



## ASX ANNOUNCEMENT

### **Actinogen Medical Investor Presentation**

**Sydney, 9 September 2020.** Actinogen Medical ASX: ACW ('ACW' or 'the Company') is pleased to release an updated Investor Presentation. This presentation will be used to update existing shareholders, potential investors, strategic parties, and is referenced in a presentation as part of the ASX Small and Mid-Cap Conference.


The presentation by Dr Bill Ketelbey, CEO and Managing Director, will be available on-demand on the ASX Small and Mid-Cap Conference virtual platform. The Conference focuses on emerging leaders from a broad range of ASX-listed small and mid-cap companies. This will provide Actinogen with an opportunity to showcase the excellent progress made with the development of Xanamem™, to a wide network of Australian investors. For more information, including registering for the event, please visit <https://www2.asx.com.au/smid>.

Actinogen has generated a substantial dataset on its lead compound, Xanamem. A comprehensive analysis of this data has been finalised, with conclusions used to optimise key parameters for next series of clinical studies, such as dosing and patient characteristics. The Company is progressing plans for multiple phase 2 clinical trials in various diseases presenting with high unmet medical need, including in an early stage of Alzheimer's disease, Mild Cognitive Impairment (MCI). This trial is designed to link the positive efficacy results seen in the XanaHES trial with an Alzheimer's disease population. The Company looks forward to providing further updates in due course.

Actinogen's presentation is attached to this announcement.

**ENDS**

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***Announcement authorised by the Board of Directors of Actinogen Medical***

#### **About Actinogen Medical**

Actinogen Medical (ASX:ACW) is an ASX-listed biotechnology company developing novel therapies for cognitive impairment associated with chronic neurological, psychiatric, and metabolic diseases. The company is currently developing its lead compound Xanamem as a promising new therapy for Alzheimer's disease, and cognitive impairment associated with schizophrenia, diabetes, and other disorders. The cognitive dysfunction associated with these conditions is significantly debilitating for patients, and there is a substantial unmet medical need for new and improved treatments.

### **About Xanamem™**

Xanamem's novel mechanism of action sets it apart from currently available therapies. It works by blocking the production of intracellular cortisol – the stress hormone – through the inhibition of the 11 $\beta$ -HSD1 enzyme in the brain. There is a strong association between persistent stress and the production of excess cortisol that leads to detrimental changes in the brain, affecting memory, cognitive function and particular behavioural symptoms. The 11 $\beta$ -HSD1 enzyme is highly concentrated in the hippocampus and frontal cortex, the areas of the brain associated with cognitive impairment in a number of diseases/disorders, including Alzheimer's disease, schizophrenia, diabetes and other conditions associated with cognitive impairment.

The Company's XanaHES Phase I trial exploring the safety and tolerability of Xanamem 20mg once daily in healthy elderly volunteers, confirmed the drug's strong safety profile with no treatment-related serious adverse events. Additionally, the trial demonstrated that Xanamem produced a statistically significant improvement in cognition, which, along with other recently generated data, confirms 11 $\beta$ -HSD1 inhibition by Xanamem as a promising potential treatment for cognitive impairment and other symptoms associated with raised cortisol.

The Company plans to initiate Phase II studies of Xanamem in various disease areas in 2020/21, including MCI due to Alzheimer's disease.

Xanamem is an investigational product and is not approved for use outside of a clinical trial by the FDA or by any global regulatory authority.

Xanamem™ is a trademark of Actinogen Medical.

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**Actinogen Medical encourages all current investors to go paperless by registering their details with the designated registry service provider, Link Market Services.**

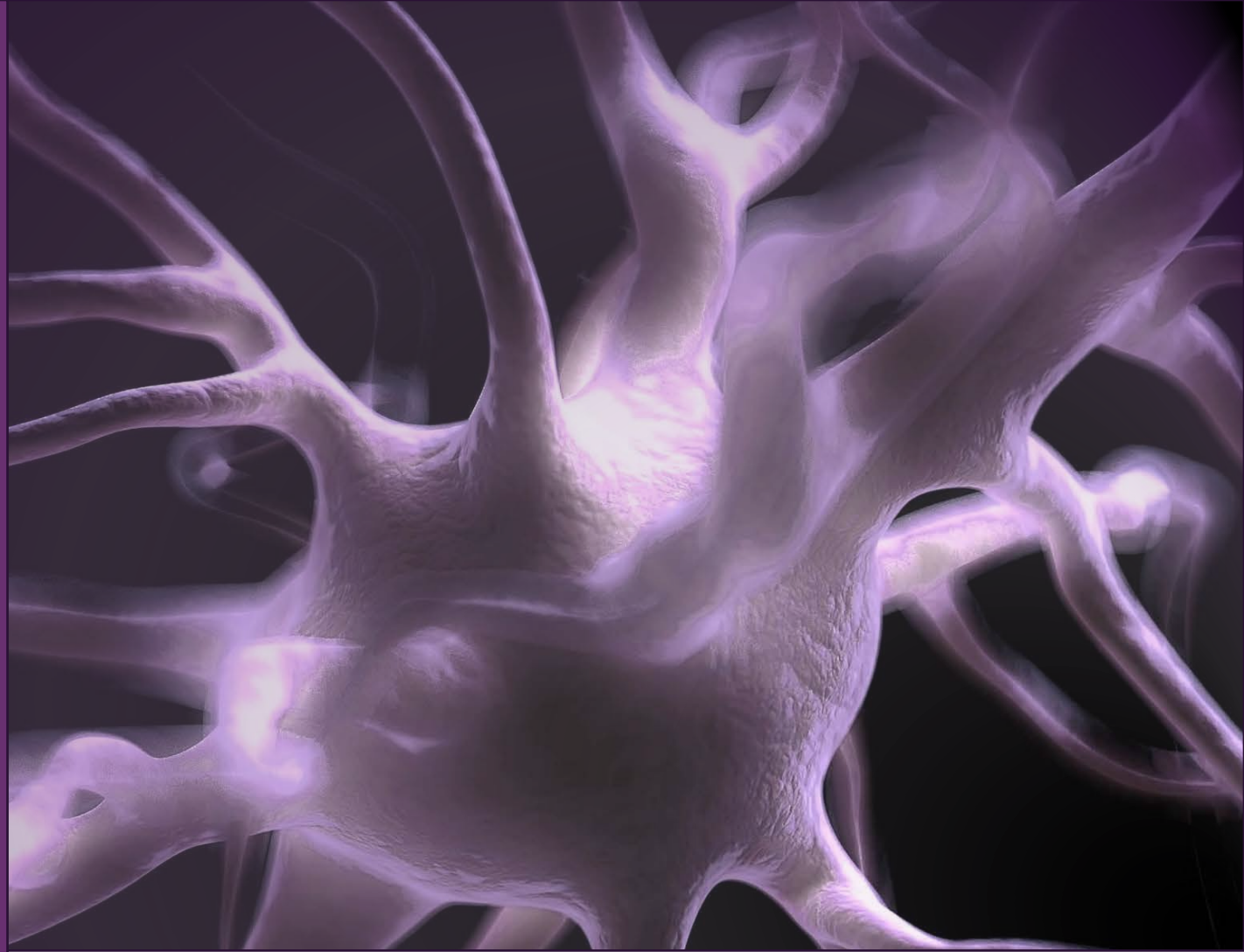
# Investor Presentation

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Dr. Bill Ketelbey: CEO & MD

September 2020

*Developing innovative treatments for cognitive impairment associated with neurological and metabolic diseases due to raised cortisol, including Alzheimer's disease*



# Xanamem™ - lead compound

A novel mechanism of action designed to inhibit cortisol production in the brain (via 11 $\beta$ -HSD1 inhibition)



**Novel MoA**  
(cortisol inhibition)



**PoC demonstrated in animal trials**



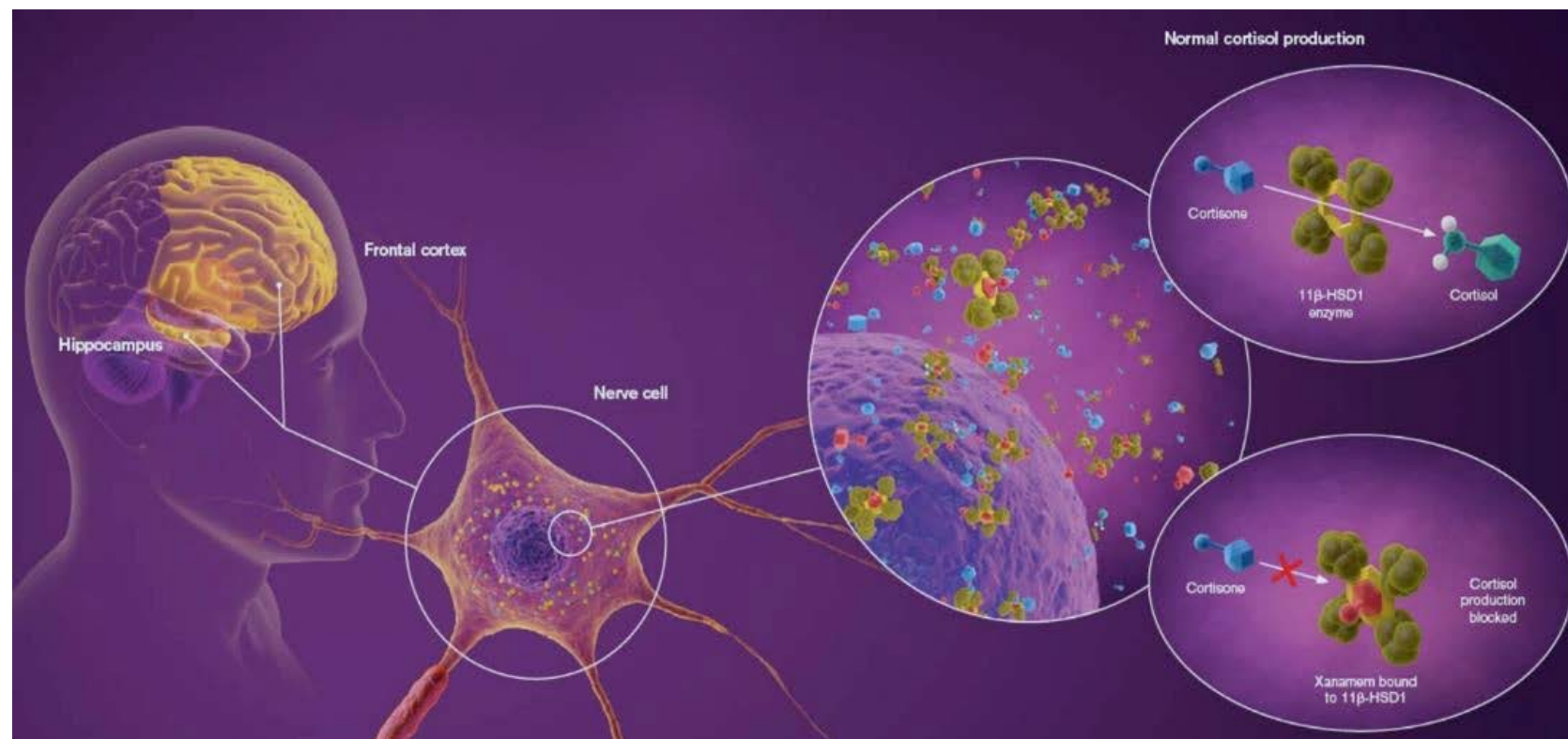
**PoC demonstrated in human trials**



**Strong safety profile**



**Excellent PK/PD profile**

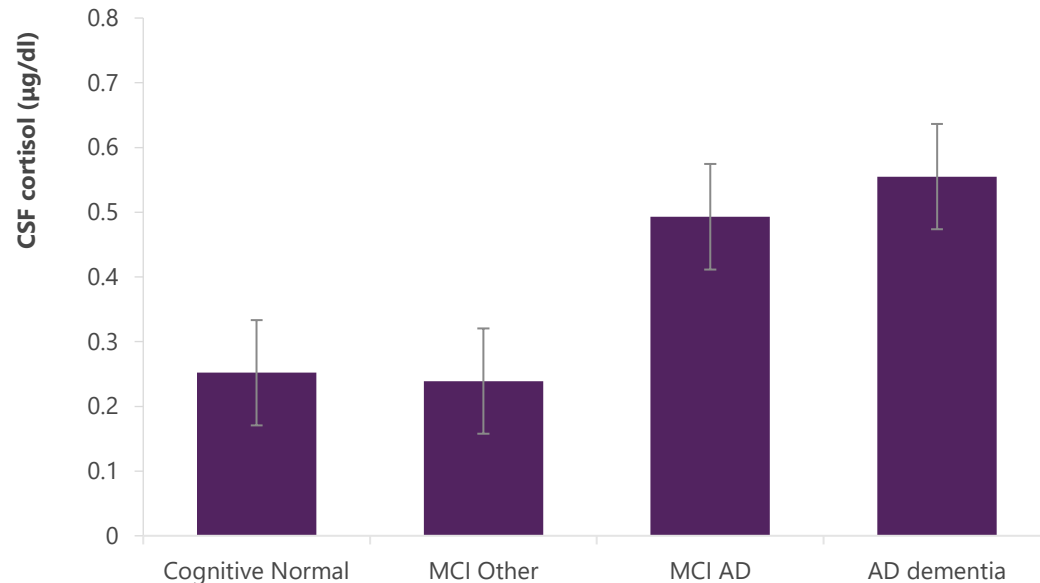


**Xanamem - an oral, brain penetrant, selective and effective 11 $\beta$ -HSD1 inhibitor with a strong safety profile**

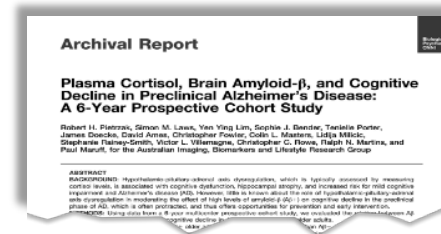
# Strategic focus underpinned by significant medical research

A growing body of medical literature supports the association between chronically raised cortisol, cognitive impairment and lower brain volumes

## Raised cortisol associated with Alzheimer's disease<sup>1</sup>



## Supported by growing body of medical literature



Many studies support the association between **cortisol** and **Alzheimer's disease** development & progression<sup>2</sup>

AIBL study<sup>3</sup> demonstrates that **50% of those aged 65+ have raised cortisol levels**

Research suggests that lowering cortisol levels may prevent the development / progression of Alzheimer's disease

1. MCI: mild cognitive impairment; AD: Alzheimer's Disease





2. Recent studies also support the association between cortisol and cognitive impairment associated with neuroendocrine dysfunction

3. Plasma Cortisol, Brain Amyloid- $\beta$ , and Cognitive Decline in Preclinical Alzheimer's Disease: a 6-Year Prospective Cohort Study. Pietrzak et al., 2017. Biological Psychiatry: Cognitive Neuroscience and Neuroimaging 2:45-52



# Highlights: Demonstration of Xanamem's promising efficacy and safety

A significantly enhanced and growing dataset

 <hr/> <i>Efficacy shown in Phase 1 clinical trial in healthy elderly patients (20mg Xanamem daily)</i>	 <hr/> <i>Phase 2 clinical trial in mild Alzheimer's disease (10mg Xanamem daily)</i>	 <b>Target Occupancy &amp; Homogenate Binding studies</b> <hr/> <i>Phase 1 Target Occupancy, &amp; Homogenate Binding Studies</i>	 <b>Comprehensive Data Analysis</b> <hr/> <i>QSP<sup>1</sup> and PK/PD<sup>2</sup> modelling analysing the substantial pre-clinical and clinical dataset</i>
✓ <b>Completed</b>	✓ <b>Completed</b>	✓ <b>Near completion<sup>3</sup></b>	✓ <b>Completed</b>

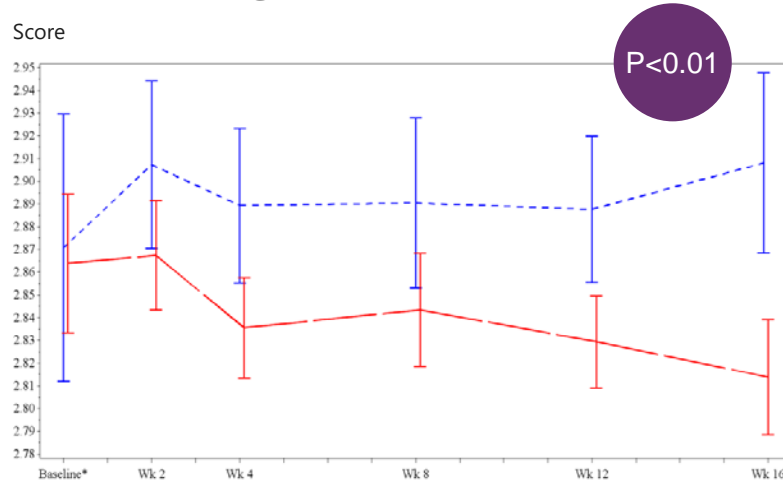
**Comprehensive review of Xanamem completed – updated clinical development plan well advanced**

# Significant cognitive efficacy signal achieved

Breakthrough results from Cogstate Cognitive Test Battery evaluation demonstrate robust statistically significant cognitive efficacy improvement in multiple domains with a rapid and sustained response

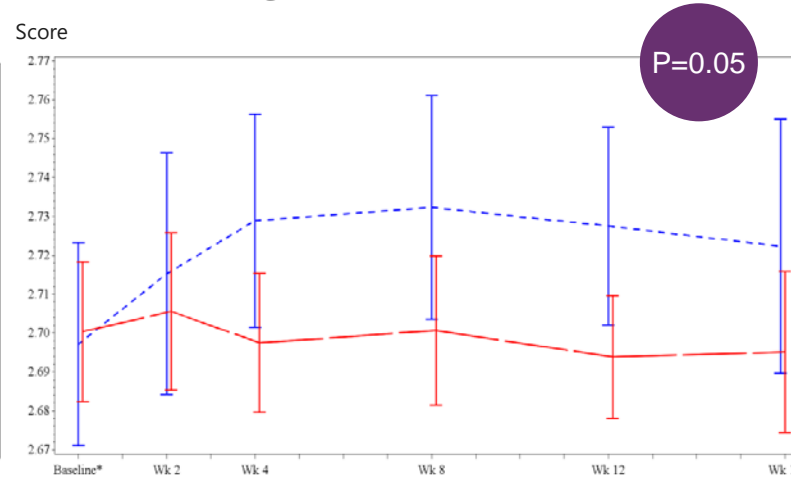
## Working memory (One Back Test)

**Strongly statistically significant result**



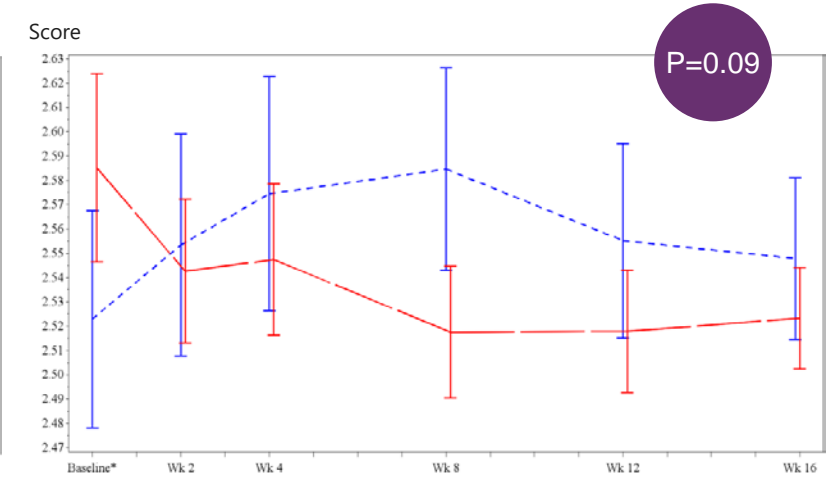
## Visual attention (Identification Test)

**Statistically significant result**



## Psychomotor function (Detection Test)

**Good trend to a positive result**



### Treatment Group

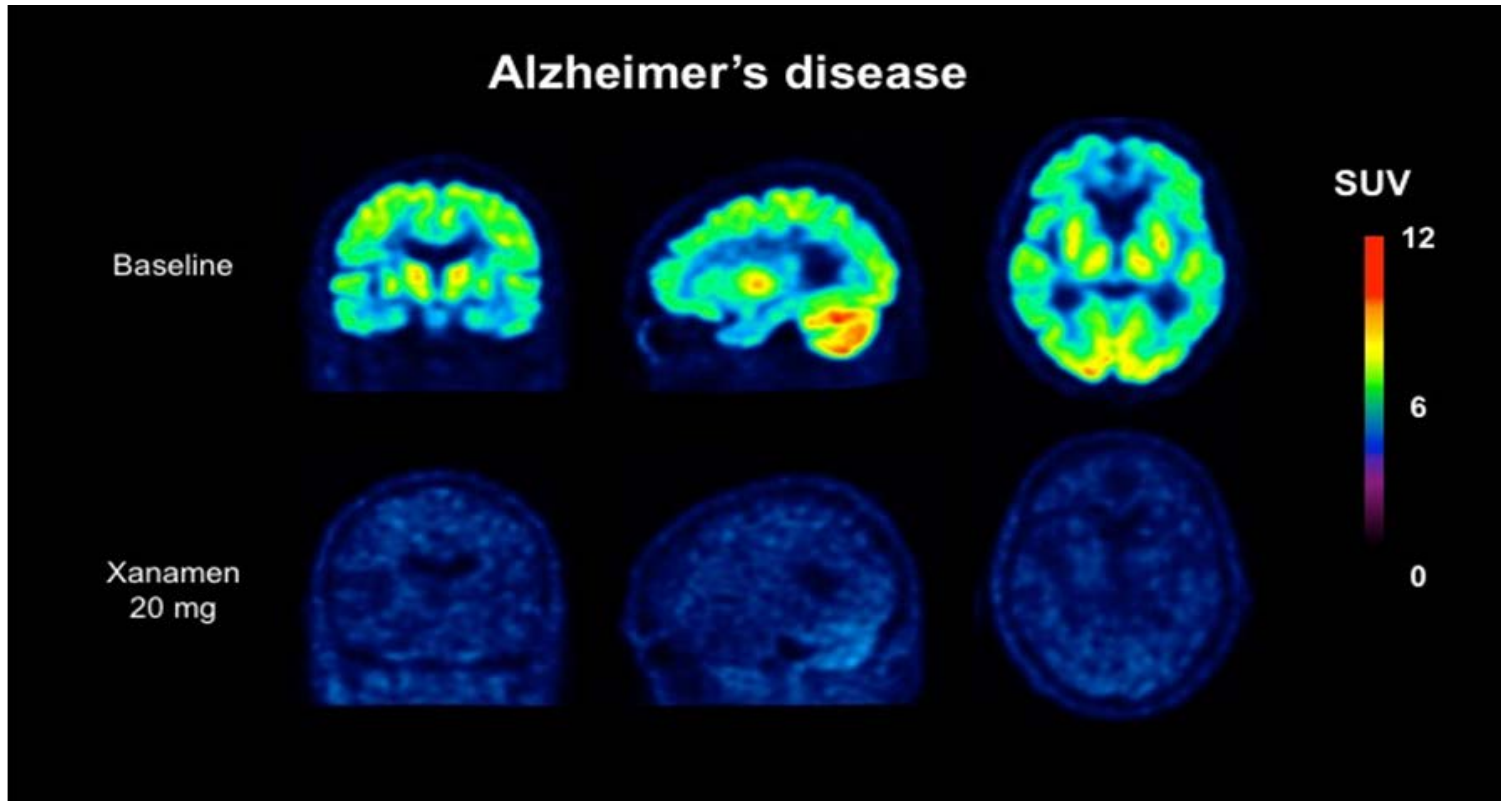
— Xanamem (30 pts)    - - - Placebo (12 pts)

**Efficacy results reflect high quality and consistent data in a small study population**



## Target Occupancy study: positive confirmatory data

Phase I target occupancy study demonstrates that 5mg to 30mg Xanamem dosed for seven days significantly occupies the neuronal 11 $\beta$ -HSD1 enzyme throughout the brain (32 of 36 patients completed)







**50% to 85% occupancy,  
dependent upon brain  
region, dosage and  
study subject<sup>1</sup>**

**Phase I Target Occupancy supports Xanamem as a potent, orally bioavailable and brain-penetrant 11 $\beta$ -HSD1 inhibitor**



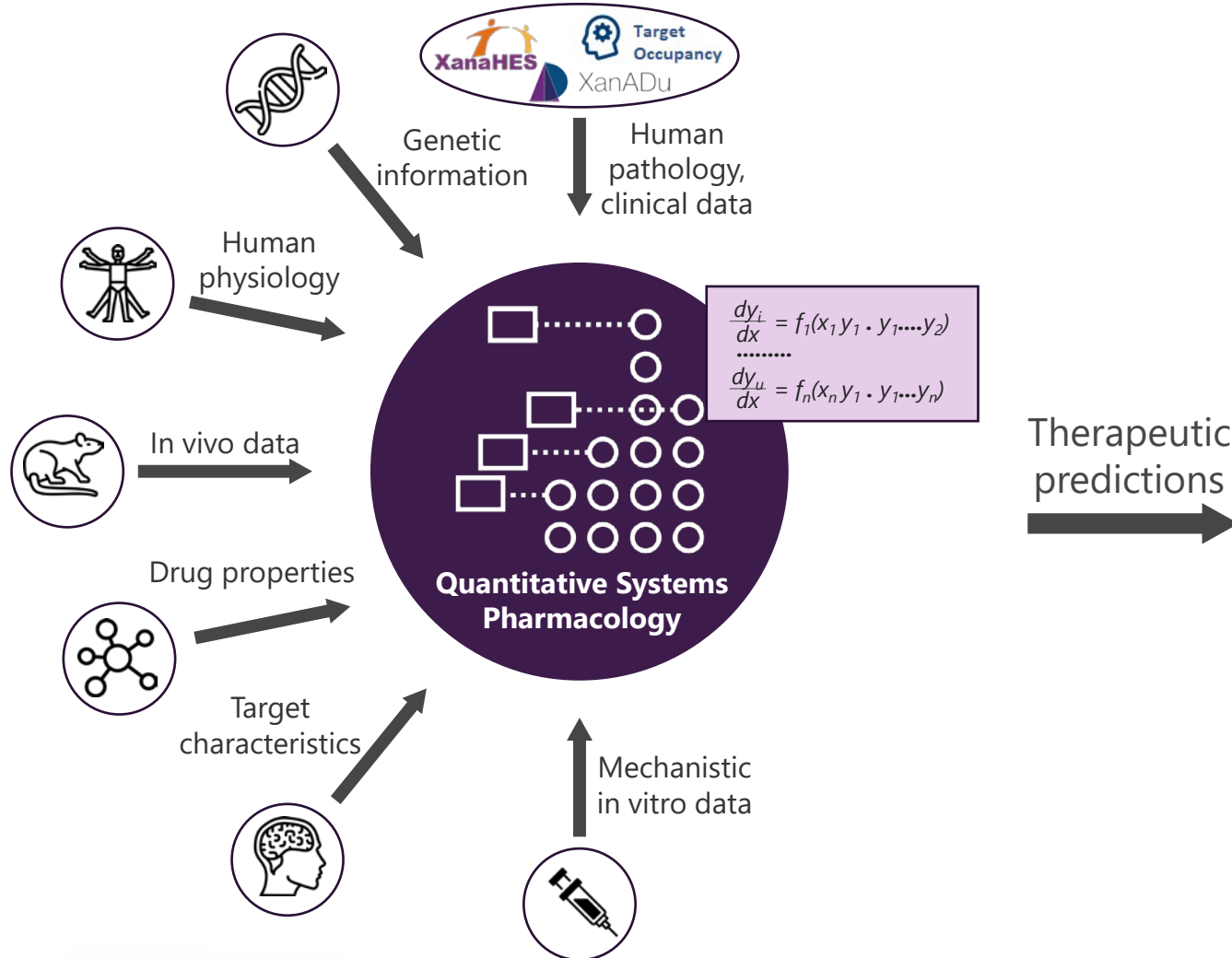
# Key outcomes from Xanamem studies

<i>Xanamem dose</i>		
 <b>Cognitive Efficacy</b>	Breakthrough results demonstrate a statistically significant clinical effect in <b>improving cognition</b> in healthy elderly patients	<i>20mg</i>
 <b>Target Occupancy</b>	Confirms <b>Xanamem works as designed</b> to penetrate the brain in concentrations that adequately inhibit the activity of 11 $\beta$ -HSD1 enzyme	<i>5mg - 30mg</i>
 <b>Cortisol inhibition</b>	<b>Cortisol inhibition</b> demonstrated in human trials	<i>10mg &amp; 20mg</i>
	<b>Statistically significant reduction</b> in serum cortisol in human trial	<i>20mg</i>
 <b>Safety</b>	<b>Strong safety profile</b> demonstrated in human trials	<i>10mg &amp; 20mg</i>



# Detailed data analysis completed

Quantitative Systems Pharmacology modelling and analysis



Analysis of entire dataset completed  
Conclusions will be used to optimise parameters for next series of clinical studies, including:



**Dose**



**Dosing Regimen**



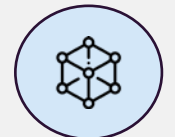
**Treatment Duration**



**Patient Characteristics**



**Endpoints & Outcomes**



**Stratification Factors**

# Strategic direction and next steps

Updated clinical development plan incorporating new Xanamem data supporting clinical development opportunities across multiple indications

## Enhanced clinical development strategy (in progress)



**Comprehensive review** of all Xanamem data, new target indications, and potential funding options, to inform strategic direction



**Clinical development plan** includes planning for and ongoing evaluation into feasibility of studies in **multiple indications**



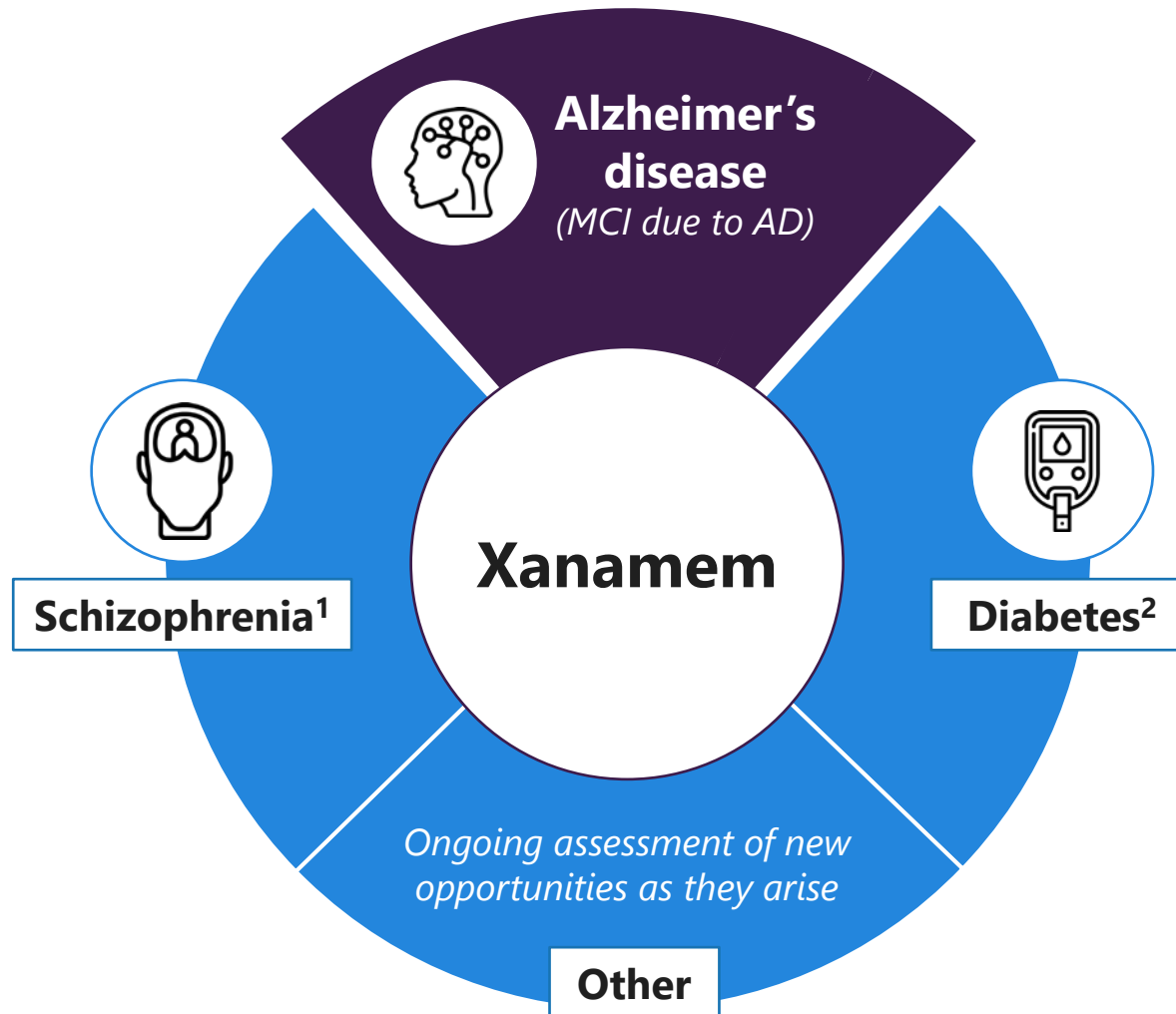
Proactive engagement with **key opinion leaders** and **relevant regulatory bodies**, and potential **collaboration and partnership** discussions ongoing

## Next steps (near future)

**Clinical studies  
expected to initiate  
in 2020/21**

# Next series of Xanamem studies

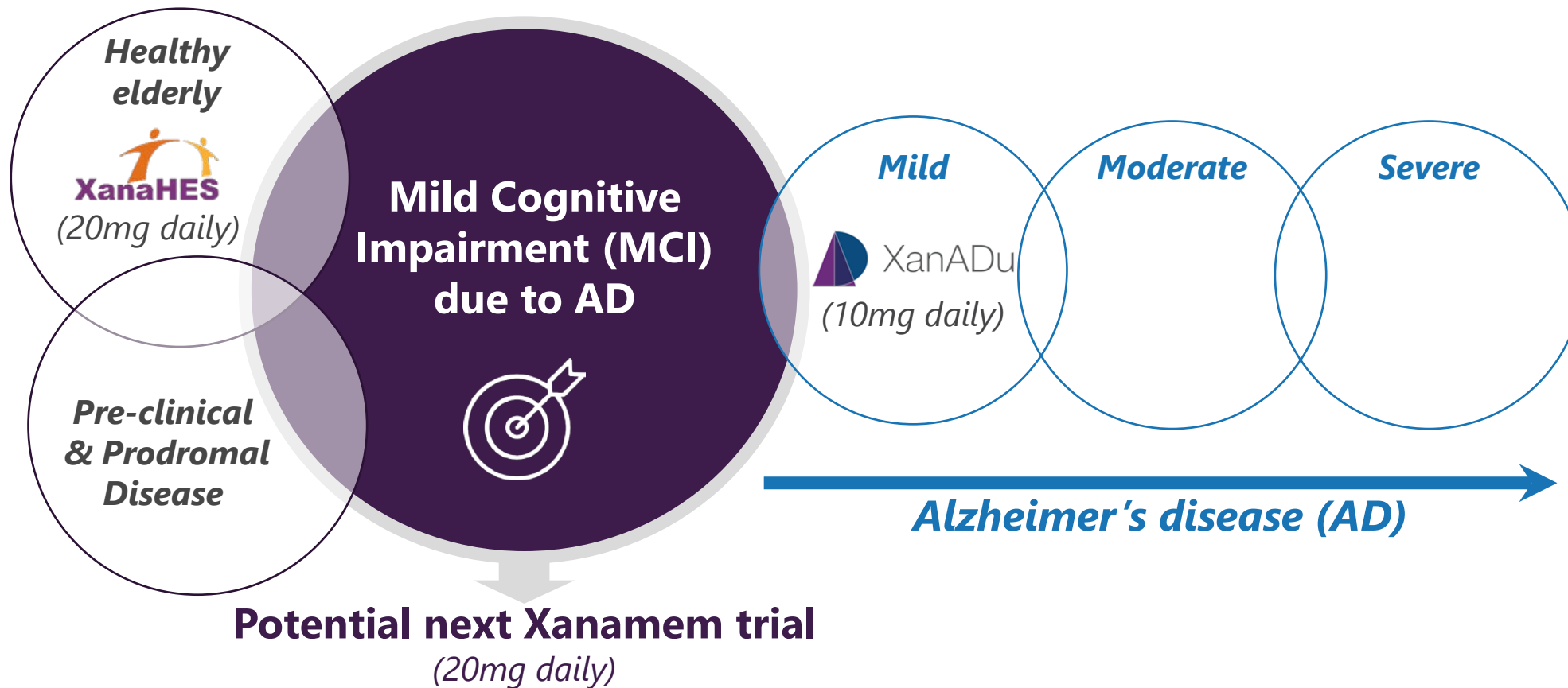
Actinogen leveraging Xanamem development across multiple target indications





## Alzheimer's disease focus

Actinogen plans to target patients with Mild Cognitive Impairment due to AD (an early stage of the AD spectrum) as part of the next phase of studies, linking the XanaHES results with Alzheimer's disease



Phase II trial in planning to demonstrate Xanamem's pro-cognitive effects on a MCI due to AD patient population





# Market dynamics of Alzheimer's disease

Early stage AD presents a compelling commercial opportunity for Actinogen to target

## High prevalence resulting in substantial target market<sup>1</sup>

Cognitively normal	Subjective memory decline	Cognitive and functional decline fulfilling dementia		
At-risk	MCI due to AD	Mild AD	Moderate AD	Severe AD
15.5m <sup>3</sup> -26.9m <sup>4</sup>	~4.3m	~1.7m	~2.3m	~1.7m

*Upside potential for earlier use*

*Key focus*

# >US\$13.7bn

Target annual peak sales<sup>2</sup>

## Underpinned by favourable market dynamics



Targeting **large addressable markets** (US, EU5, JP)



Currently approved drugs are symptomatic treatments only, **providing limited benefit**



Treatment **prices are robust**, with users paying for modest clinical efficacy

# Investment summary

Actinogen is developing Xanamem as a potential treatment for cognitive impairment associated with raised cortisol in a range of diseases, with a primary focus on Alzheimer's disease

- ✓ Xanamem – a **differentiated compound** with a **validated novel MoA** and **strong safety profile**
- ✓ Target Occupancy studies demonstrate **Xanamem works as designed to safely inhibit cortisol**
- ✓ XanaHES trial **achieved robust cognitive efficacy signal with Xanamem 20mg daily**
- ✓ Next phase of clinical development to investigate Xanamem across **multiple indications**, including a Phase II clinical trial **targeting patients with Mild Cognitive Impairment due to AD**
- ✓ **Optimised study parameters, including dose**, following latest trial results and data analysis
- ✓ Exploring potential **partnership and collaboration funding** opportunities
- ✓ Development targeting **huge unmet medical needs** associated with **unsustainable healthcare costs**

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