

# Developing Xanamem™ for Alzheimer's Dementia

---

Dr. Bill Ketelbey CEO, Actinogen Medical

Investor Presentation  
February 2015



**Actinogen**  
Medical

# Forward Statements



This presentation has been prepared by Actinogen Limited. (“Actinogen” or the “Company”) based on information available to it as at the date of this presentation. The information in this presentation is provided in summary form and does not contain all information necessary to make an investment decision.

This presentation does not constitute an offer, invitation, solicitation or recommendation with respect to the purchase or sale of any security in Actinogen, nor does it constitute financial product advice or take into account any individual’s investment objectives, taxation situation, financial situation or needs. An investor must not act on the basis of any matter contained in this presentation but must make its own assessment of Actinogen and conduct its own investigations. Before making an investment decision, investors should consider the appropriateness of the information having regard to their own objectives, financial situation and needs, and seek legal, taxation and financial advice appropriate to their jurisdiction and circumstances. Actinogen is not licensed to provide financial product advice in respect of its securities or any other financial products. Cooling off rights do not apply to the acquisition of Actinogen securities.

Although reasonable care has been taken to ensure that the facts stated in this presentation are accurate and that the opinions expressed are fair and reasonable, no representation or warranty, express or implied, is made as to the fairness, accuracy, completeness or correctness of the information, opinions and conclusions contained in this presentation. To the maximum extent permitted by law, none of Actinogen its officers, directors, employees and agents, nor any other person, accepts any responsibility and liability for the content of this presentation including, without limitation, any liability arising from fault or negligence, for any loss arising from the use of or reliance on any of the information contained in this presentation or otherwise arising in connection with it.

The information presented in this presentation is subject to change without notice and Actinogen does not have any responsibility or obligation to inform you of any matter arising or coming to their notice, after the date of this presentation, which may affect any matter referred to in this presentation.

The distribution of this presentation may be restricted by law and you should observe any such restrictions.

This presentation contains certain forward looking statements that are based on the Company’s management’s beliefs, assumptions and expectations and on information currently available to management. Such forward looking statements involve known and unknown risks, uncertainties, and other factors which may cause the actual results or performance of Actinogen to be materially different from the results or performance expressed or implied by such forward looking statements. Such forward looking statements are based on numerous assumptions regarding the Company’s present and future business strategies and the political and economic environment in which Actinogen will operate in the future, which are subject to change without notice. Past performance is not necessarily a guide to future performance and no representation or warranty is made as to the likelihood of achievement or reasonableness of any forward looking statements or other forecast. To the full extent permitted by law, Actinogen and its directors, officers, employees, advisers, agents and intermediaries disclaim any obligation or undertaking to release any updates or revisions to information to reflect any change in any of the information contained in this presentation (including, but not limited to, any assumptions or expectations set out in the presentation).

# Actinogen Medical - Overview



## **Developing a novel treatment for Alzheimer's disease (AD) and Mild Cognitive Impairment (MCI)**

- Lead compound Xanamem™ (UE2343) blocks production of cortisol – the stress hormone – in the brain. A novel mechanism of action

## **Successful early development – Phase II planning underway**

- Positive results in pre-clinical and first Phase I study – early development funded by the Wellcome Trust
- Initiating second Phase I study and final pre-clinical studies – results due mid-2015. Research fully funded.
- Phase II study planned for 2016 in AD and MCI
- US FDA's designation of Mild Cognitive Impairment as a recognised indication, shifts the landscape for AD drug development to much earlier treatment

## **Alzheimer's – a significant and growing unmet medical need**

- AD population expected to triple over the next generation, increasing prevalence underpinned by shifting age demographics
- American Alzheimer's Association estimates the direct healthcare cost in 2013 of US\$250bn

# 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
- Chair of Oncosil (ASX.OCL), Rhinomed (ASX.RWO) and Non-Executive Director of Cellmid (ASX.CDY)



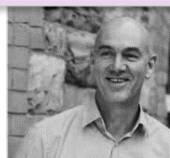
**Bill Ketelbey**  
**CEO**

- 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 venture investor with involvement in more than 24 biotech start-ups
- Non-executive Director of Resonance Health (ASX.RHT)



**Anton Uvarov**  
**Non-Executive Director**

- Healthcare equities analyst
- Executive Director of Sun Biomedical

# A significant, unmet need



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

- One person develops AD every minute in the US<sup>1</sup>, and every 4 seconds globally
- AD cost the US healthcare system **\$US250 billion** in 2013
- Estimated to increase to **US\$1 trillion** by 2050, outstripping the cost of treating all other diseases
- Current medications are of limited benefit. New and alternative treatments are desperately needed
- Xanamen™ has the potential to be a multi-billion dollar product



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.

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

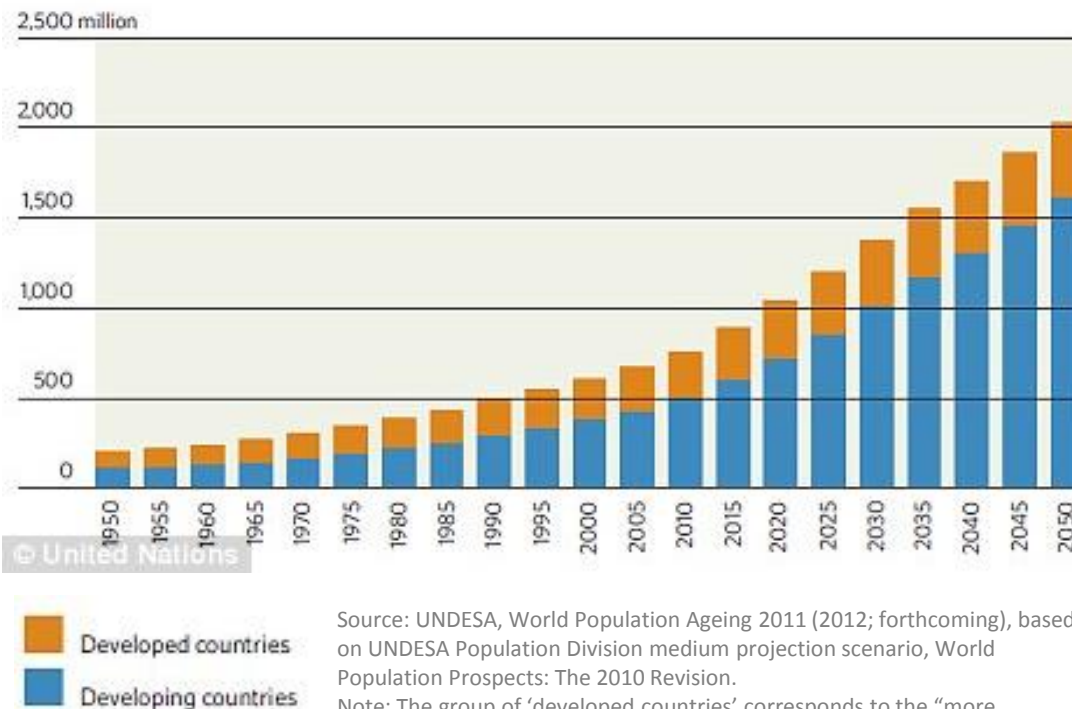
[http://www.alz.org/downloads/Facts\\_Figures\\_2014.pdf?utm\\_content=bufferb49b5&utm\\_medium=social&utm\\_source=twitter.com&utm\\_campaign=buffer](http://www.alz.org/downloads/Facts_Figures_2014.pdf?utm_content=bufferb49b5&utm_medium=social&utm_source=twitter.com&utm_campaign=buffer)



# 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.

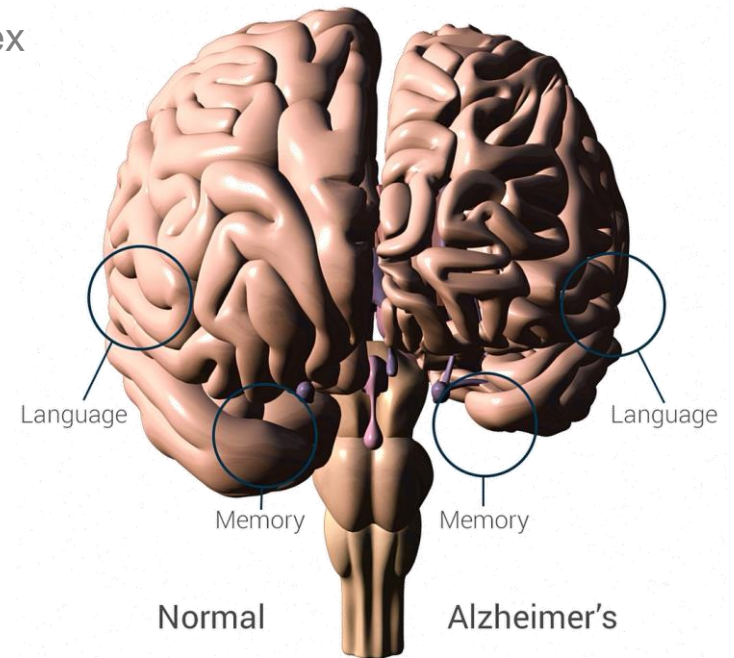
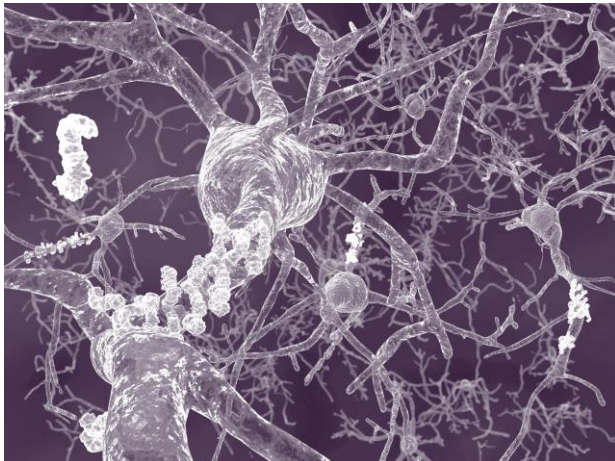
- Commonly diagnosed in patients in their 60's, with 25% of 85 year olds and up to **50% of 95 year olds** developing the disease
- Affects nearly **36 million patients** worldwide<sup>1</sup>
- In Australia, there are currently **320,000 AD** sufferers – by 2050, this is expected to rise to close to **1 million**.
- AD is the **sixth leading cause** of death in the US<sup>2</sup>

# The hallmarks of AD



Memory, language and behavioural impairment with

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



# 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



# Overview of Xanamem™



## Xanamem™ - under development as a treatment for Alzheimer's and its precursor Mild Cognitive Impairment



THOMSON REUTERS

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

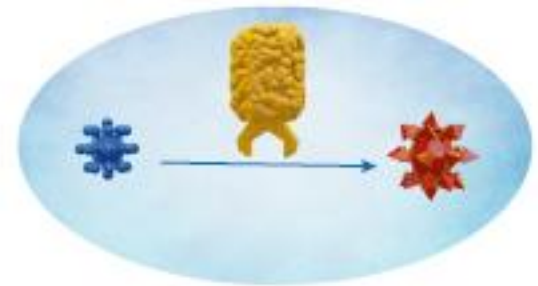
- A novel mechanism of action blocking the production of cortisol in the brain
- Excess cortisol (the stress hormone) has been shown to lead to reversible memory loss, amyloid plaques and neural death – the hallmarks of AD
- Link between excess cortisol and cognitive decline identified in patients with Cushing's disease, Alzheimer's, depression and normal aging
- Early development of Xanamem™ (UE2343) funded by the Wellcome Trust: \$25m over seven years
- Second Phase I clinical study underway - data expected mid-2015
- Phase II efficacy and safety study to target Mild Cognitive Impairment – the early onset of AD
- Patent protection to 2030, additional patents pending

# Mechanism of action: a key differentiator

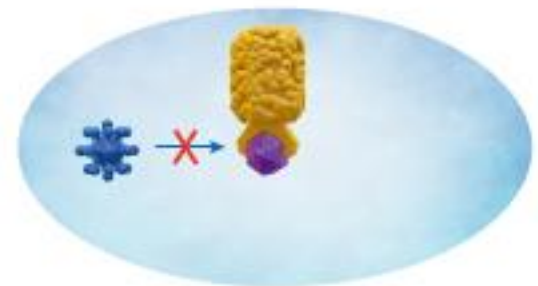


## Xanamem's novel mechanism of action sets it apart from other AD treatments

- Xanamem™ blocks the HSD1 enzyme, preventing the production of cortisol, from cortisone
- Excess cortisol contributes to the memory loss, amyloid plaques and neural death, hallmarks of AD
- HSD1 enzyme most concentrated in the hippocampus and frontal cortex – the areas of the brain most impacted by AD
- Pre-clinical and clinical data suggests Xanamem™ has the potential to treat AD and its early prodromal stage, Mild Cognitive Impairment and to significantly alter the course of the disease



HSD1 enzyme activates cortisone, producing cortisol



Xanamem binds to HSD1, blocking cortisol production

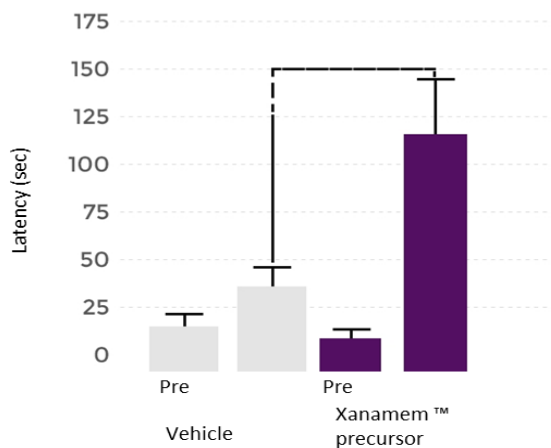
# Pre-clinical data



Xanamem™ (UE2343) - a highly selective HSD1 inhibitor in pre-clinical animal models.

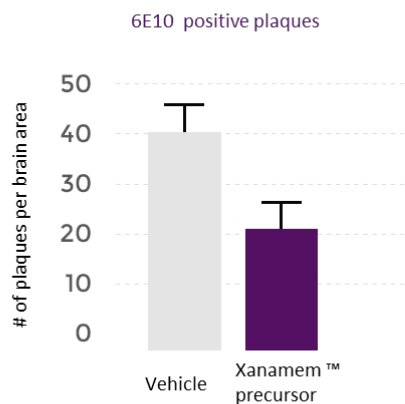
- Inhibition of HSD1 improves cognition in ageing and AD models
- Inhibition of HSD1 reduces A $\beta$  plaque burden and plasma A $\beta$  in AD models

**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*

# Clinical trials overview



## Second Phase 1 clinical 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
- Two follow on studies:
  - A fast-fed study in a cohort of 12 patients
  - A study in 4 patients to confirm the central nervous system pharmacokinetics of Xanamem™
- Full results expected by mid 2015



**Phase II efficacy and safety study in patients with AD and Mild Cognitive Impairment. Planned for 2016 in the US, Australia and EU**

# Pipeline



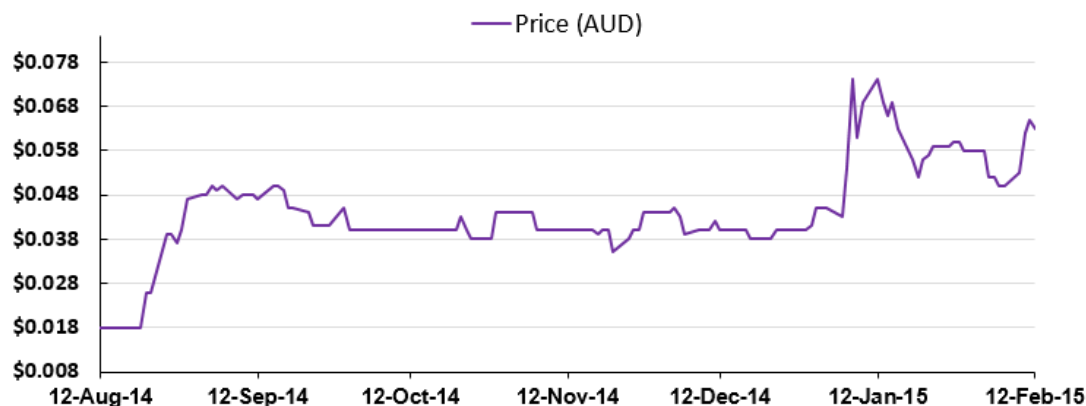
Xanamem's novel mechanism of action – blocking cortisol production through the inhibition of the HSD1 enzyme – offers many additional potential applications.

- Relevant to diseases of the central nervous and endocrine/metabolic systems
- Assessing potential development opportunities in:
  - Cognitive dysfunction in schizophrenia
  - Cognitive dysfunction in depression
  - Type 2 diabetes
  - Obesity
  - Cardiovascular disease
  - Neuroprotection in metabolic disease





# Financial Profile

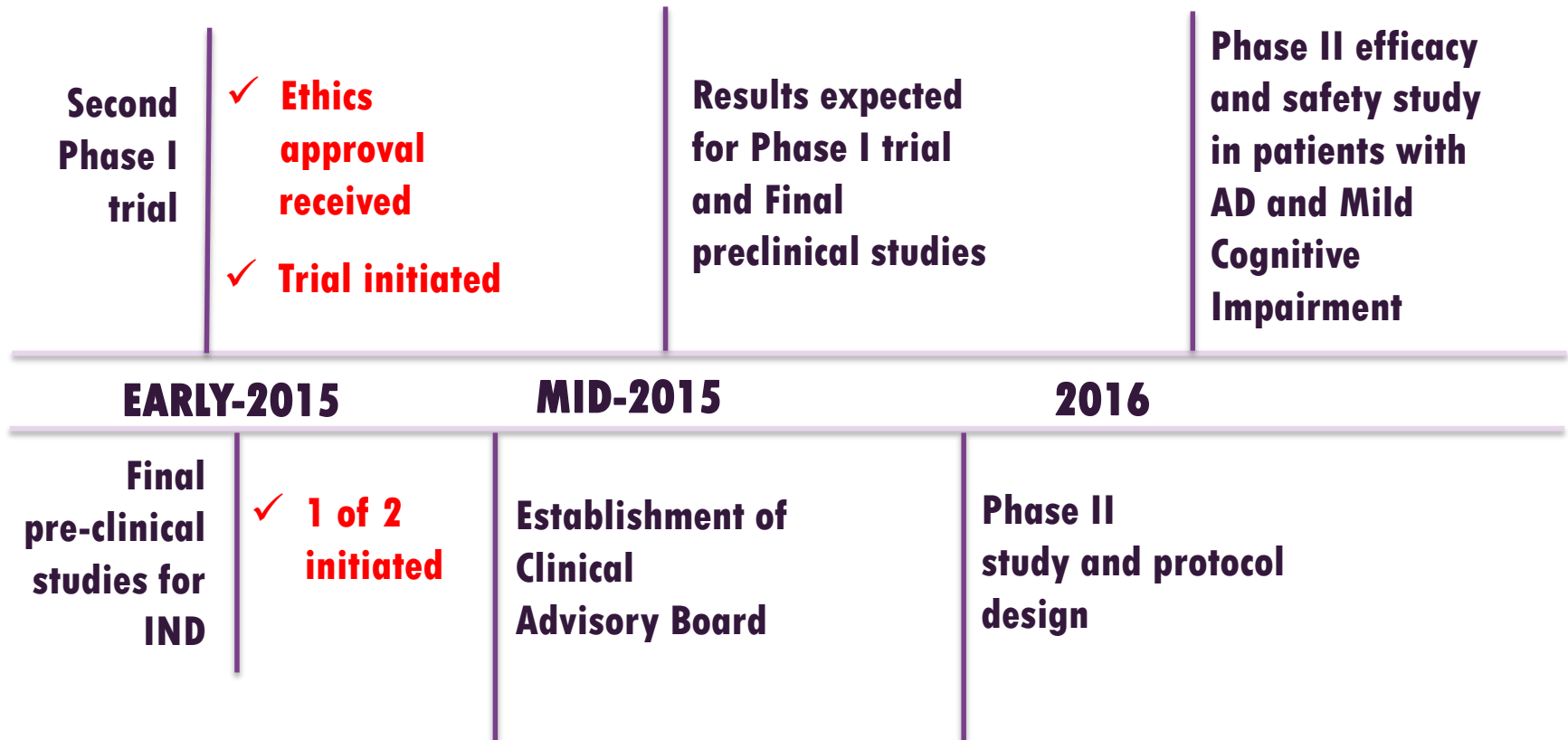


## Key Corporate Data:

Market Cap:	30.47 m
Share Price	0.063
Cash as of 31 Dec 2014	2.05 m
Shares on issue	492 m

Top Ten Shareholders	Percentage
Edinburgh Technology Fund Limited	9.78%
JK Nominees Pty Ltd	7.05%
Tisia Nominees Pty Ltd	6.83%
Mr Martin Rogers	5.08%
Warmbi SARL	4.41%
Denlin Nominees Pty Ltd	4.06%
Mr Jason Peterson & Mrs Lisa Peterson	3.56%
Webinvest Pty Ltd	3.35%
Oaktone Nominees Pty Ltd	2.99%
Dr John William Ketelbey	2.48%

# Milestones



# Investment Highlights



- Xanamem™ a potential treatment for AD and its precursor stage Mild Cognitive Impairment
- Significant unmet need in a huge and growing global market
- Novel mechanism of action, suppressing production of 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 clinical and preclinical results due mid-2015; funded through to completion of these studies
- IND filing and Phase II efficacy study planned for 2016
- HSD1 inhibition offers many additional potential applications
- Patent protection to 2030, additional patents pending
- Tight capital structure with top 20 shareholders owning more than 70%





Thank you

---