



Developing Xanamem™ for treatment of Alzheimer's Dementia –  
A Therapeutic Area with Largest Potential

AusBiotech Invest – Crown Casino Melbourne 2014

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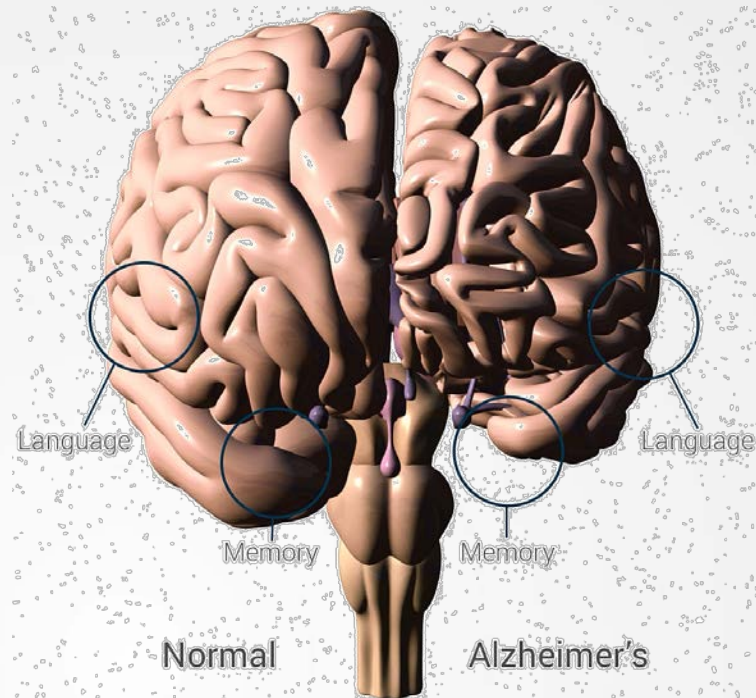
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# Company Snapshot

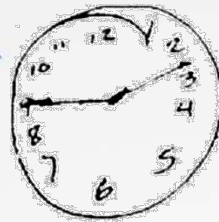
- ~> Stock code ASX: ACW – market cap approximately A\$20 million
- ~> Developing treatments for chronic degenerative neurological conditions
  - ⊙ One of the largest drug potential with an unmet medical need with Alzheimer's dementia
  - ⊙ American Alzheimer's Association estimates a healthcare cost last year of US\$250bn
- ~> Fully funded for next stage of clinical development
  - ⊙ Tight capital structure with top 20 shareholders owning > 70% equity
  - ⊙ 6 month turnaround on next clinical trial results
- ~> Successful clinical and pre-clinical demonstration
  - ⊙ Funded by the charity Wellcome Trust for \$25m invested over 7 years
  - ⊙ Excellent thesis of mechanism of action around Cortisol the "Stress" hormone and Cushing's disease
  - ⊙ US FDA changed indication on Alzheimer's dementia recently to "Mild Cognitive Impairment"

# Alzheimer's Disease & Dementia

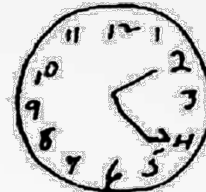


- Alzheimer's dementia is a degenerative brain disease around loss of memory and also the loss of use and understanding of language
- There is no known cure or treatment to slow progression of the disease
- It takes a disastrous toll on not only the patient but everyone around them
- Patients are robbed of their independence, their relationships and their very identity

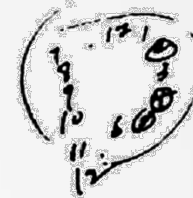
# Affects Cognitive Function



Normal  
Score 10



Mild  
Cognitive  
Impairment  
(Numbers error  
and  
placement  
of hands)  
Score 8



Moderate  
Cognitive  
Impairment  
Score 4



Severe  
Cognitive  
Impairment  
Score 2

Dementia is typically documented by poorer performance on neuropsychological tests which assess memory, general knowledge, language, abstract reasoning and the ability to perform certain tasks of minimal skill (i.e. *'Please draw a clock. Put the hours on it and set the time at 2:45'* ).



# Lead Candidate

## Xanamem™

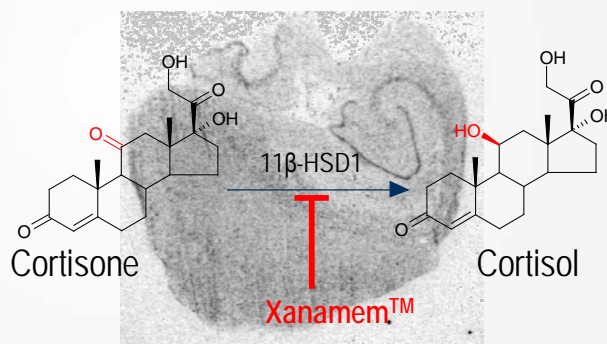
- ~> Xanamem™ is a patented (year 2028 and above) inhibitor of 11β-HSD1 – a novel target for AD
- ~> Prevents regeneration of Cortisol – a stress hormone. Evidence suggests chronic stress and high cortisol levels lead to formation of amyloid plaques and neural death
- ~> Xanamem™ has been developed to target CNS
  - ⊙ Disease modifying effects observed in pre-clinical models with Xanamem™ precursors
  - ⊙ Pre-clinical and clinical proof of concept for cognition obtained for Xanamem™
  - ⊙ Xanamem™ successfully completed single dose Phase I study in humans

# Xanamem™

## How it Works?

### Pre-clinical proof of concept data

- 11 $\beta$ -HSD1 in brain is inversely associated with cognitive decline
- 11 $\beta$ -HSD1 knockout models are protected against age-related cognitive impairment
- Xanamem™ as small molecule inhibition of 11 $\beta$ -HSD1 improves cognition in ageing and AD models
- Xanamem™ as small molecule inhibition of 11 $\beta$ -HSD1 reduces A $\beta$  plaque burden and plasma A $\beta$  in AD models



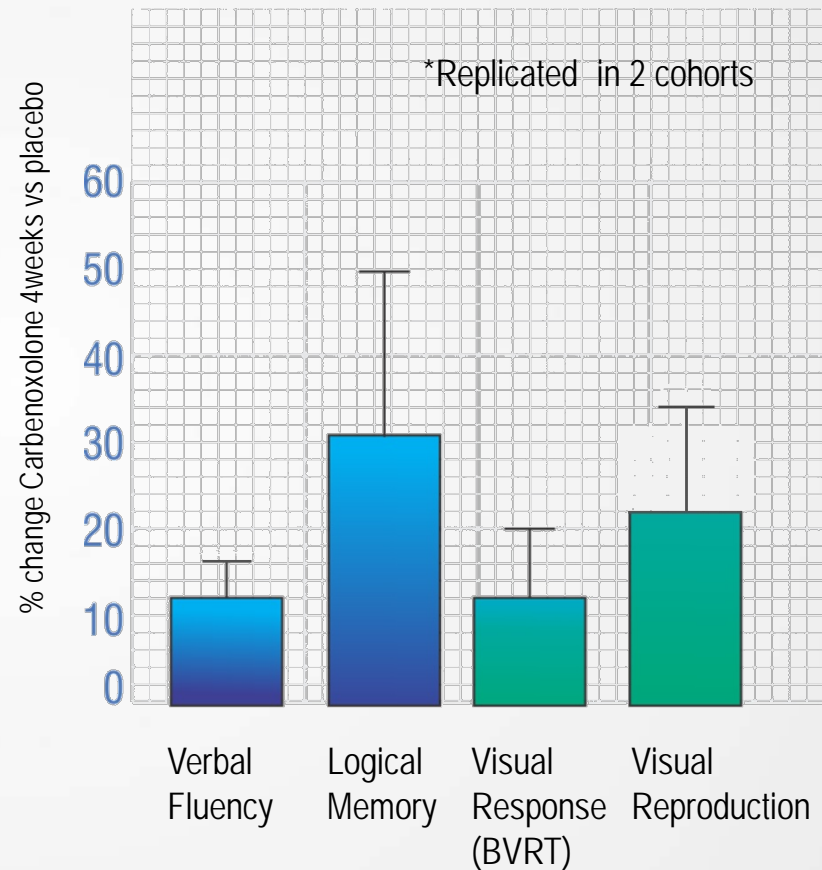
### Proof of concept in humans

- ⊙ 11 $\beta$ -HSD1 generates cortisol in brain regions important for cognition
- ⊙ Patients with cortisol excess (Cushing's syndrome) display reversible memory loss with hippocampal atrophy
- ⊙ Elevated cortisol levels associate with cognitive decline in ageing and AD
- ⊙ 11 $\beta$ -HSD inhibition with non-selective inhibitor Xanamem™ improves cognition in humans

# Human Proof of Concept Completed

Administration of the  $11\beta$ -HSD1 inhibitor Xanmem™ Carbenoxolone improved verbal fluency ( $p < 0.01$ ) after 4 weeks in 10 healthy elderly men (aged 55-75 y) and improved verbal memory ( $p < 0.01$ ) after 6 weeks in 12 patients with type 2 diabetes (52-70 y)

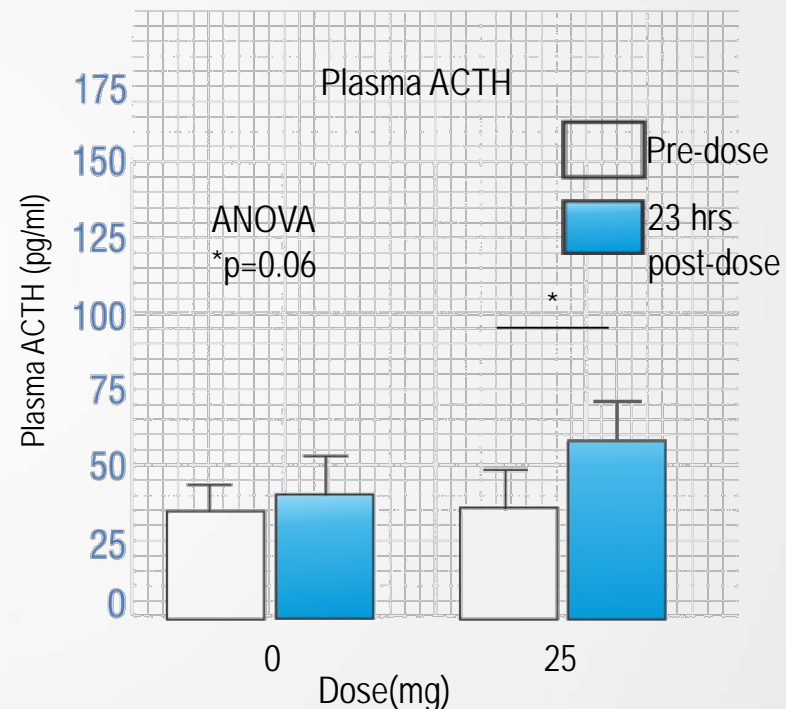
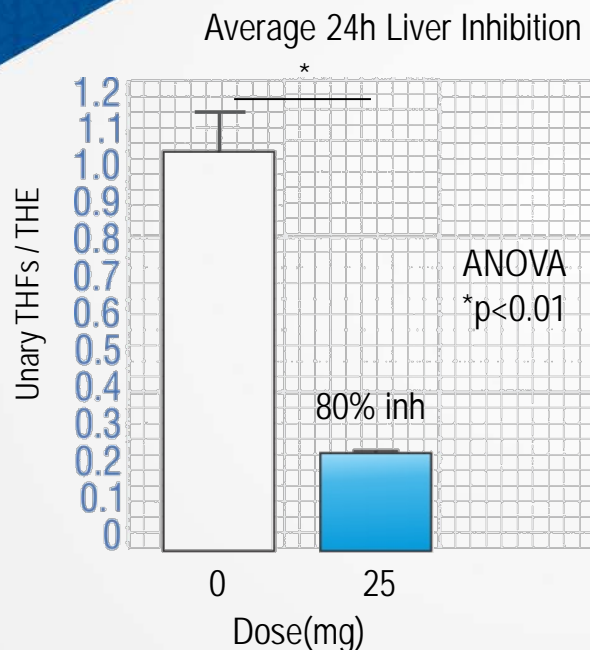
Pharmacological inhibition of HSD1 with Xanmem™ improves memory in humans





# XANAMEM™ Phase I SAD Study

## Xanamem™ Pharmacodynamics Phase I study (Single Dose)



Maximal enzyme inhibition achieved over 24h with a single 25mg dose of Xanamem™ in Phase I study in humans

# Clinical Development Steps

- ~> Confirmed stability of active pharmaceutical ingredient (API)
- ~> Capsules been manufactured to support Phase I multiple ascending dose (MAD) study
- ~> Second Phase I (MAD) and fast-fed study to start early 2015 (6 months to complete)
- ~> Phase I MAD study data in mid-2015
- ~> Phase II symptomatic efficacy study in patients with Mild Cognitive Impairment to start late 2015 / early 2016
  - ~> stratified patient group
  - ~> cognitive testing
  - ~> functional MRI and biomarkers

## Future Development in Indications with High Unmet Need

- ~> Cognitive dysfunction in schizophrenia
- ~> Cushing's Syndrome



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