

# Developing Xanamem™

Presented by,  
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CEO & Managing Director



**Actinogen**  
Medical

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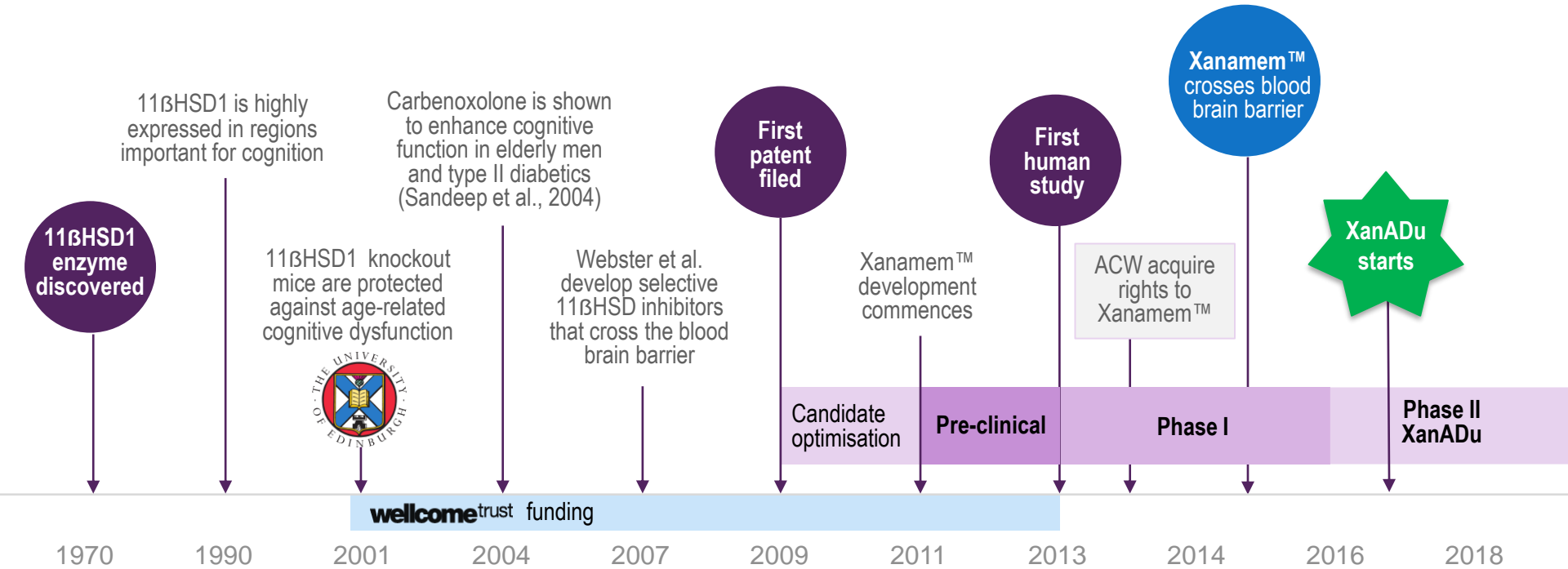
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Focusing on an innovative approach, through the inhibition of cortisol production, for treating **cognitive impairment** in chronic neurodegenerative and metabolic diseases.

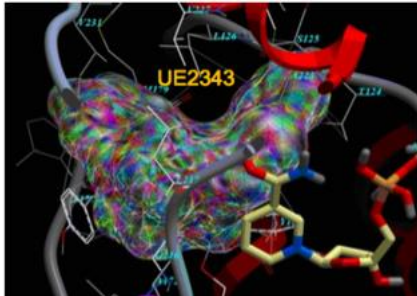
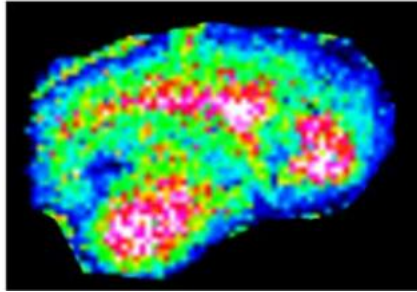
# Xanamem™: A prime investment opportunity

- Alzheimer's - a significant unmet need in a huge and growing global market
- Xanamem™'s innovative, differentiated mechanism of action targeting the stress hormone cortisol
- Evidence Xanamem™ is **both symptomatic and disease modifying**
- Phase II study **funded through to completion**
- Patent protected to 2031 – composition of matter
- Value enhancing additional indications in substantive markets of interest to big pharmaceutical companies – Alzheimer's disease, Diabetes, Parkinson's disease

# Actinogen's journey of discovery












# Xanamem™ unique value proposition



- High potency at low oral doses
- Highly selective and specific enzyme binding
- Safe and well tolerated in humans
- Delivered to the brain to target site of action
- Established proof of principle in models of Alzheimer's Disease

# Leadership Team

<p><b>Dr. Bill Ketelbey</b> CEO &amp; MD</p>	
<p><b>Martin Rogers</b> Executive Chairman</p>	  
<p><b>Dr. Jason Loveridge</b> Non-Executive Director</p>	  
<p><b>Dr. Anton Uvarov</b> Non-Executive Director</p>	 

# Clinical Advisory Board:

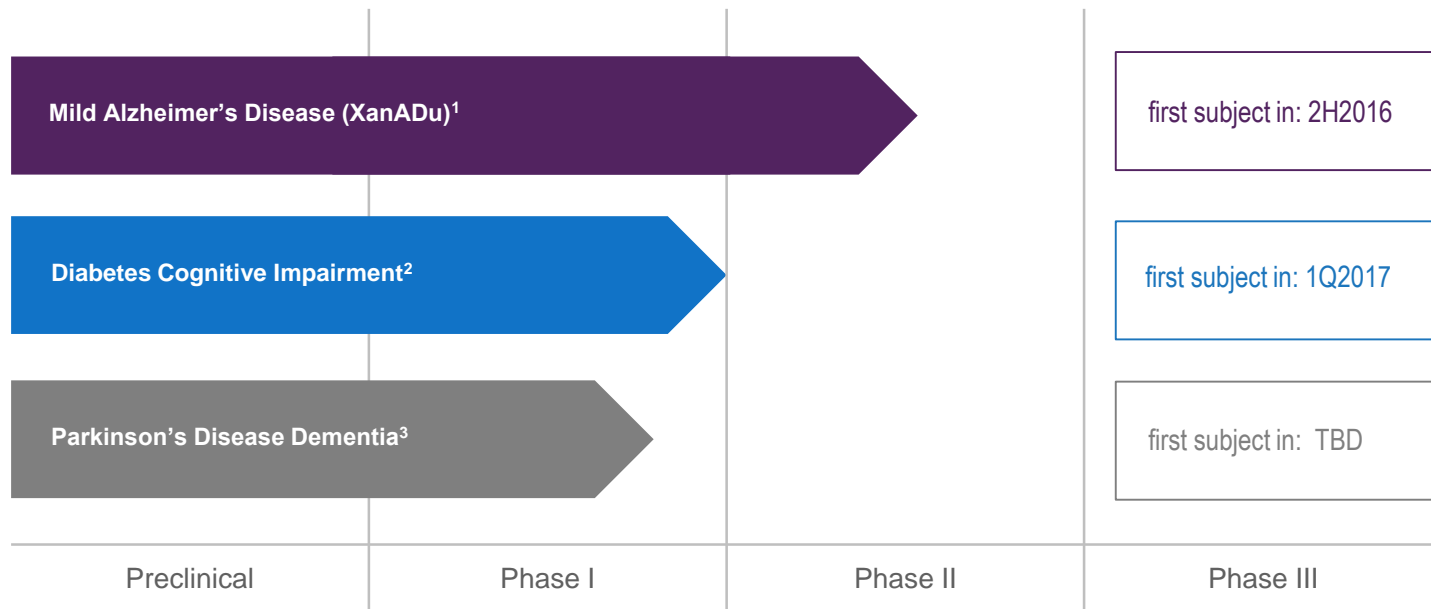
world renowned neuroscience leaders

<p><b>Professor Craig Ritchie</b> Chair, Xanamem™ Clinical Advisory Board</p>	 <p>THE UNIVERSITY <i>of</i> EDINBURGH</p>
<p><b>Professor Colin Masters</b> Xanamem™ Clinical Advisory Board</p>	 <p>THE UNIVERSITY OF MELBOURNE</p>  <p>THE FLOREY INSTITUTE OF NEUROSCIENCE &amp; MENTAL HEALTH</p>  <p>The Royal Melbourne Hospital</p>
<p><b>Professor Jeffrey Cummings</b> Xanamem™ Clinical Advisory Board</p>	 <p><b>Cleveland Clinic</b></p>



# Xanamem™ research pipeline

milestone timelines are estimates

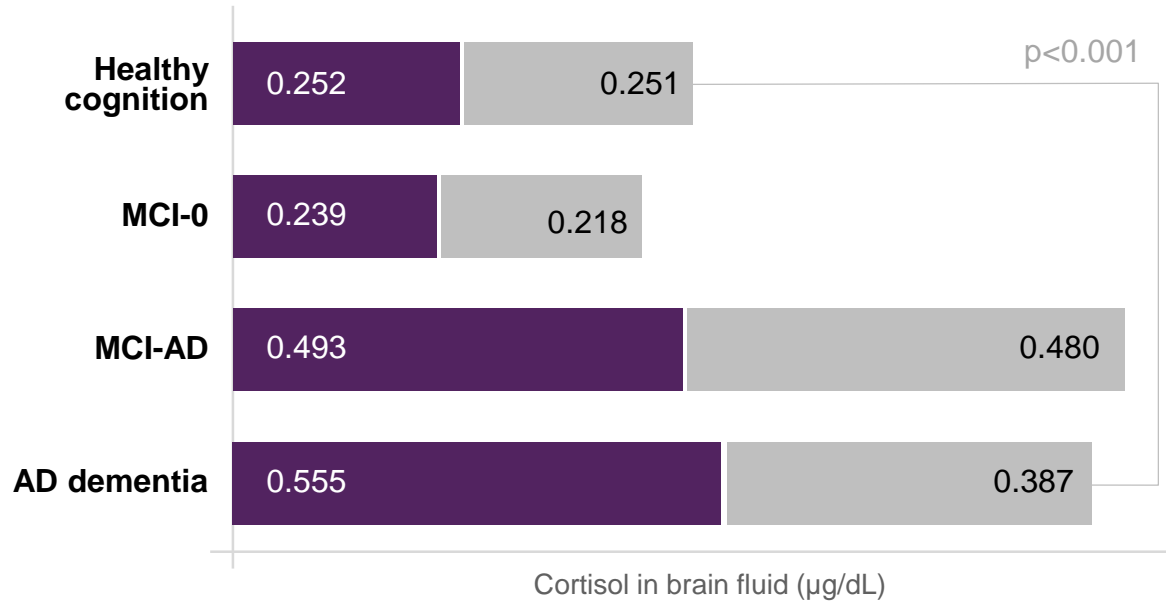


<sup>1</sup> Trial initiated 2016.

<sup>2</sup> Phase II trial design complete. Final operational planning underway. Trial expected to start late 2016.

<sup>3</sup> Planning ongoing for Phase II trial design

# Cortisol and Alzheimer's disease



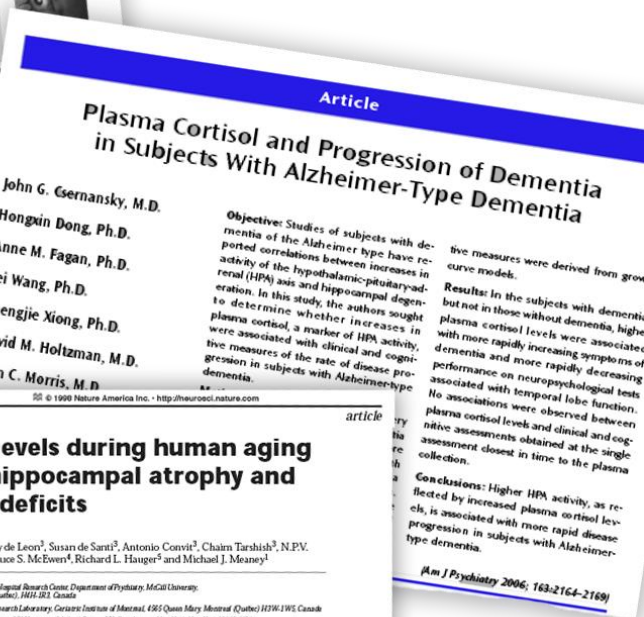
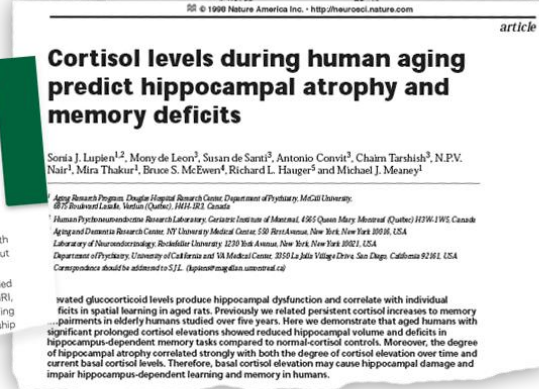
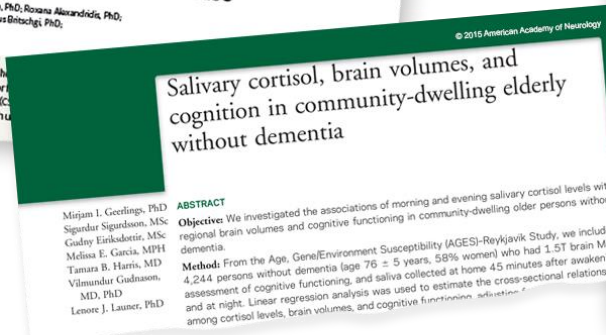
**Neuroendocrine dysfunction leading to elevated cortisol precedes disease state in AD dementia**

**Elevated cortisol was associated with progressive cognitive decline**

The transitional stage between 'normal' functional ability and a full-blown clinical picture of dementia is described as mild cognitive impairment (MCI). The term MCI refers to decrease in cognitive function, from a formerly normal level towards a mildly impaired level. (Kornhuber et al., 2009).

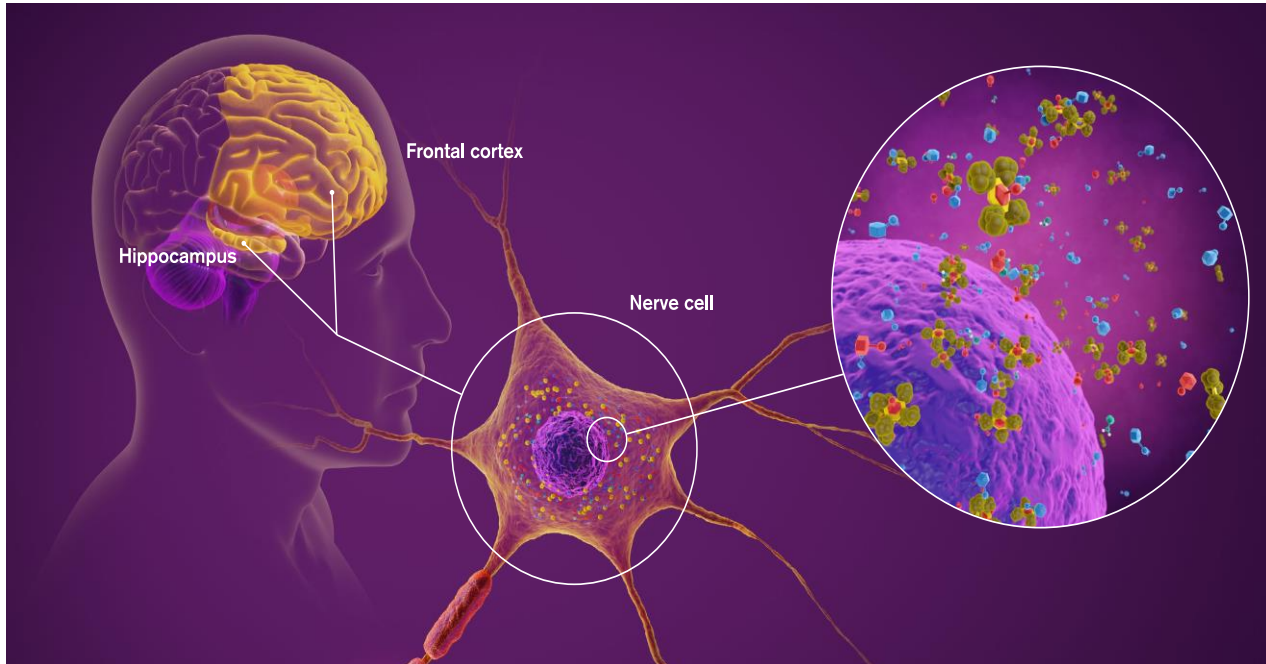
Source: Popp et al., 2015  
MCI-AD = MCI of Alzheimer's type  
MCI-O = MCI of other type

# Publications confirm links to cortisol and AD

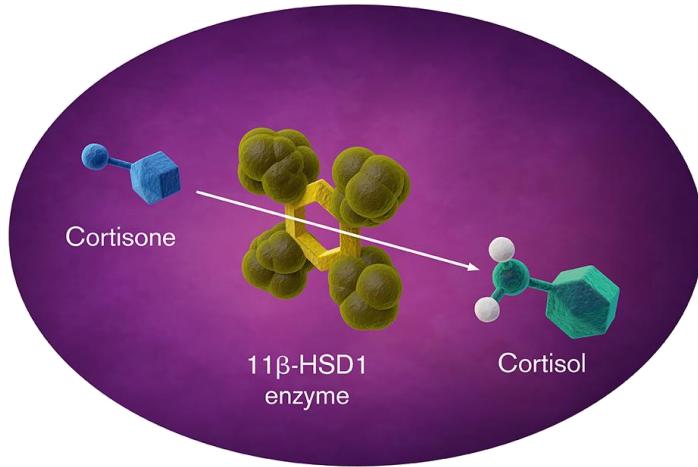


Plasma cortisol, amyloid-β, and cognitive decline in preclinical Alzheimer's disease. Pietrzak et al for the AIBL Research Group, 2016. Under review for publication.

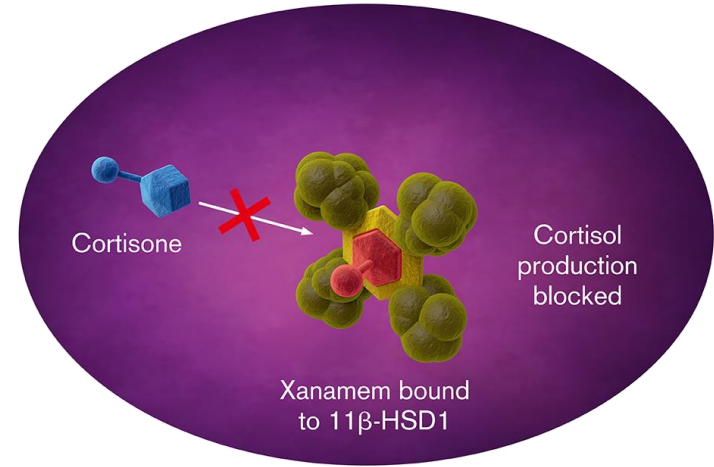
# Targeting elevated cortisol at the site of action



# Xanamem™ - inhibiting action of 11βHSD1



11βHSD1 enzyme activates  
cortisone producing cortisol

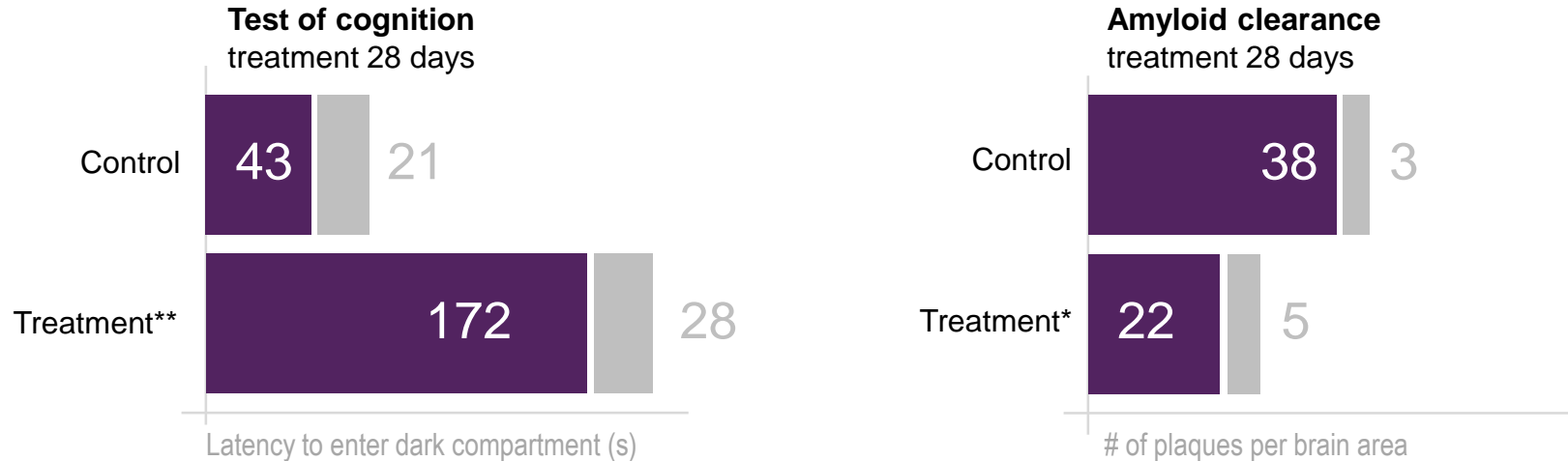


Xanamem™ binds to 11βHSD1,  
blocking cortisol production

\*11β-HSD1 =11β-hydroxysteroid dehydrogenase type 1

# Xanamem™

## Symptomatic and disease modifying effects in mouse models



Significant improvement in cognition in only 28 days treatment which continues 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.

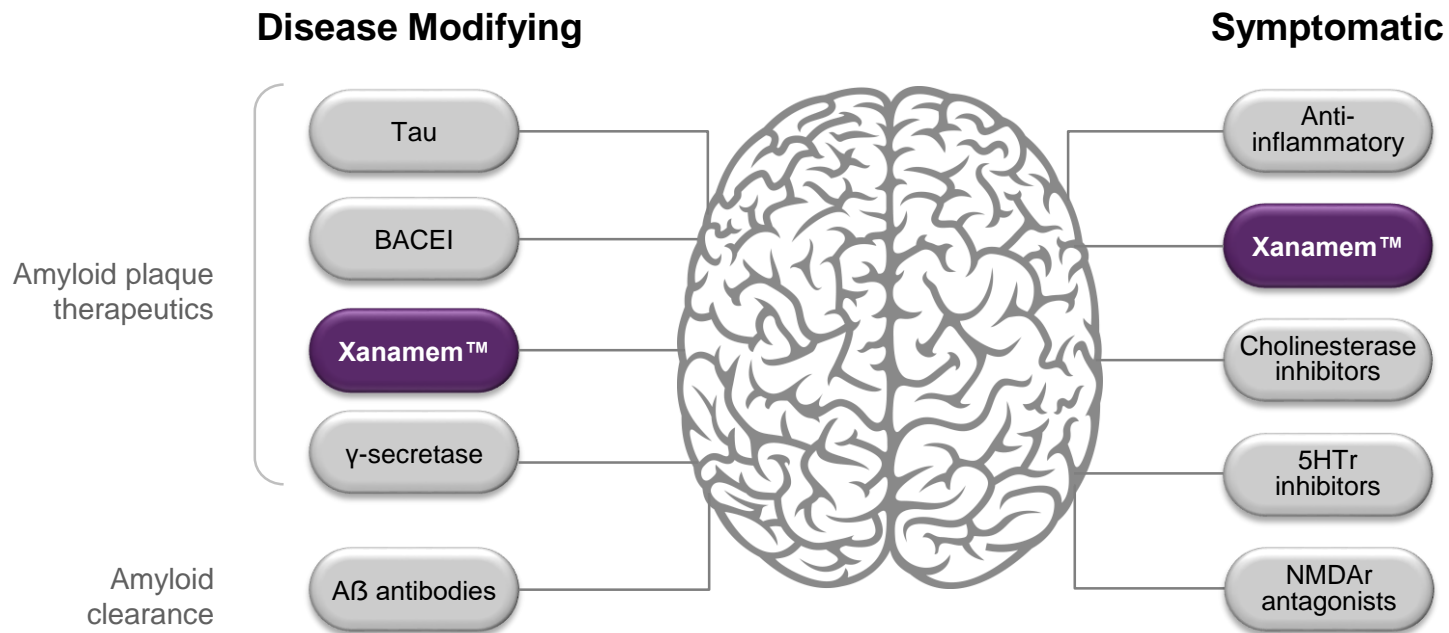
# Xanamem™ development: proposed study design

*XanADu* – Phase II double blind, randomised, placebo-controlled study to assess the efficacy of Xanamem™ in participants with mild AD

Treatment course <b>12 weeks</b>	<b>200</b> Mild Alzheimer's patients	Co-primary end points <b>ADAS-Cog</b> <b>ADCOMS +</b>
Xanamem™ twice daily dosage <b>35mg</b>	Being trialled in <b>AUS, USA</b> <b>and UK</b>	<b>Secondary end-points</b> Multiple: MMSE CDR-SOB, RAVLT, NPI, NTP & CSF A $\beta$ and Tau

ADCOMS: AD Composite Score. Wang et al., 2016. *J. Neurol. Neurosurg. Psychiatry* 0:1-7. Clinicaltrials.gov: NCT02727699.

# Xanamem™ potential for dual mechanism of action





# Target clinical positioning

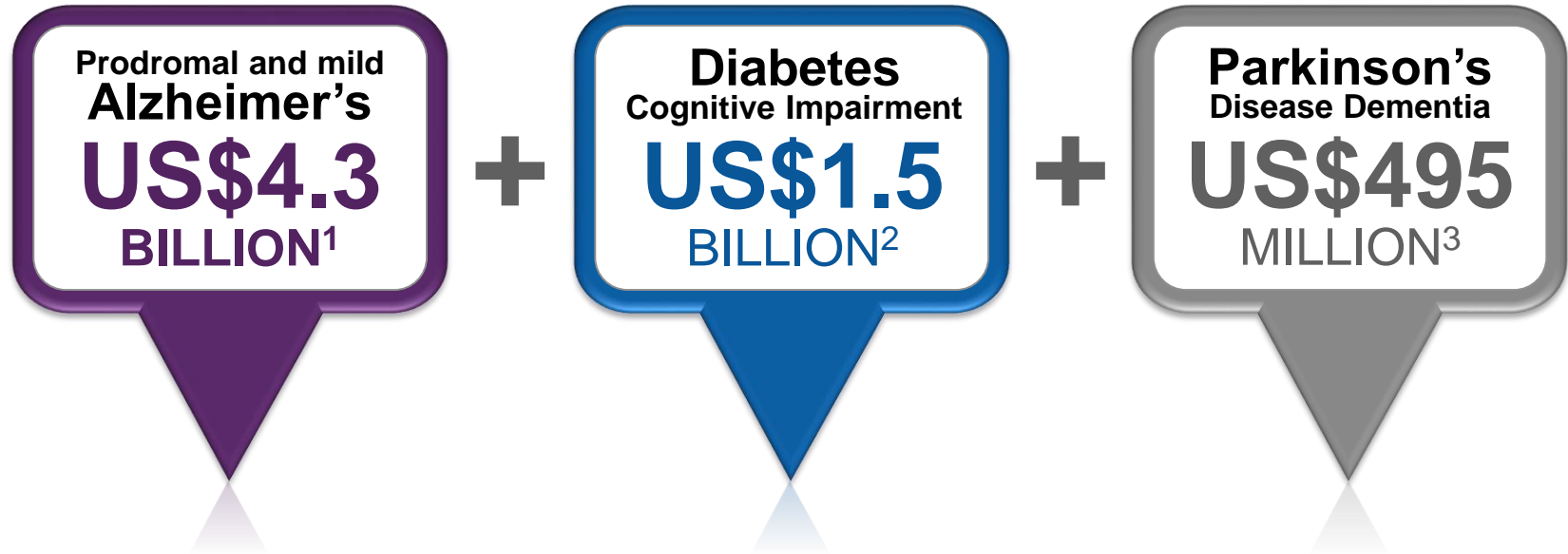
An oral agent that provides durable symptomatic and disease modifying benefits in mild Alzheimer's disease by direct inhibition of excess cortisol production.

**Xanamem™ is a novel agent likely to be used in combination with other AD therapies.**



# Xanamem's™ estimated market share

Global peak sales in 2031



<sup>1</sup> Reference Baker Young Initiation Coverage, August 2015.

<sup>2</sup> Price comparator Aricept, assumes 10% market share at peak sales, optimistic scenario.

<sup>3</sup> Price comparator Exelon patch, assumes 10% market share at peak sales, optimistic scenario.

# ACW financials

Key Corporate Data	
Market Cap*	~AU\$43 million
Entity	Public company listed on the Australia Stock Exchange (ACW)
Share Price*	AU\$0.071
Shares on issue^	~606 million
Cash position**	AU\$7.87 million
Ownership by top 20	55%

\*market cap and share price data as at 24 Jun, 2016

> post placement and SPP

\*\*As at 31<sup>st</sup> December, 2015, Appendix 4D.

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**THANK YOU**



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# Supplemental Slides

# Alzheimer's disease is emerging as the most significant health challenge of our time



**One person every 3 seconds**

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



**Numbers will double every 20 years**



**Total cost rise to US\$2 trillion by 2030**

Dementia will become a trillion dollar disease by 2018

The World Alzheimer's Report was independently researched by King's College London and supported by BupaC.



# Alzheimer's cannot currently be prevented, cured, or even slowed

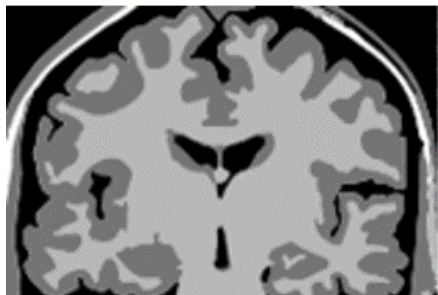


50% of 85 year olds  
have Alzheimer's Disease

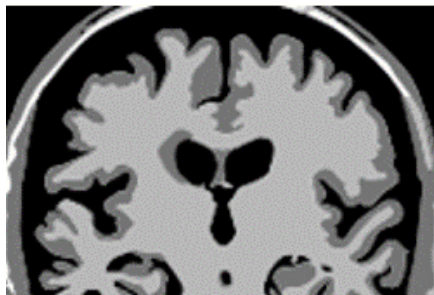
1 in 3 seniors will die with Alzheimer's  
disease or other dementia

The Alzheimer's Association Facts and Figures, 2014.

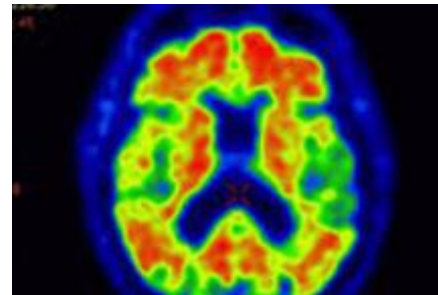
# Hallmarks of Alzheimer's Disease



Normal brain  
(volumetric MRI)



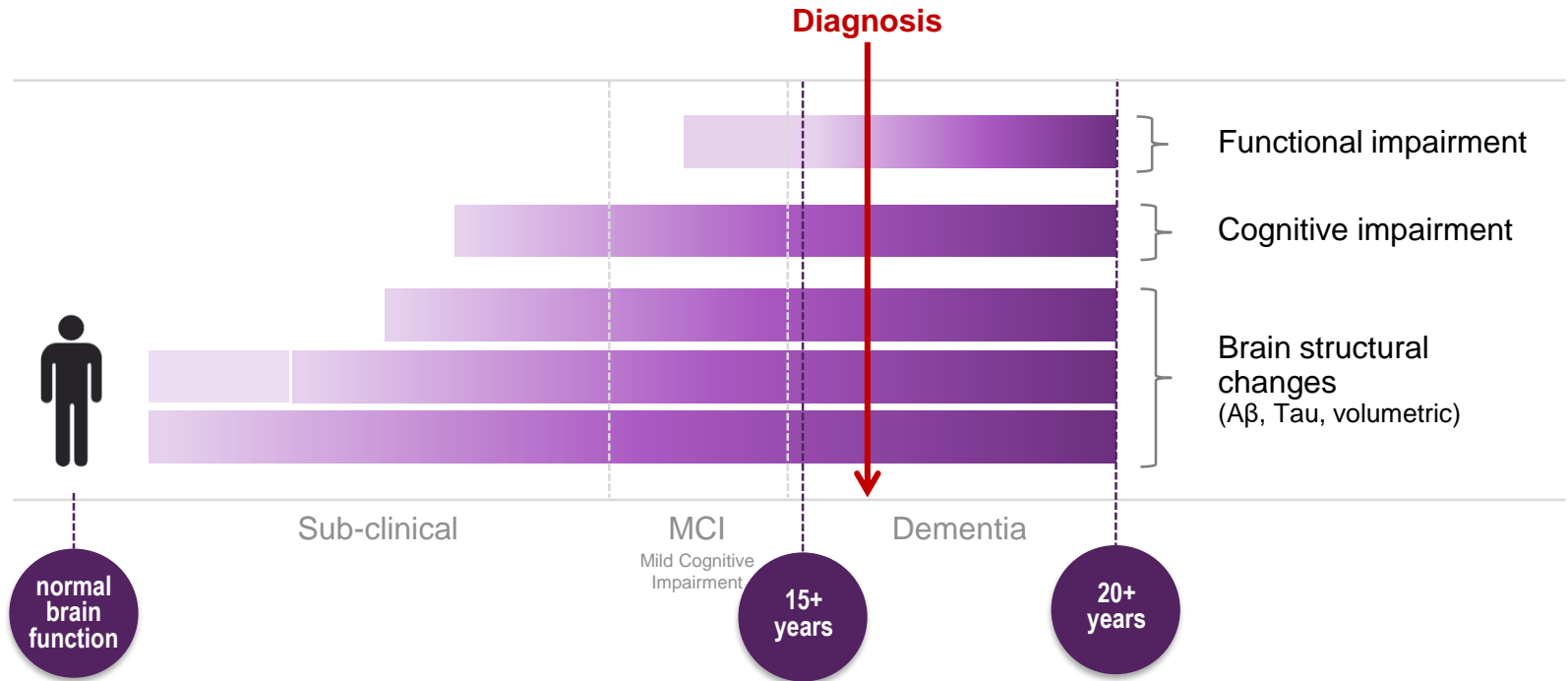
Neural death and brain  
shrinkage



Abnormal  $\beta$ -amyloid  
plaque build up (red)

Alzheimer's research aspiration - earlier detection  
and treatment to slow disease progression

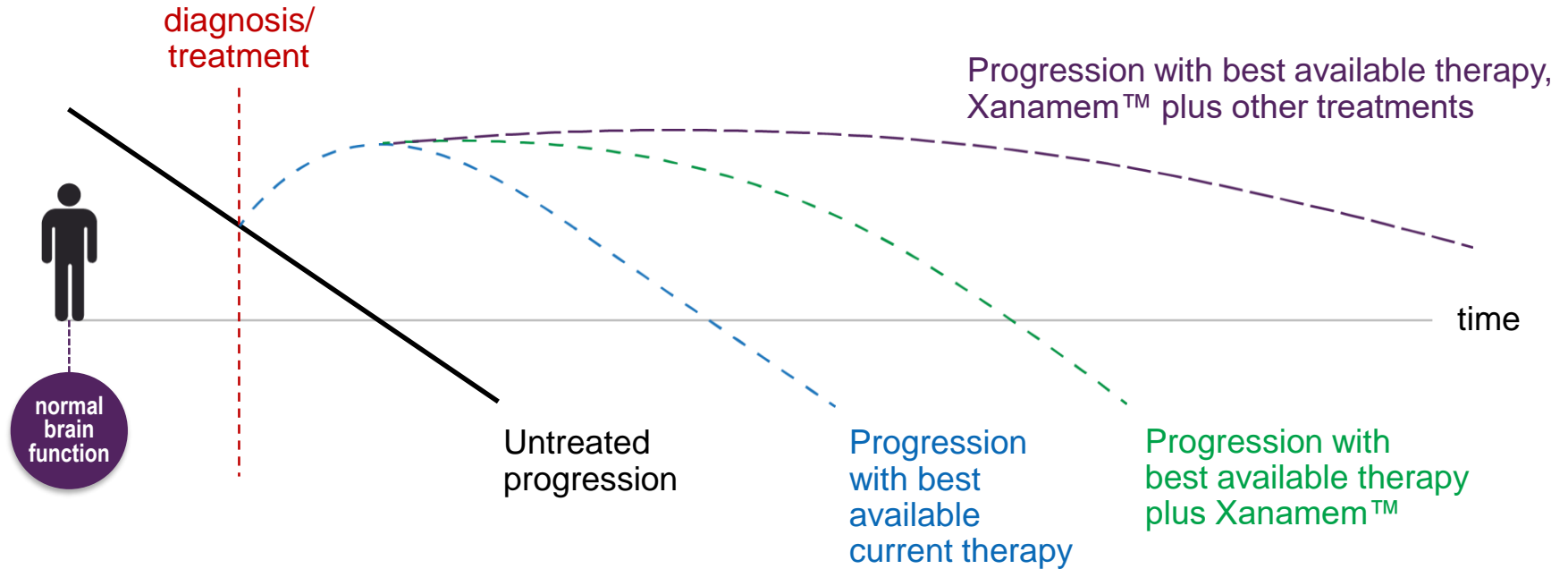
# Disease progression and diagnosis



Source: adapted from <http://www.re-cognitionhealth.com>

# Clinical goal for Xanamem™

Filling an unmet need in the market



Hypothetical Results

# Focusing on markets with high risk of progressive cognitive decline

**Alzheimer's**

**Diabetes**

**Parkinson's**

# Unmet need in Diabetes Cognitive Impairment



**422M<sup>1</sup>**  
Suffer from  
Diabetes globally



**Twice the risk  
of dementia**  
14.77M<sup>2</sup> suffer  
from dementia



**Treatment  
inertia**  
No-one is looking  
for a solution

<sup>1</sup> WHO Diabetes Fact Sheet March, 2016.

<sup>2</sup> Biessels et al., 2006.

# Unmet need in Parkinson's Disease Dementia



**7-10M<sup>1</sup>**

Living with  
Parkinson's  
Disease



**31%**

Progress from MCI to  
dementia  
100% penetrance  
after 10 years



**symptomatic  
relief**

Treatments are  
short term

<sup>1</sup> Parkinson's Disease Foundation [http://www.pdf.org/en/parkinson\\_statistics\\_Medtrack](http://www.pdf.org/en/parkinson_statistics_Medtrack) Report, 2015.