

# Developing Xanamem™ for Alzheimer's Dementia

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ASX Spotlight – Singapore, Hong Kong  
May 2015



**Actinogen**  
Medical

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# Alzheimer's - a significant unmet need



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

- A person develops AD almost every minute in the US<sup>1</sup>
- AD is the second leading cause of death in Australia behind ischaemic heart disease
- Estimated to increase to **US\$1 trillion** by 2050, outstripping the cost of treating all other diseases
- Current treatments are of limited benefit. New and alternative treatments are desperately needed

<sup>1</sup>Alzheimer's Association- Facts and Figures 2014)

[http://www.alz.org/downloads/Facts\\_Figures\\_2014.pdf?utm\\_content=bufferb49b5&utm\\_medium=social&utm\\_source=twitter.com&utm\\_campaign=buffer](http://www.alz.org/downloads/Facts_Figures_2014.pdf?utm_content=bufferb49b5&utm_medium=social&utm_source=twitter.com&utm_campaign=buffer)



Alzheimer's is the only cause of death among the top 10 in America that

**CANNOT BE PREVENTED, CURED OR EVEN SLOWED.**



1 in 3 Seniors

**DIES WITH ALZHEIMER'S**  
or another dementia.

# Xanamem™



Under development as a treatment for Alzheimer's disease and prodromal Alzheimer's/mild cognitive impairment



- A novel mechanism of action blocking the production of cortisol (the stress hormone) in the brain
- Excess cortisol leads to reversible memory loss, amyloid plaques and neural death – hallmarks of AD
- Link between excess cortisol and cognitive decline identified in patients with Cushing's disease, Alzheimer's, depression, and in normal aging
- Early development of Xanamem™ funded by the Wellcome Trust - \$25m over seven years
- Second Phase I study underway - data expected mid-2015
- Phase II to target early and prodromal AD in 2016.
- Expected to be used in combination with other AD therapies – marketed and in research
- Patent protection to 2031



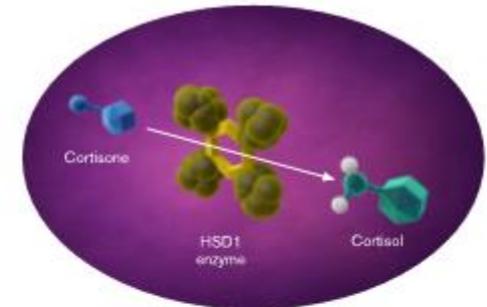
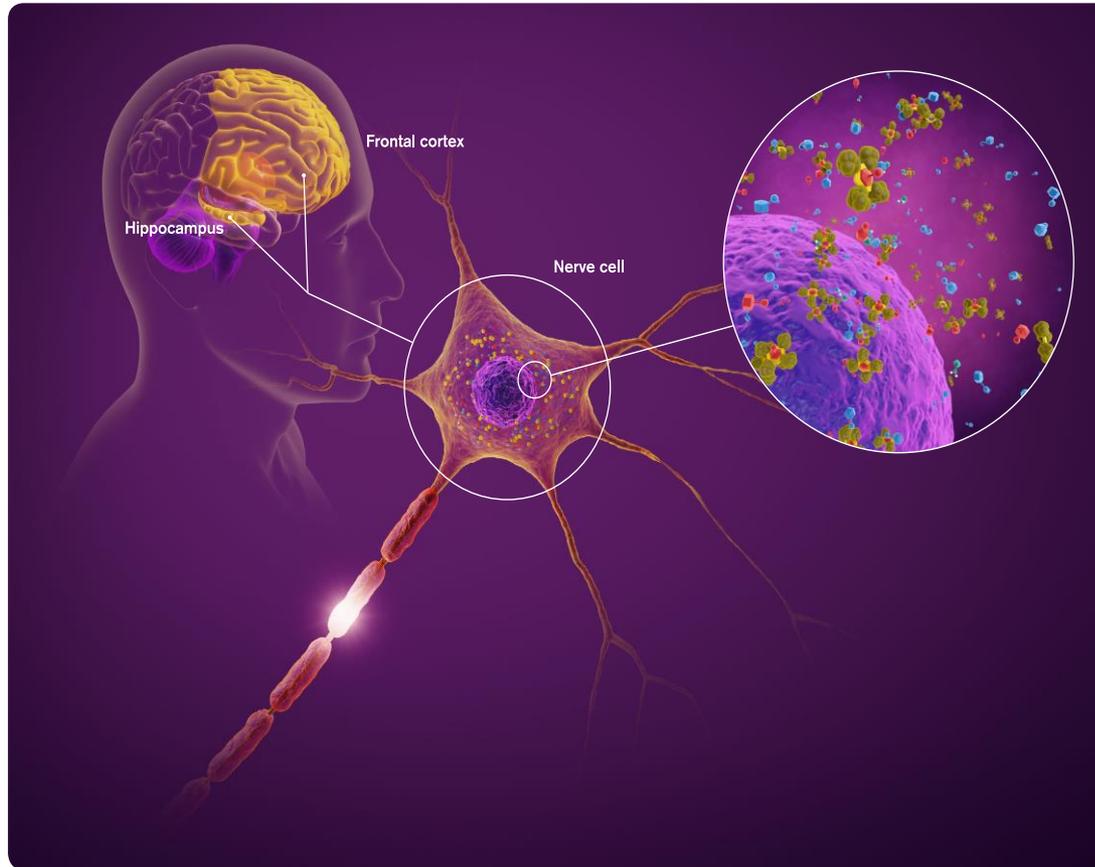
THOMSON REUTERS

recently named Xanamem™ as one of the top five drugs in Phase 1 development in the global pharmaceutical or biotech industries

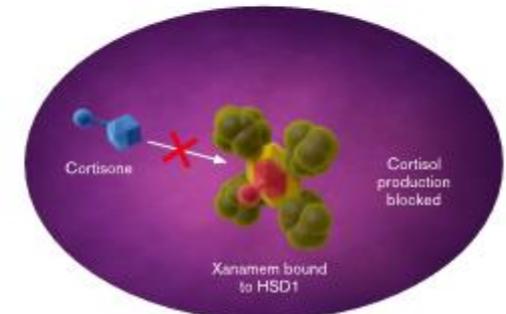
# Mechanism of action - a key differentiator



Xanmem™'s novel mechanism of action sets it apart from other AD treatments



HSD1 enzyme activates cortisone producing cortisol



Xanmem™ binds to HSD1, blocking cortisol

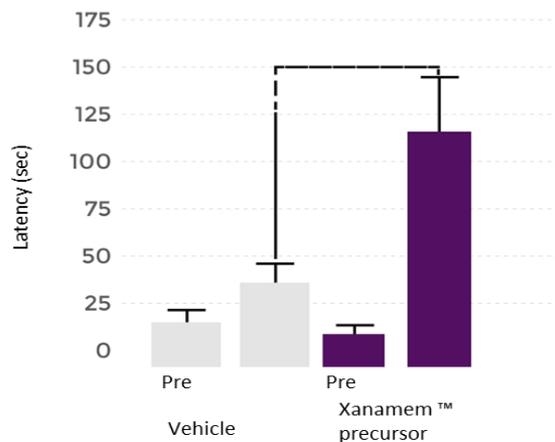
# Pre-clinical data



Xanamem™- a highly selective HSD1 inhibitor in pre-clinical animal models.

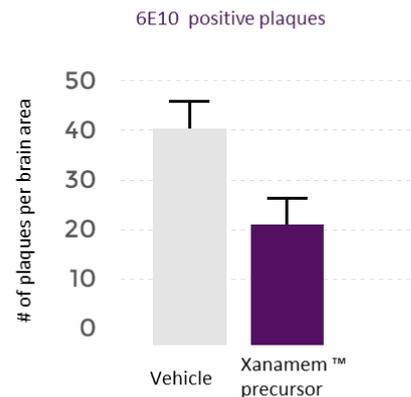
- Inhibition of HSD1 improves cognition in ageing and AD models
- Inhibition of HSD1 reduces A $\beta$  plaque burden and plasma A $\beta$  in AD models

**Cognitive Enhancement with Xanamem™ in AD** (Performance in Passive Avoidance Test, treatment for 28 days)



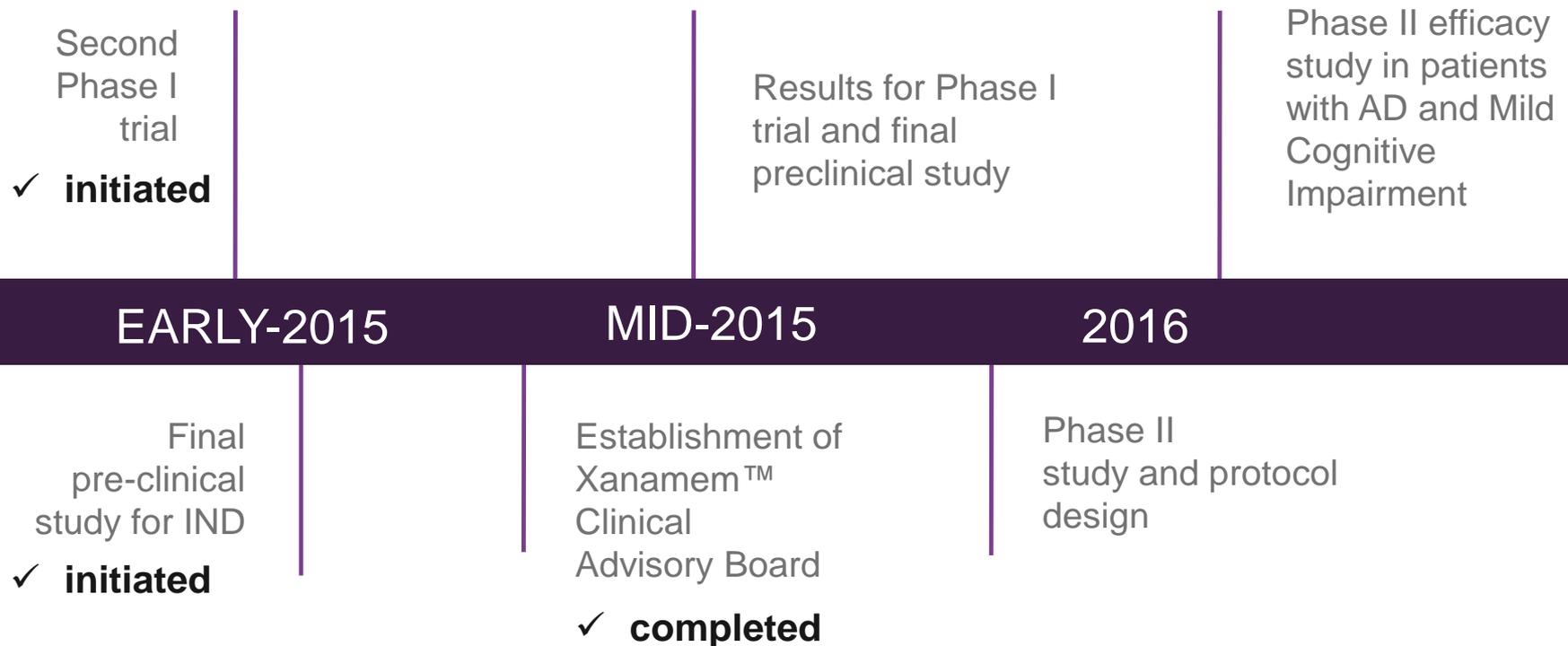
*AD - progressive cognitive decline*

**Xanamem™ reduces number of A $\beta$  plaques in AD brain** (28 day treatment)



*AD - associated with amyloid plaques in the brain*

# Xanamem™ development milestones



# Xanamem™ Clinical Advisory Board



Powerhouse Advisory Board to drive Xanamem™'s clinical development. World experts to help design the optimum Phase II efficacy trial for Xanamem™ in early and prodromal Alzheimer's patients



**Prof. Craig Ritchie**

- Professor of Psychiatry of Aging, University of Edinburgh, UK
- Senior Investigator in over 30 Alzheimer's clinical trials
- Published extensively on dementia



**Prof. Colin Masters**

- Professor, University of Melbourne, Australia
- Executive Director of Mental Health Research Institute
- Senior Deputy Director of the Florey Institute of Neuroscience and Mental Health



**Prof. Jeffrey Cummings**

- Professor of Medicine (Neurology), Cleveland Clinic, Ohio and Nevada, USA
- Chair of the Neurological Institute of Cleveland Clinic
- edited 39 books and published over 650 papers

# Xanamem™ pipeline

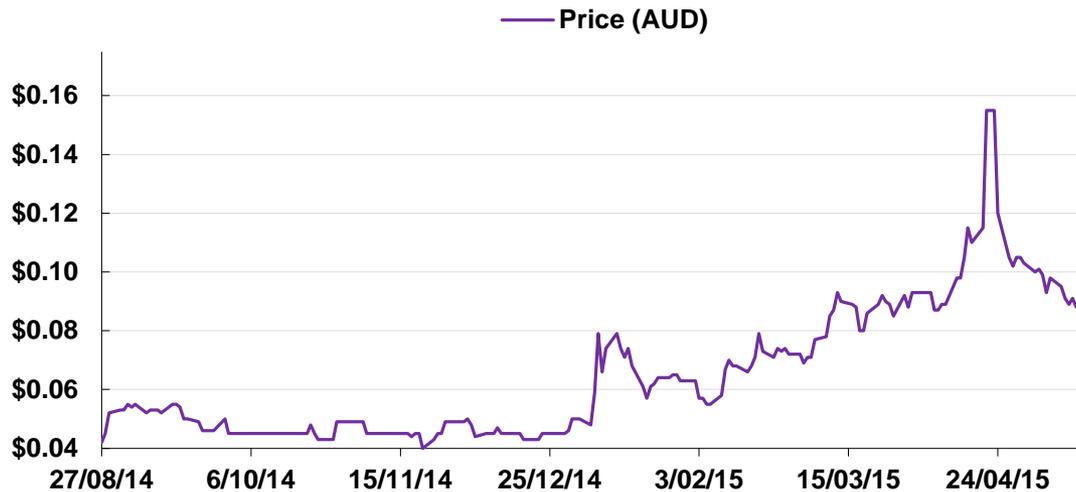


Xanamem™'s novel mechanism of action – blocking excess cortisol production – offers many additional possible applications relevant to diseases of the central nervous and endocrine/metabolic systems

- Potential development opportunities:
  - Cognitive dysfunction in schizophrenia, depression
  - PTSD (post traumatic stress disorder)
  - Diabetes – cognitive dysfunction and treatment
  - Cardiovascular disease
  - Post myocardial infarction
  - Obesity
  - Neuroprotection in metabolic disease



# Financial profile



## Key Corporate Data:

Market Cap.*	~\$51m
Share Price*	\$0.083
Cash**	\$10.4m
Shares on issue^	606.16m

\*market cap and share price data as of May 19, 2015  
 \*\*includes the proceeds from the Placement and SPP  
 ^post Placement and SPP

Top Ten Shareholders	Percentage
Edinburgh Technology Fund Limited	7.94%
Tisia Nominees Pty Ltd	5.55%
JK Nominees Pty Ltd	5.44%
Mr Martin Rogers	4.12%
Warmbi SARL	3.61%
Webinvest Pty Ltd	3.54%
Denlin Nominees Pty Ltd	3.15%
Mr Jason Peterson & Mrs Lisa Peterson	3.05%
Oaktone Nominees Pty Ltd	2.43%
Dr John William Ketelbey	2.04%

# Investment highlights



- Xanamem™ a potential treatment for early and prodromal AD/mild cognitive impairment
- Significant unmet need in a huge and growing global market
- Novel mechanism of action, targeting the stress hormone cortisol – a key differentiator
- Hypothesis backed by good pre-clinical and clinical evidence. Early development funded by Wellcome Trust
- Final Phase I and preclinical results due mid-2015; funded through to completion of these studies
- IND filing and Phase II study planned for 2016
- Expected to be used in combination with other AD therapies – marketed and in research
- Patent protection to 2031
- Tight capital structure with top 20 shareholders owning more than 70%



# Board and Management



A highly experienced Board and Management team with a wealth of drug development, commercialisation and clinical research expertise



**Martin Rogers**  
Chairman

- Biotechnology entrepreneur and executive
- Non-Executive Director of OncoSil (ASX:OSL), Chair of Rhinomed (ASX:RNO) and Non-Executive Director of Cellmid (ASX:CDY)



**Bill Ketelbey**  
CEO

- MD with 30 years' experience in pharmaceuticals
- Senior roles at Pfizer, including development of Aricept™, the current leading AD treatment



**Vince Ruffles**  
VP Clinical  
Research

- Extensive drug development experience over 20 years
- Responsible clinical development and regulatory strategy



**Jason Loveridge**  
Non-Executive  
Director

- Former head of Nomura Life Sciences Fund in the UK with 28 out of 34 investment wins in investing in Biotech



**Anton Uvarov**  
Non-Executive  
Director

- Healthcare and biotech equities analyst, formerly Citibank NY
- Executive Director of Sun Biomedical

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Thank you and  
questions

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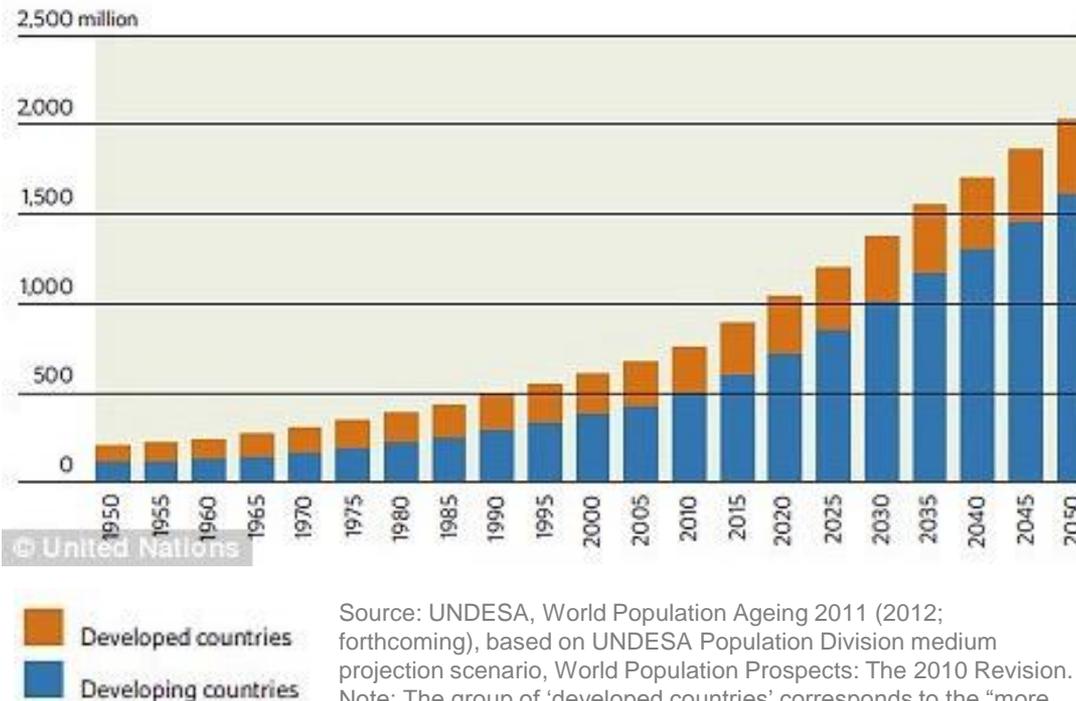
# Appendix

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# AD consequence of a rapidly ageing population



## Number of people aged 60 or over: World, developed and developing countries, 1950-2050



Source: UNDESA, World Population Ageing 2011 (2012; forthcoming), based on UNDESA Population Division medium projection scenario, World Population Prospects: The 2010 Revision. Note: The group of 'developed countries' corresponds to the "more developed regions" of the World Population Prospects: The 2010 Revision, and the group "developing countries" corresponds to the "less developed regions" of the same publication.

- Affects nearly 36 million patients worldwide
- In Australia, there are currently 320,000 AD sufferers – by 2050, this is expected to rise to close to 1 million.
- Commonly diagnosed in patients in their 60's, with 25% of 85 year olds and up to 50% of 95 year olds developing the disease
- AD is the second leading cause of death in Australia. (ABS)

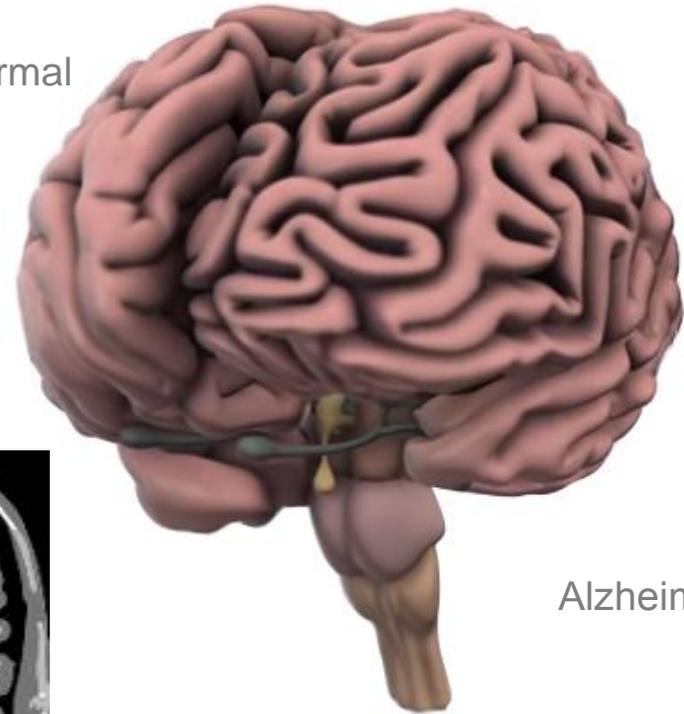
# The hallmarks of AD



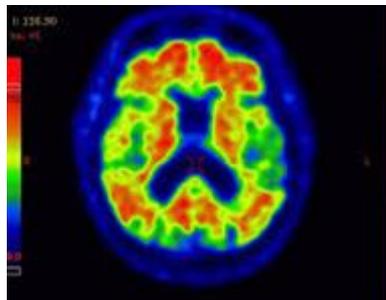
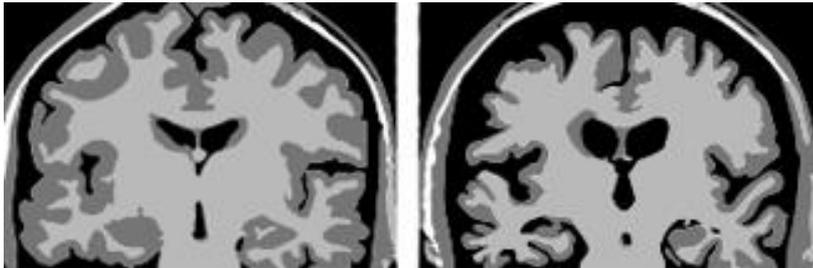
Memory, language and abstract reasoning impairment with

- brain shrinkage – particularly hippocampus and cortex
- neuronal loss
- amyloid plaques
- neurofibrillary tangles

Normal



Alzheimer's



# Signs of AD



Dementia is typically documented by decreasing performance on neuropsychological tests assessing memory, general knowledge, language, abstract reasoning and the ability to perform particular tasks requiring minimal skill:

*‘ Please draw a clock. Put the hours on it and set the time at 2:45’*



**Score 10:**  
Normal



**Score 8:**  
Mild Cognitive Impairment  
(numbers error and placement of hands)

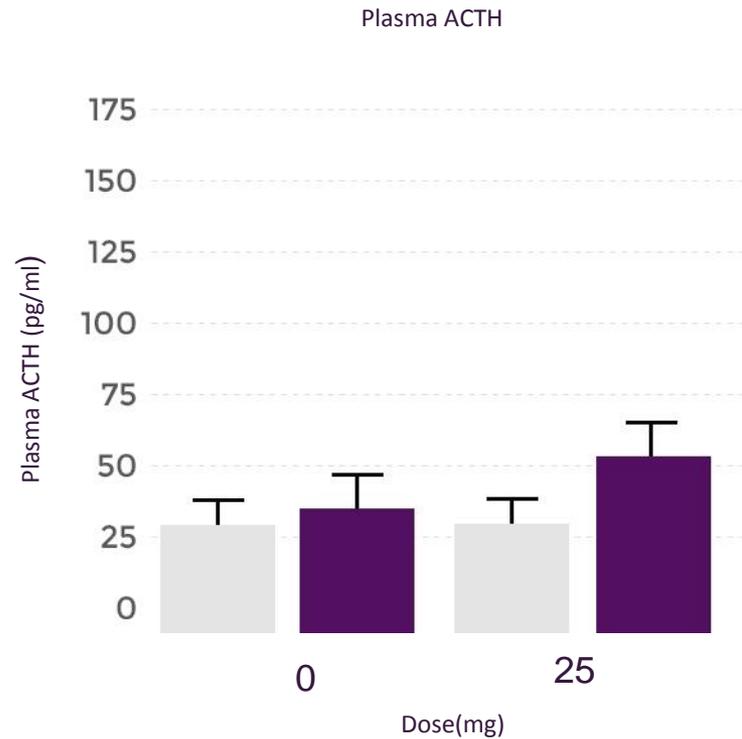
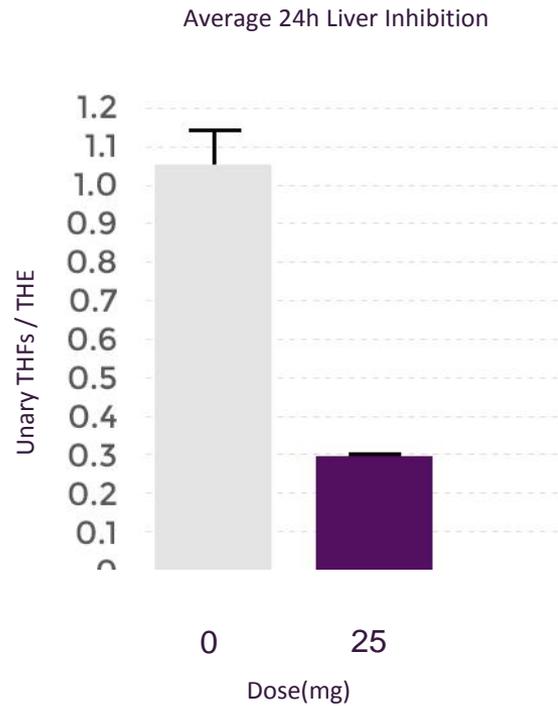


**Score 4:**  
Moderate cognitive impairment



**Score 2:**  
Severe cognitive impairment

# Xanamem™ Phase I SAD study

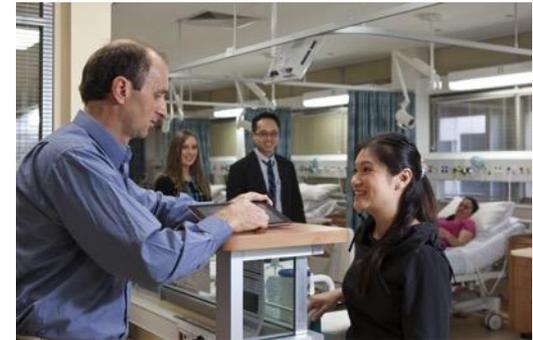


# Clinical trials overview



## Second Phase 1 study in healthy volunteers underway

- Trial conducted at Linear Clinical Research, Sir Charles Gairdner Hospital Perth, Western Australia.
- 40 healthy volunteers enrolled across 3 studies
- First study to confirm how the body absorbs and metabolises Xanamem™ and the optimal dose - **completed**
- Two follow-on studies:
  - Fast-fed study in a cohort of 12 patients – **underway with results in July**
  - Central nervous system pharmacokinetics of Xanamem™ in participants
  - Trial on-time and on-budget. Results expected by mid 2015



**Phase II efficacy and safety study in patients with early and prodromal AD/ mild cognitive impairment. On track to start in 2016 in US, Australia and UK**