

**ASX ANNOUNCEMENT****Actinogen at SACHS Forum and JP Morgan week**

- Actinogen to present at the 3<sup>rd</sup> Annual SACHS Neuroscience Innovation Forum and participate in partnering meetings during JPM Week in San Francisco, USA
- Excellent opportunity for the Company to present the breakthrough XanaHES results and Xanamem's expanded dataset on a global stage
- Xanamem has been demonstrated to be an efficacious, brain penetrant and appropriately safe oral drug, with clinical results in line with its intended mechanism of action
- Actinogen will engage with investors, potential strategic partners and the scientific and medical communities during the JPM week

**Sydney, 8 January 2020. Actinogen Medical ASX: ACW ('ACW' or 'the Company')** will present at the 3<sup>rd</sup> Annual SACHS Neuroscience Innovation Forum and participate in numerous partnering meetings during JPM week in San Francisco, USA in January 2020.

The SACHS Forum and JPM Week provides the Company with an excellent opportunity to update the pharmaceutical industry and major global investors interested in Neuroscience on the compelling results achieved with XanaHES, and the expanded Xanamem dataset generated during 2019.

Latest Xanamem developments that will be discussed at both events include:

- Breakthrough XanaHES results demonstrating a robust and statistically significant effect on improving cognition in healthy elderly patients taking 20mg Xanamem daily
- Target Occupancy results confirming that Xanamem works as designed to penetrate the brain in concentrations that adequately inhibit the activity of the 11 $\beta$ -HSD1 enzyme
- Strong safety profile and cortisol inhibition demonstrated in human trials with 10mg and 20mg Xanamem

Following the Forum, Actinogen will participate in multiple partnering meetings during the week, which is concurrent with the 38<sup>th</sup> Annual J.P. Morgan Healthcare Conference. This preeminent global investment and business development conference attracts numerous international pharmaceutical leaders and investors.

Attached is the latest investor presentation that will be utilised in the SACHS presentation and discussed during the Company's numerous partnering meetings.

If you are interested in a meeting with Actinogen in San Francisco from 13 to 16 January 2020, please contact the Company using the details below.

**ENDS****Actinogen Medical**

Dr. Bill Ketelbey  
CEO & Managing Director  
P: +61 2 8964 7401  
E: bill.ketelbey@actinogen.com.au

 @BillKetelbey

**Investor and Media Enquiries**

Arthur Chan  
WE Communications  
P: +61 2 9237 2805  
E: arthurc@we-worldwide.com

**ACTINOGEN MEDICAL LIMITED** TRADING AS ACTINOGEN MEDICAL ACN 086 778 476 ASX | ACW

Suite 901, Level 9, 109 Pitt Street, Sydney NSW 2000 AUSTRALIA

TELEPHONE +61 2 8964 7401

WEB [www.actinogen.com.au](http://www.actinogen.com.au)

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

### **About SACHS Neuroscience Innovation Forum**

The 3<sup>rd</sup> Annual Neuroscience Innovation Forum for BD&L and Investment in Therapeutics and Technology is to take place at the Marines' Memorial Club, San Francisco on the 12 January 2020. The program will cover BioPartnering for CNS, with industry keynotes and panels on AD, PD, Neuropsychiatry and Pain Management. The Forum brings together biotech companies focused on central nervous system conditions with partnering executives from pharm, biotech and medtech companies and analysts from investment banks and funds.

### **About Actinogen Medical**

Actinogen Medical (ASX: ACW) is an ASX-listed biotechnology company developing novel therapies for cognitive impairment associated with chronic neurological 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 and mood 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 other therapies for Alzheimer's disease. It works by blocking the excess production of intracellular cortisol – the stress hormone – through the inhibition of the 11β-HSD1 enzyme in the brain. There is a strong association between persistent stress and the production of excess cortisol that leads to changes in the brain, affecting memory. The 11β-HSD1 enzyme is highly concentrated in the hippocampus and frontal cortex, the areas of the brain associated with cognitive impairment in neurological diseases, including Alzheimer's disease, schizophrenia and the mood disorders. The Company's XanaHES Phase I trial exploring the safety and tolerability of Xanamem™ 20mg once daily in healthy elderly volunteers, showed that the drug exhibited a good 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 data recently generated, confirms the underlying mechanism of action of Xanamem.

The Company plans to initiate Phase II studies of Xanamem in various disease areas in 2020, including in Alzheimer's disease, and in cognitive impairment associated with schizophrenia, mood disorders and diabetes.

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

# Investor Presentation

## 3<sup>rd</sup> Annual Neuroscience Innovation Forum

*Developing innovative treatments for cognitive impairment associated with a number of medical conditions, including Alzheimer's disease*

Dr. Bill Ketelbey: CEO & MD

12 January 2020



# Xanamem – our lead compound under development

A novel MoA designed to inhibit cortisol production in the brain, with proof of concept in animals and in humans, a strong safety profile and significant data on dosing



**Novel MoA**  
(*cortisol inhibition*)



**POC demonstrated in animal trials**



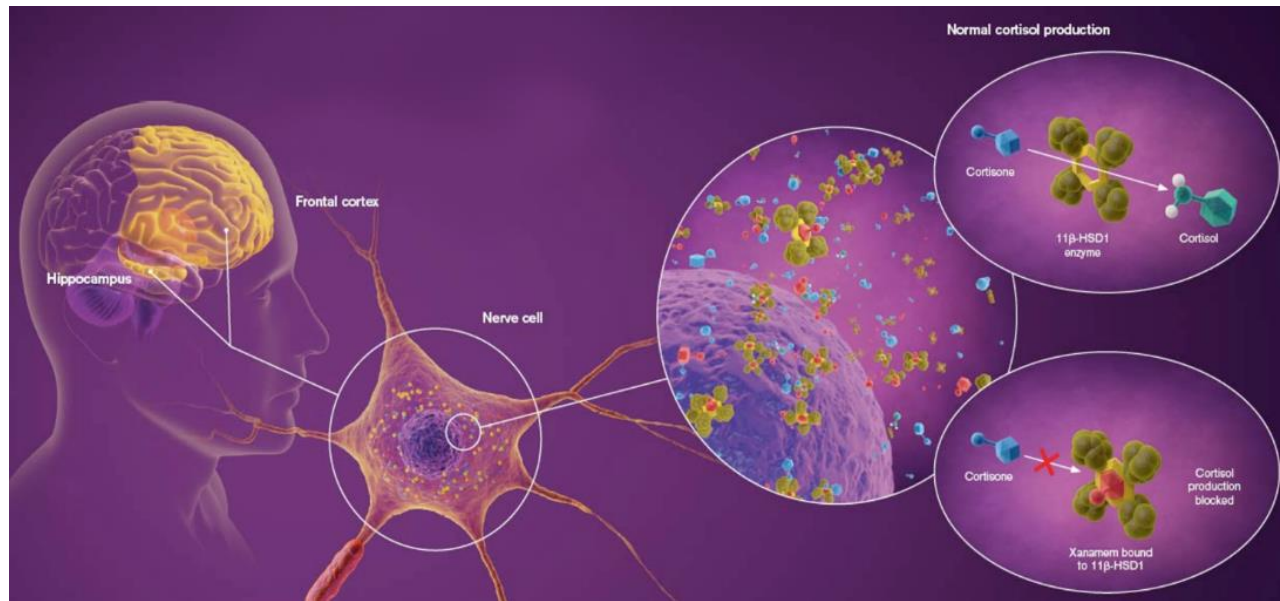
**POC demonstrated in human trials**



**Strong safety profile**







**Excellent dosing data**



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

# 2019 highlights: Xanamem's efficacy demonstrated!

Deepened the understanding and significantly enhanced the dataset on Xanamem

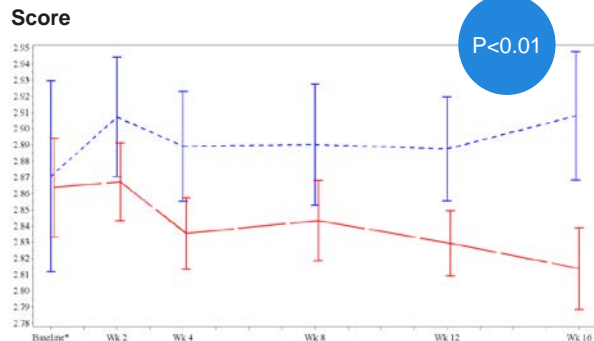
	 <b>Target Occupancy &amp; Homogenate Binding Studies</b>	 XanADu	 <b>Additional Toxicology Studies</b>
<i>Efficacy shown in Phase 1 clinical trial in healthy elderly patients (20mg Xanamem daily)</i>	<i>Phase 1 Target Occupancy, &amp; Homogenate Binding Studies</i>	<i>Phase 2 clinical trial in mild Alzheimer's disease (10mg Xanamem daily)</i>	<i>Pre-clinical safety and toxicology studies to allow longer treatment periods</i>
✓ <b>Completed</b>	✓ <b>Progressing on schedule</b>	✓ <b>Completed</b>	✓ <b>Progressing on schedule</b>

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

Breakthrough XanaHES results demonstrate strong statistically significant cognitive efficacy improvement in multiple cognition domains – based on Cogstate Cognitive Test Battery

## Working memory (One Back Test)

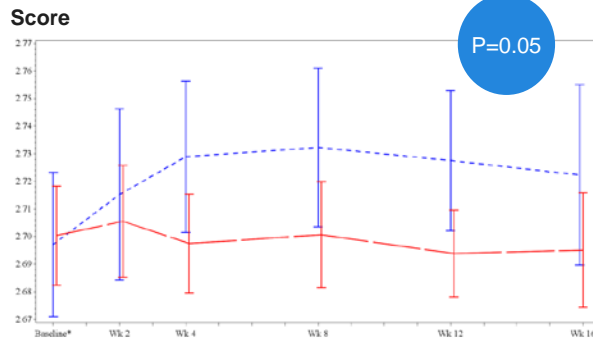
**Strongly statistically significant result**



**Rapid response, evident by week 4, and sustained response out to end of therapy (wk 12)**

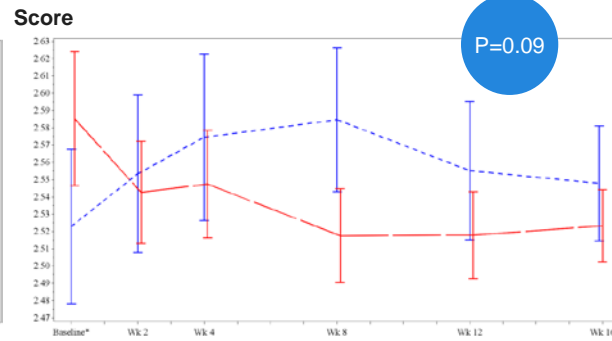
## Visual attention (Identification Test)

**Statistically significant result**



## Psychomotor function (Detection Test)

**Good trend to a positive result**



**Treatment Group**  
 — Xanemem — Placebo

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

Cogstate Cognitive Test Battery evaluated six domains. Statistically significant cognitive improvement in three domains with significant effect size demonstrated. Rapid and sustained response achieved.

## XanaHES 20mg Cogstate Cognitive Test Battery: p values and Cohen's d effect size

Cognitive Evaluation (Test)	p value			Treatment Effect Size: Cohen's d			
	All	Male	Female	Week 2	Week 4	Week 8	Week 12
Working Memory (One Back Test)	<0.01*	<0.01*	0.03*	0.64#	0.78#	0.64#	0.83 <sup>Δ</sup>
Visual Attention (Identification Test)	0.05*	0.04*	0.60	0.19	0.67#	0.62#	0.67#
Psychomotor Function (Detection Test)	0.09 <sup>^</sup>	0.94	0.13	0.47	0.65#	1.12 <sup>Δ</sup>	0.76#
Paired Associate Learning (CPAL <sup>1</sup> Test)	0.21	0.34	0.49	0.87 <sup>Δ</sup>	0.01	0.66#	0.08
Memory (CPAL <sup>1</sup> – Delayed Test)	0.50	0.55	0.21	0.34	0.23	0.06	0.48
Visual Learning (One Card Learning Test)	0.92	0.41	0.64	0.11	0.12	0.60#	0.19

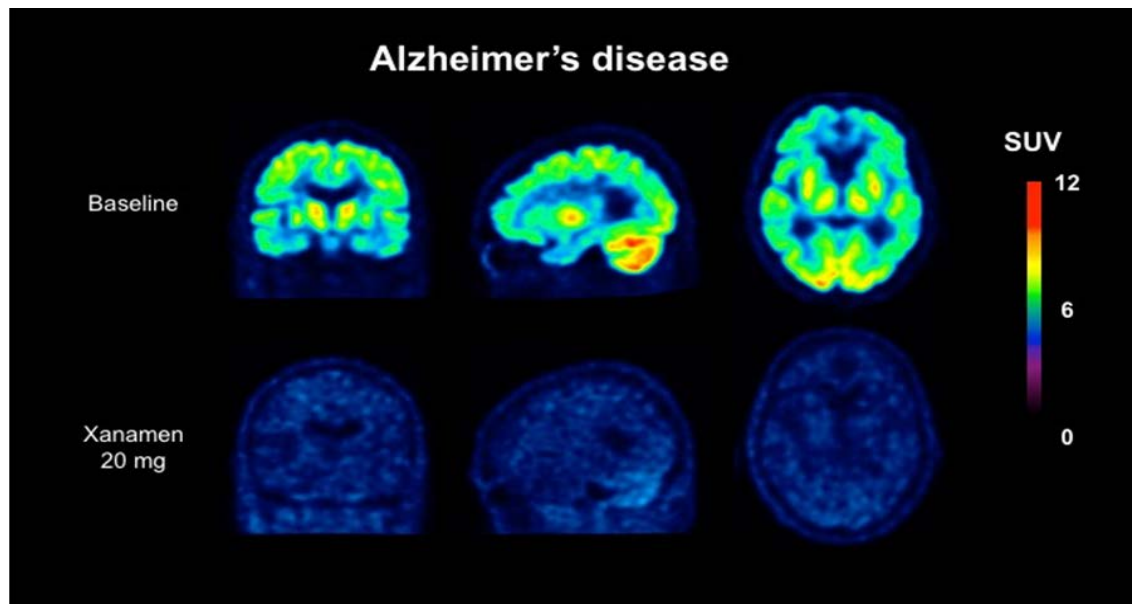
Notes: \* statistical significance achieved; ^ strong trend to statistical significance; # effect size >0.5 (moderate treatment effect); Δ effect size >0.8 (large treatment effect)

1: CPAL – Continuous Paired Associate Learning



# Target Occupancy Study: preliminary results

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



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





**Additional ongoing cohorts at 10mg  
Xanamem with delayed PET imaging  
to demonstrate CNS PK**

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

1. Study population consisted of ~50% healthy subjects (cognitively normal) and ~50% with Alzheimer's disease



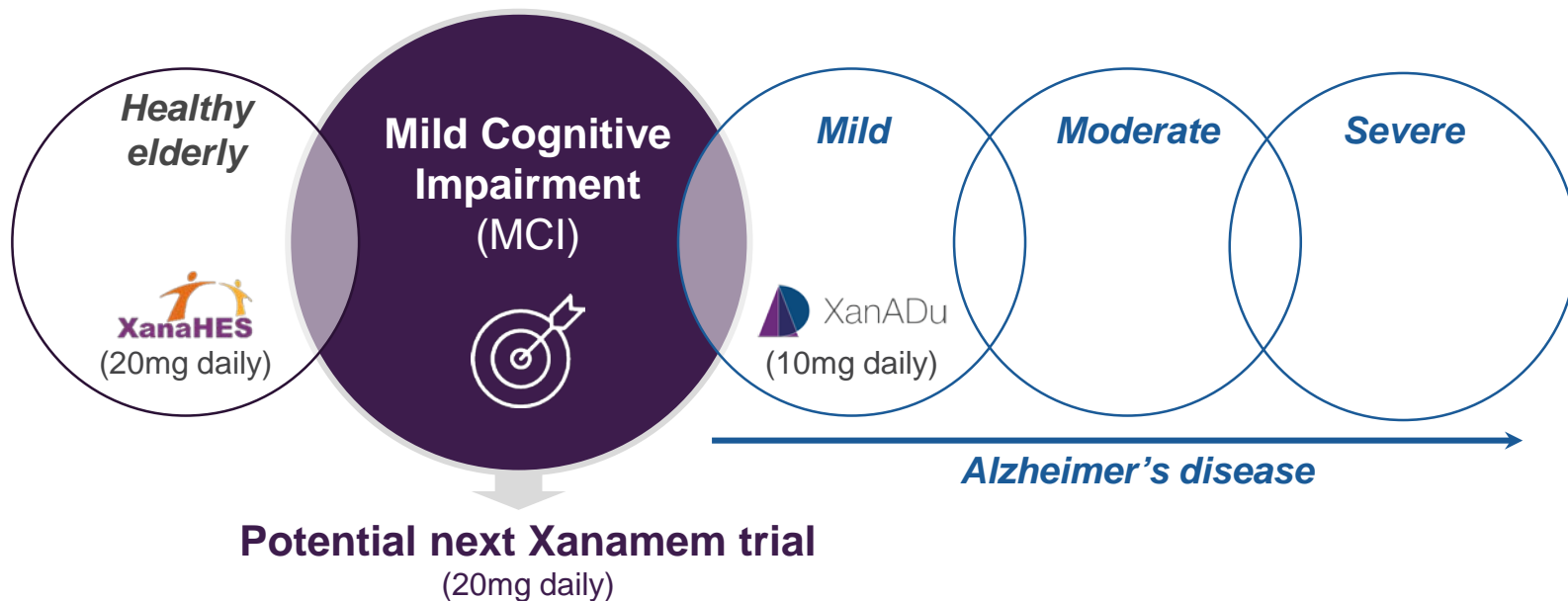
# Key outcomes from Xanamem studies

		<i>Xanamem dose</i>
 <b>Cognitive Efficacy</b>	Breakthrough results demonstrate a statistically significant clinical effect on improving cognition in healthy elderly patients <sup>1</sup>	<i>20mg</i>
 <b>Target Occupancy</b>	Confirms Xanamem works as designed to penetrate the brain in concentrations that adequately inhibit the activity of 11 $\beta$ -HSD1 enzyme	<i>5mg - 30mg</i>
 <b>Cortisol inhibition</b>	Cortisol inhibition demonstrated in human trials Statistically significant reduction in serum cortisol in human trial	<i>10mg &amp; 20mg</i> <i>20mg</i>
 <b>Safety</b>	Strong safety profile demonstrated in human trials <sup>2</sup>	<i>10mg &amp; 20mg</i>

1. After 12 weeks therapy; effect apparent after only 4 weeks, and sustained on therapy  
 2. No treatment related serious adverse events reported after 12 weeks therapy

# Alzheimer's disease – the primary development focus

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

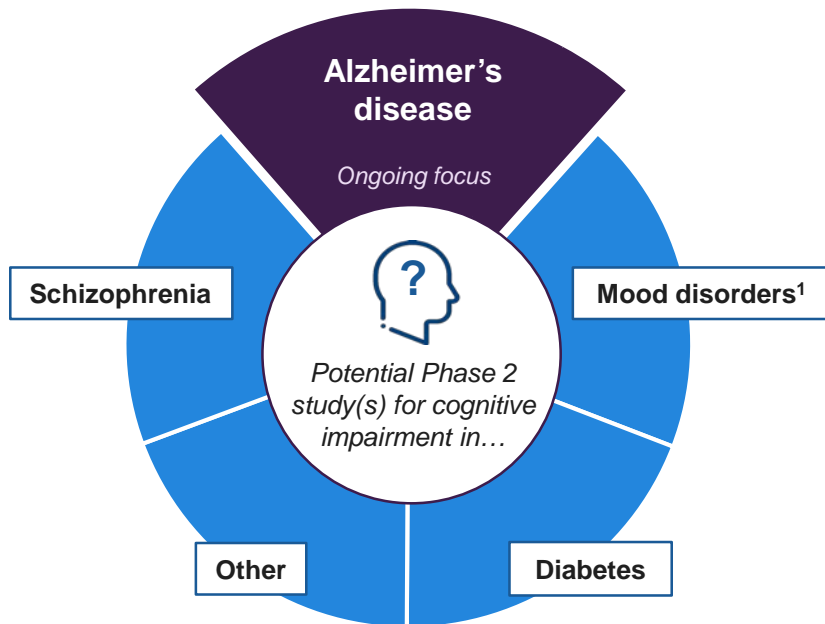


Study design to be confirmed and refined following discussions with the FDA and other regulators

# Determining the next set of Xanamem studies

Actinogen is considering how to best leverage Xanamem development across multiple target indications and determining the optimal study parameters going forward

## Leveraging platform technology



## Optimising study parameters



Dose



Dosing  
regimen



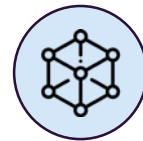
Duration



Size



Measurement  
tools



Patient  
populations

1. Cognitive impairment in Mood disorders, such as bipolar disorder

# Strategic direction and next steps

Updated clinical development plan is currently well advanced, incorporating Xanamem data gathered and potential clinical development opportunities across multiple indications

## Update clinical development strategy (in progress)

- **Comprehensive review** of all Xanamem data, new target indications and potential funding options – informs strategic direction
- **Clinical development plan** includes new studies in Alzheimer's disease and cognitive impairment associated with schizophrenia, bipolar disorder and diabetes
- **Grant applications** submitted for non-dilutive funding alternatives
- Proactive engagement with **key opinion leaders** and **relevant regulatory bodies**
- Potential **collaboration and partnership** discussions continue

## Next steps (near future)

**Clinical studies expected to initiate in 2020**

**Actinogen to present data and results at AD/PD in April 2020<sup>1</sup>**

1. International Advancement in Alzheimer's and Parkinson's Disease Therapies (AD/PD) Focus Meeting - includes all the latest breakthroughs in drug development, translational R&D, early diagnosis, and clinical trials

# Investment summary

Actinogen is developing innovative treatments for cognitive impairment associated with a number of medical conditions, with a primary focus on Alzheimer's disease

---

- ✓ Xanamem – a **differentiated compound** (efficacious, oral, brain penetrant, selective 11 $\beta$ -HSD1 inhibitor) with a **validated novel mechanism of action** and **strong safety profile**
- ✓ XanaHES trial **achieved robust cognitive efficacy signal** with results supporting the cortisol hypothesis
- ✓ Next phase of Alzheimer's disease clinical development to **target patients with Mild Cognitive Impairment (MCI)** – based on recently completed XanaHES results
- ✓ Leverage Xanamem platform technology across **multiple indications**, including cognitive impairment associated with schizophrenia, bipolar and diabetes
- ✓ **Study parameters optimised, including dose**, following latest trial results
- ✓ Exploring potential **partnership and collaboration funding** opportunities
- ✓ Xanamem development targeting a **huge unmet medical need** with **unsustainable healthcare costs**

# Disclaimer

This presentation has been prepared by Actinogen Medical 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).

# **Appendix: Background information**

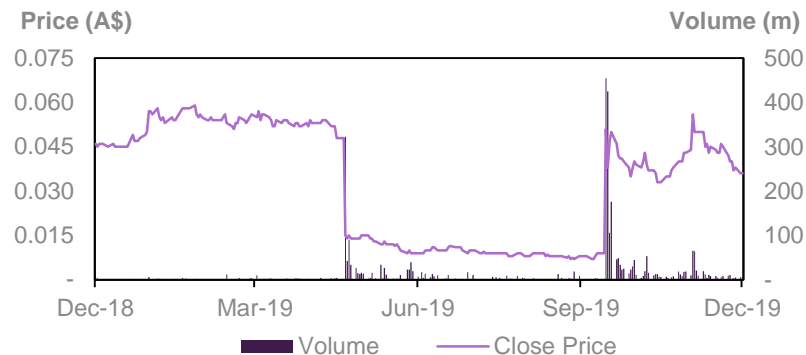




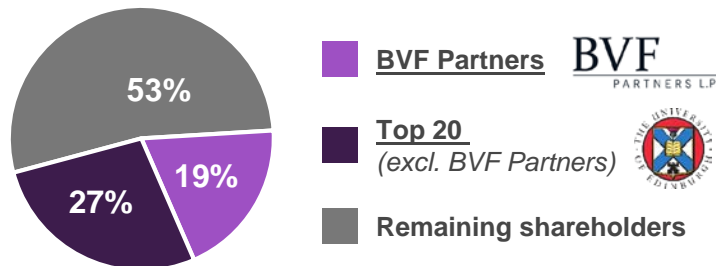
# Corporate overview ASX:ACW

Actinogen is an ASX-listed biotech company focused on innovative approaches to treating cognitive impairment associated with neurological and metabolic diseases

## LTM share price performance



## Key shareholding metrics



## Board of Directors



**Dr. Geoff Brooke**

**Chairman**

MBBS; MBA

- **30+ years experience** in the healthcare investment industry
- Founder and MD of Medvest Inc and GBS Venture Partners



**Dr. Bill Ketelbey**

**CEO & MD**

MBBCh; FFPM; MBA; GAICD

- **30+ years experience** in healthcare, biotech and pharmaceutical industries
- Formerly senior international roles at Pfizer and Director at Westmead Institute of Medical Research



**Dr. George Morstyn**

**Non-executive director**

MBBS; PhD; FRACP; MAICD

- **25+ years experience** in biotech investment and drug development
- Board member of Biomedvic, Cancer Therapeutics and Symbio; Former Senior VP and SMO at Amgen



**Mr. Malcolm McComas**

**Non-executive director**

BEC, LLB; FAICD; SF Fin

- **25+ years experience** in the financial services industry
- Chairman of Pharmaxis and Fitzroy River Corporation; formerly senior leadership roles in investment banking



# Advisory Boards

World's premier academics involved in the development of Xanamem and as a novel treatment for Alzheimer's disease

## Clinical Advisory Board (Alzheimer's disease)

*Positions Xanamem at the forefront of  
Alzheimer's drug development*



**Prof. Craig  
Ritchie** *Chair*



THE UNIVERSITY  
of EDINBURGH



**Prof. Colin  
Masters** *AO*



The Royal  
Melbourne Hospital

THE  
**FLOREY**  
INSTITUTE OF NEUROSCIENCE & MENTAL HEALTH



**Prof. Jeffrey  
Cummings**



**Cleveland  
Clinic**



**Prof. Jonathan  
Seckl**



THE UNIVERSITY  
of EDINBURGH



**Prof. Brian  
Walker**



**Newcastle  
University**



**Prof. Scott  
Webster**



THE UNIVERSITY  
of EDINBURGH

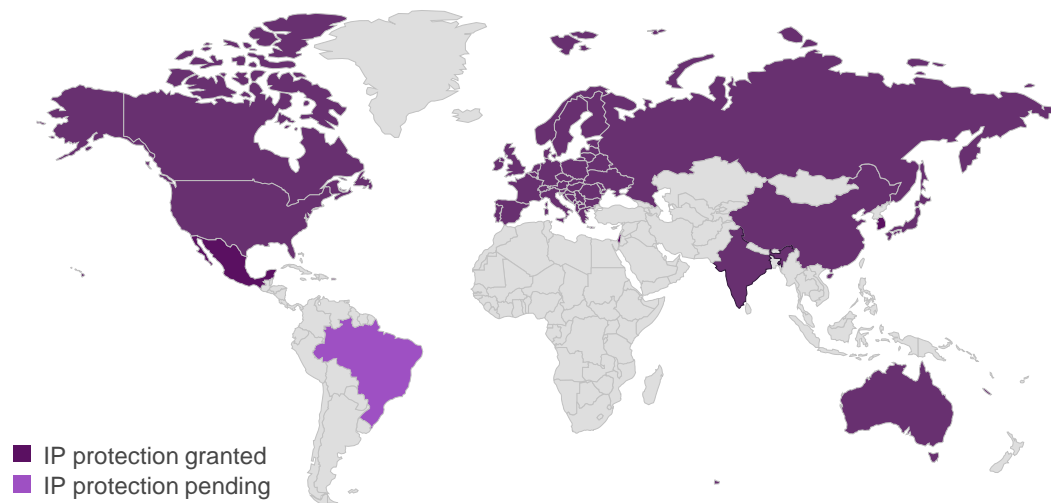
## Scientific Advisory Board

*Combining deep understanding of cortisol,  
11 $\beta$ -HSD1 and drug discovery*

# IP protection

Actinogen maintains a broad granted composition of matter patent estate, with key patents granted in all major target markets

## Geographic patent overview



- Actinogen's patent portfolio **covers a broad range of neurological and metabolic diseases** including Alzheimer's disease
- Xanomem **patents granted in key markets** that account for over 90% of the global Alzheimer's market
- Additional patents and patent extension being actively prosecuted**

**>90%** of the global Alzheimer's disease market

A novel drug designed to inhibit cortisol production in the brain, with the potential to treat cognitive impairment



## Well researched

>15 years of R&D completed



## Well tolerated

Dosed >200 patients with strong clinical safety, toxicity & PK / PD<sup>1</sup> profile



## Well protected

Composition of matter IP coverage, patents granted in all major markets



## Validated in Alzheimer's model

Symptomatic and disease modifying effects (in vivo) and demonstrated effect of cortisol hypothesis (in humans)

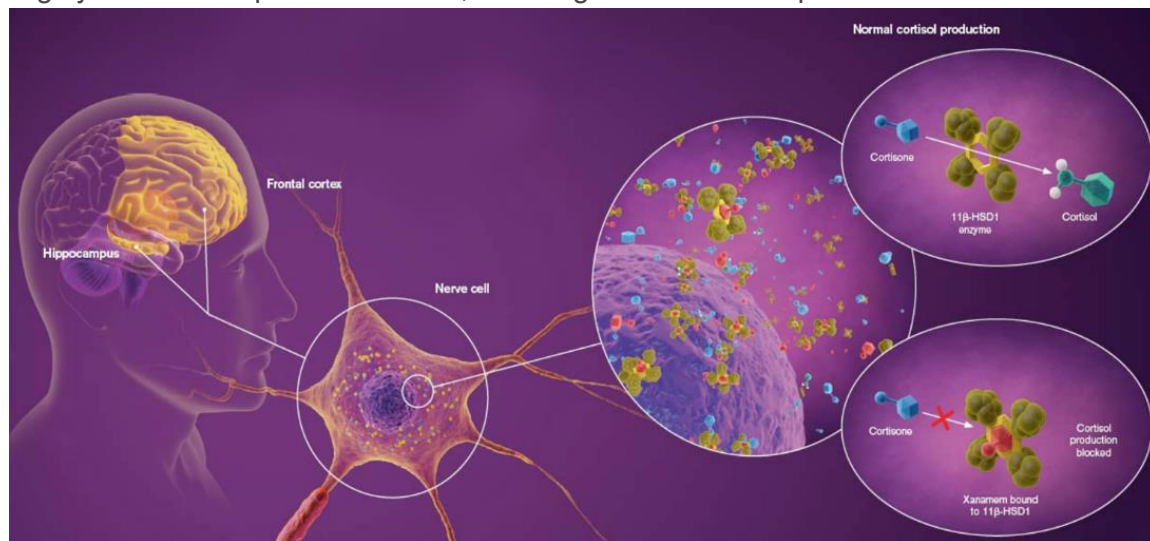


## Potential in other diseases

Cognitive impairment in schizophrenia, mood disorders and diabetes

## Differentiated mechanism of action:

Highly selective 11 $\beta$ HSD1 inhibitor, reducing excess cortisol production in the brain



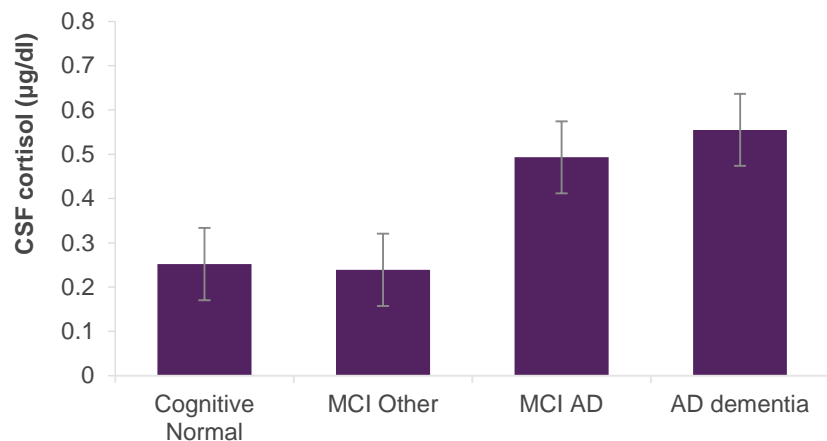
**Xanamem is a novel, first-in-class, potent, orally bioavailable and brain-penetrant 11 $\beta$ -HSD1 inhibitor**

1. PK / PD: pharmacokinetic / pharmacodynamic

# Alzheimer's strategic focus underpinned by medical research

A growing body of medical literature supports the association between cortisol and Alzheimer's disease

## 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 and progression<sup>2</sup>**

AIBL<sup>3</sup> study provides compelling evidence that elderly subjects with **higher plasma cortisol levels are at much greater risk of developing Alzheimer's disease**

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

# Market dynamics of Alzheimer's disease

Presents a compelling commercial opportunity for Actinogen to target initially

## Substantial target market with significant upside<sup>1</sup>

Cortisol-high, cognition normal	Subjective memory decline	Cognitive and functional decline fulfilling dementia		
At-risk	Prodromal	Mild	Moderate	Severe
~25.0m (50% over 65 yrs)	~4.0m	~1.5m	~1.7m	~2.5m

Upside potential for earlier use      Key focus

  
**>US\$7.5bn**

Target annual peak sales (mild AD)<sup>2</sup>

Source: Drugs.com, Biogen, Roche, Datamonitor, Alzheimer's Association

1. Target market statistics based on the current US treatment landscape

2. Base case annual peak sales assumes: (1) Launch: US 2024, EU5, JP and ROW 2025; (2) Penetration: 30% of mild AD market in 5 years (i.e. ~470,000 in the US); (3) Pricing: US – US\$19/day gross (US\$12/day net), ROW: 50% of US price

## Underpinned by favourable market dynamics

- ✓ Targeting **large addressable** markets (US, EU5, JP)
- ✓ All **currently approved drugs are symptomatic treatments** (that do not affect disease progression) **providing limited benefit**
- ✓ Treatment **prices are robust** (despite generic competition) – with users paying for modest clinical efficacy

## US branded products (gross price)



US\$10/day



US\$8/day



US\$18/day

# Big Pharma interest

Global Big Pharma demonstrating strong M&A interest in acquiring or partnering with companies and licensing novel mechanism of action assets with Alzheimer's disease as the lead/key indication

