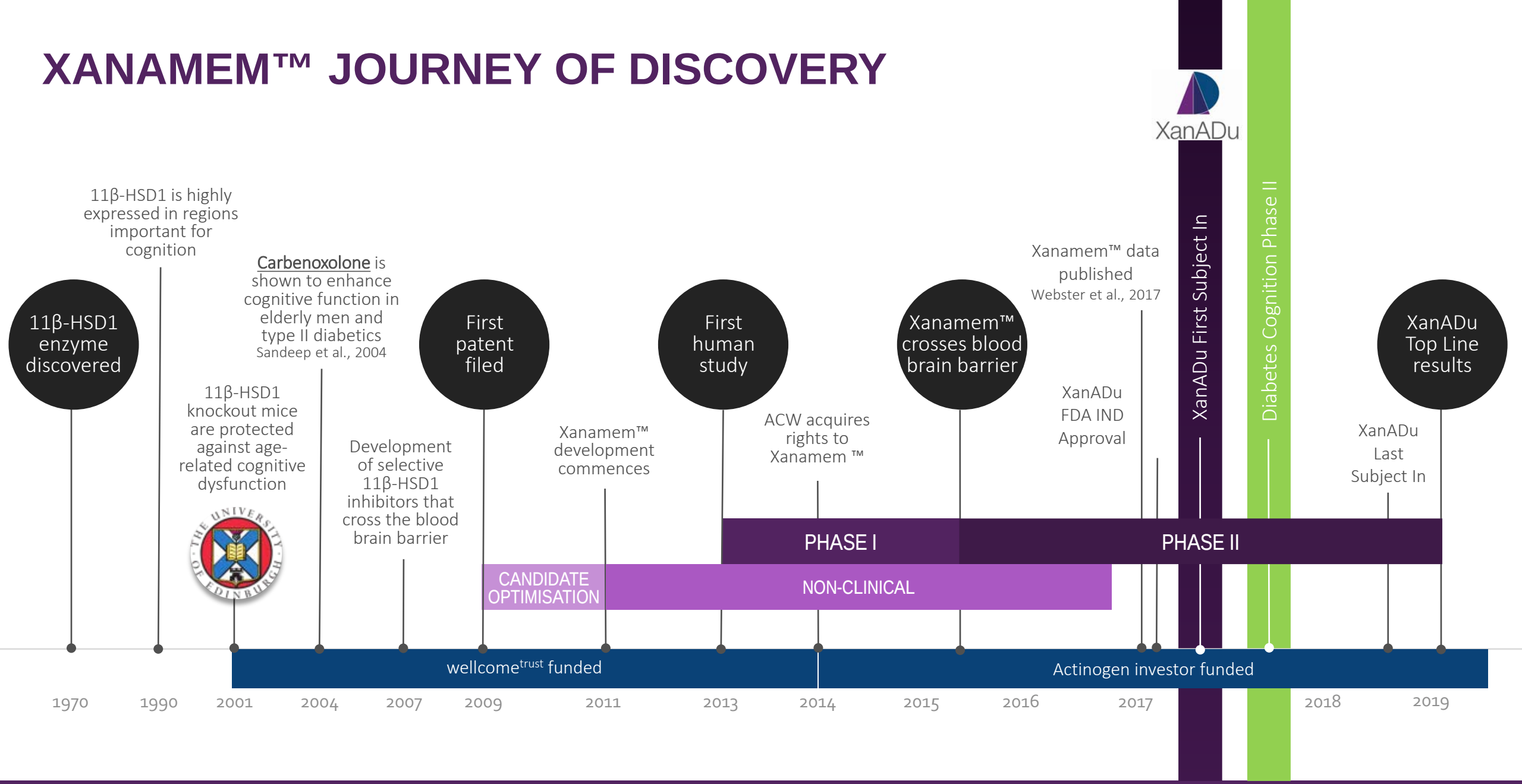
XANAMEM™ JOURNEY OF DISCOVERY



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XANAMEM™ COMPLETED CLINICAL STUDIES

(Building on extensive historic 11βHSD1 class safety data from metabolic disease focus)

- A phase I single ascending dose (SAD) study[1]
  - 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[1]
  - 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[1]
  - Xanamem **readily achieves CSF concentrations higher than its IC_{50}** (4 healthy males)
  - TEAEs mild to moderate in intensity.

[1] Webster *et al.*, 2017, British J Pharmacol 174:396-408;

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*

- First patient in 15th May 2017, recruitment ongoing to plan
- Top line results 2019

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

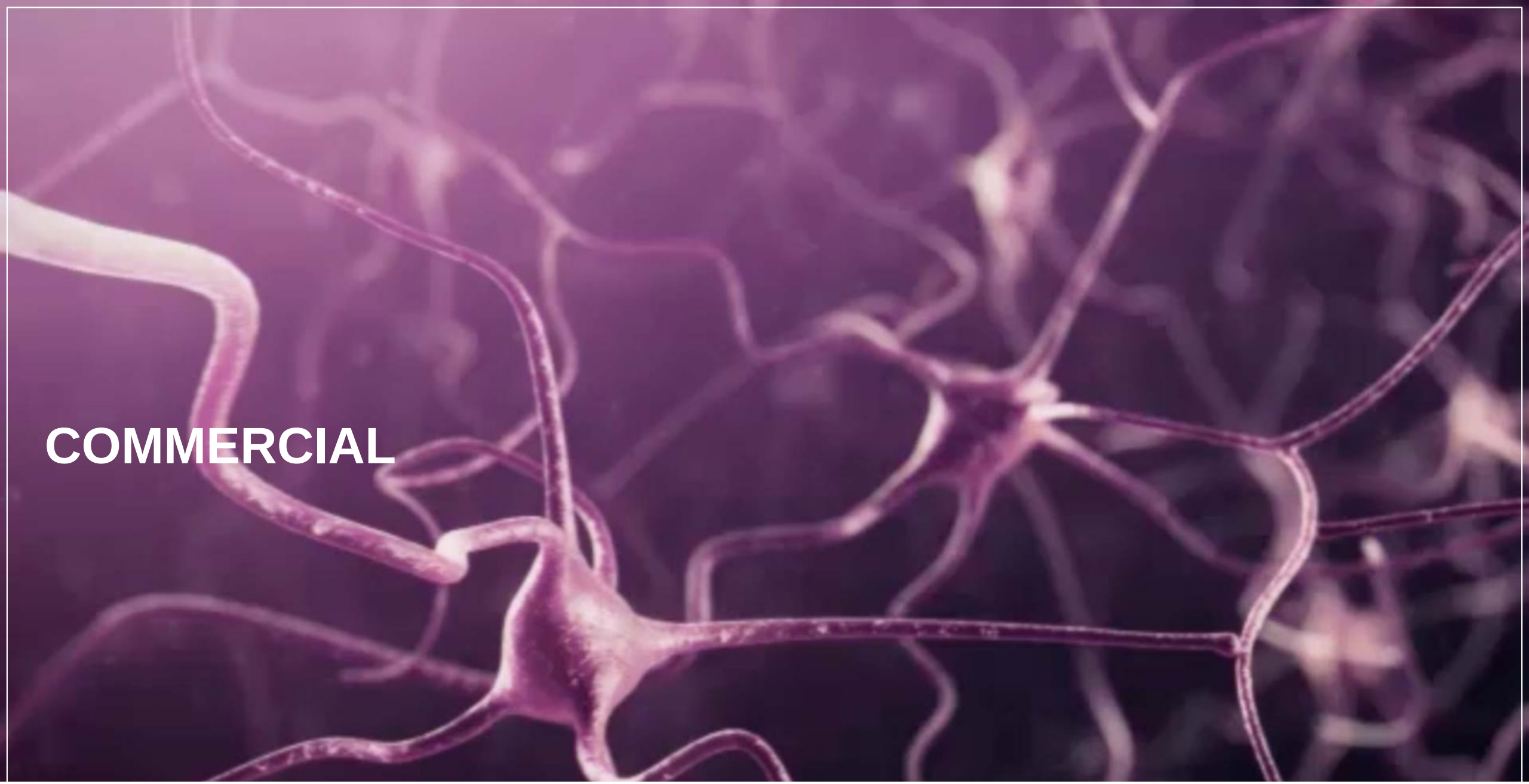
*Registered on Clinicaltrials.gov: NCT02727699

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** [1-4]
  - T2DM patients are more likely to show abnormalities in hypothalamic–pituitary adrenal (HPA) axis regulation [5]
  - Non-selective 11βHSD1 inhibitor **carbenoxolone demonstrated cognitive improvements in cognitively normal patients with T2DM** [6]
  - Large potential patient population, **>15M diabetes patients with dementia**
  - Expert clinical development partner (University of Edinburgh, UK)
  - Planning on track for **commencement in 2017**

[1] Saedi *et al.*, 2016, World J Diabetes 7(17):412-422; [2] Whitmer *et al.*, 2009, JAMA 301(15):1565-1572; [3] Saczynski *et al.*, 2008, Am J Epidemiology 168(10):1132–1139;
[4] Cukieman-Yaffe *et al.*, 2009, Diabetes Care 32(2):221-226; [5] Fienkohl *et al.*, 2015, Alzheimer's Research and Therapy 7:46; [6] Sandeep *et al.*, 2004, Proc Natl Acad Sci USA 101:6734–6739.



COMMERCIAL

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VALUE PROPOSITION

- Strong therapeutic rationale, differentiated mechanism of action
- Complementary to anti-Aβ, anti-Tau and other AD therapeutic strategies
- Solid non-clinical and clinical data set
- First in class compound, designed for brain penetration
- 11βHSD1 class safety data
- Positive dialogue with regulatory agencies
- Significant opportunities in AD and DCI; positive outcomes to broaden indications
- Deep commercial, scientific and clinical expertise
- Strong commercial and clinical interest

INTELLECTUAL PROPERTY

- Broad suite of intellectual property
- 7 granted and pending composition of matter patent families
- Global coverage to at least 2031
- Opportunities for new chemical entity market and data regulatory exclusivities
- Granted Xanamem™ trademark

COMMERCIAL STRATEGY

- Adding value through proof of concept XanADu and DCI trials
- Pursuing partnering for post phase II development and commercialisation
- Opportunistic on deal structures

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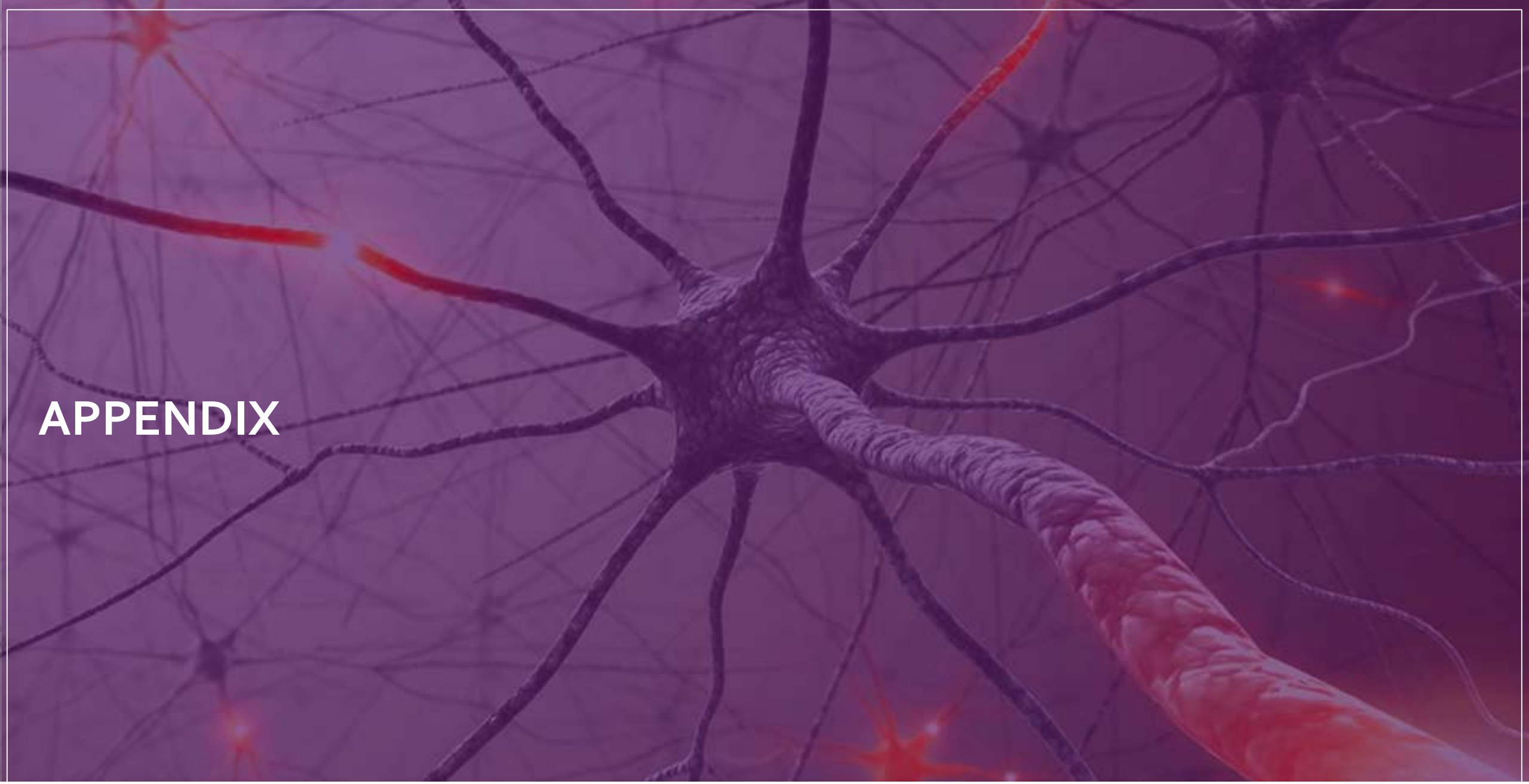

APPENDIX

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XANAMEM™ BRAIN PENETRANCE

- Substantial data package supporting brain penetrance [1]
- In the Phase I studies, CNS access was assessed by determining plasma Cmax in the CSF
- CSF concentrations ranged from 7.46 to 11.9% of total plasma levels and 25 to 40% of free plasma levels, indicating moderate brain penetration
- Data were consistent with rat preclinical studies where UE2316 (Xanamem analog) levels in brain were 43% of the free plasma concentration
- 10mg daily dosing CSF concentrations expected to be safe and efficacious
- Sub-maximal inhibition of 11β-HSD1 in the brain in rodent studies is sufficient to reverse memory impairments in aging and Alzheimer's disease [2,3]

[1] Webster *et al.*, 2017, British J Pharmacol 174:396-408; [2] Sooy *et al.*, 2010, J Neurosci 30:13867–13872; [3] Sooy *et al.*, 2015, Endocrinology 156: 4592–4603.

A SIMPLE BUT COMPELLING STORY

1	2	3	4	5
Xanamem™ - a novel therapy for Alzheimer's disease that reduces cortisol (stress hormone) production in the brain.	Independent research shows a strong association between excess cortisol in the brain and Alzheimer's disease.	Human trial of cortisol inhibition in the brain demonstrates cognitive improvement in the elderly.[1]	Xanamem™ demonstrated a significant improvement in cognition in a mouse model of AD after only 28 days treatment, which continued out to 41 weeks.[2]	Phase I human trials confirm that Xanamem™ successfully crosses the blood-brain barrier and is safe for use in humans.[3]

[1] Sandeep *et al.*, 2004, Proc Natl Acad Sci USA 101:6734–6739; [2] Sooy *et al.*, 2015. Endocrinology 156(12):4592-4603;
[3] Webster *et al.*, 2017, British J Pharmacol 174:396-408.

VALIDATION

CORTISOL and ALZHEIMER'S:

- Recent Independent studies support the association between **cortisol and the development and progression of Alzheimer's disease**.[1-5]

- Compelling evidence provided by the Australian Imaging, Biomarker & Lifestyle Study of Ageing (AIBL) study (2017).
    - Followed 416 healthy elderly Australians over nearly six years.
    - **Conclusions: subjects with higher blood cortisol have much greater chance of developing AD.** [5]

Archival Report

Biological Psychiatry: CNNI

Plasma Cortisol, Brain Amyloid-β, and Cognitive Decline in Preclinical Alzheimer's Disease: A 6-Year Prospective Cohort Study

Robert H. Pietrzak, Simon M. Laws, Yen Ying Lim, Sophie J. Bender, Tenielle Porter, James Doecke, David Ames, Christopher Fowler, Colin L. Masters, Lidija Milicic, Stephanie Rainey-Smith, Victor L. Villemagne, Christopher C. Rowe, Ralph N. Martins, and Paul Maruff, for the Australian Imaging, Biomarkers and Lifestyle Research Group

ABSTRACT

BACKGROUND: Hypothalamic-pituitary-adrenal 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's disease (AD). However, little is known about the role of hypothalamic-pituitary-adrenal axis dysregulation in moderating the effect of high levels of amyloid-β (Aβ+) on cognitive decline in the preclinical phase of AD, which is often protracted, and thus offers opportunities for prevention and early intervention.

BJP British Journal of Pharmacology

British Journal of Pharmacology (2017) •• ••–•• 1

RESEARCH PAPER

Selection and early clinical evaluation of the brain-penetrant 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) inhibitor UE2343 (Xanamem™)

Correspondence Scott P Webster, Centre for Cardiovascular Science, University of Edinburgh, Queen's Medical Research Institute, 47 Little France Crescent, Edinburgh EH16 4TJ, UK. E-mail: scott.webster@ed.ac.uk

Received 23 August 2016; Revised 21 November 2016; Accepted 15 December 2016

Scott P Webster[1], Andrew McBride[1], Margaret Binnie[1], Karen Sooy[1], Jonathan R Seckl[1], Ruth Andrew[1], T David Pallin[2], Hazel J Hunt[3], Trevor R Perrior[4], Vincent S Ruffles[5], J William Ketelbey[5], Alan Boyd[6] and Brian R Walker[1]

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.[6,7]

[1] Geerlings *et al.,* 2015, Neurology 85: 1-8; [2] Lehallier *et al*., 2015, JAMA Neurology 14:1-10; [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 Neuroimagery, 2:45-52; [6] Sooy *et al*., 2015. Endocrinology 156(12):4592-4603; [7] Webster *et al.*, 2017, British J Pharmacol 174:396-408.

INVESTMENT SUMMARY

Huge unmet medical need: The total cost of Alzheimer's to rise to $US 1 trillion by 2020 and there are currently only four drugs approved to treat the symptoms of Alzheimer's disease. None significantly alters the course of the disease.

Novel approach: The association between cortisol and Alzheimer's disease is strongly supported by numerous studies, including the leading AIBL study funded by the CSIRO and various leading research institutes and universities.

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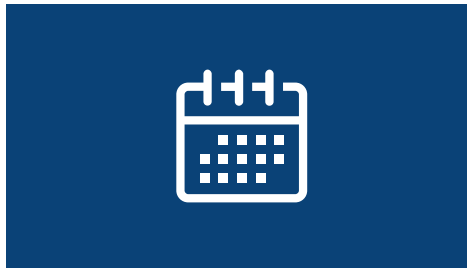
Multiple Potential Indications: Actinogen has identified a number of potential indications for Xanamem™ that substantially increases the scope of the Company's development pipeline.



Xanamem™ has a long patent life: Xanamem has composition-of-matter patent protection through to 2031 giving Actinogen a substantial window to benefit from a successful commercialisation.

Highly experienced Board and management team: Board and management have invaluable expertise in drug development, commercialisation and clinical research.