ASX ANNOUNCEMENT

Managing Director's AGM Presentation

Sydney, 25 November 2019. Actinogen Medical ASX: ACW ('ACW' or 'the Company') is pleased to release an updated Investor Presentation that will be used in part for the Managing Director's AGM presentation.

Key Highlights

- XanaHES trial (20mg Xanamem daily) achieved a robust cognitive efficacy improvement, with results supporting the cortisol hypothesis
- Actinogen's lead compound, Xanamem, demonstrated to be an efficacious, oral, brain penetrant, selective 11β-HSD1 inhibitor, with a validated novel mechanism of action and strong safety profile
- Next phase of Xanamem's Alzheimer's disease clinical development, expected to target patients with Mild Cognitive Impairment – based on recently completed XanaHES results
- The Company plans to leverage its Xanamem platform technology across multiple other indications, including cognitive impairment associated with schizophrenia, bipolar and diabetes
- Future study parameters being optimised, including dose and dosing regimen following latest trial results. Also exploring potential partnership and collaborative funding opportunities
- Xanamem development is targeting huge unmet medical needs with unsustainable healthcare costs

ENDS

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About Actinogen Medical

Actinogen Medical (ASX: ACW) is an ASX-listed biotechnology company focused on innovative approaches to treating cognitive decline that occurs in chronic neurological and metabolic diseases. Actinogen Medical is developing its lead compound Xanamem, as a promising new therapy for Alzheimer's disease, a condition with multibillion-dollar market potential and material human impact. In the US alone, the cost of managing Alzheimer's disease is estimated to be US$250bn and is projected to increase to US$2tn by 2050, outstripping the treatment costs of all other diseases. Alzheimer's disease is now the leading cause of death in the UK and second only to ischaemic heart disease in Australia. In addition, Actinogen is currently planning an expanded clinical development program for Xanamem in cognitive impairment in mood disorders and schizophrenia. In the US alone, the collective economic costs of mood disorders and schizophrenia are estimated to exceed $550bn, with the burden increasing every year. The cognitive dysfunction associated with these conditions is significantly debilitating for affected patients, with a substantial unmet medical need for novel, improved treatments.

About Xanamem™

Xanamem's novel mechanism of action sets it apart from other Alzheimer's treatments. It works by blocking the excess production of cortisol - the stress hormone – through the inhibition of the 11β-HSD1 enzyme in the brain. There is a strong association between chronic stress and 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, mood disorders and schizophrenia.

About XanADu

XanADu is a Phase II double-blind, 12-week, randomised, placebo-controlled study to assess the safety, tolerability and efficacy of Xanamem 10mg daily in subjects with mild dementia due to Alzheimer's disease. XanADu has fully enrolled 186 patients from 25 research sites across Australia, the UK and the USA. The trial is registered on www.clinicaltrials.gov with the identifier: NCT02727699, where more details on the trial can be found, including the study design, patient eligibility criteria and the locations of the study sites.

About XanaHES

XanaHES is a Phase I, randomised, single blinded, central reader blinded, placebo-controlled, dose escalation study to assess the safety and tolerability of Xanamem™ 20mg once daily in healthy elderly volunteers. Changes in cognitive performance from baseline to end-of-treatment are measured as an exploratory efficacy outcome.

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

AGM Presentation

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

Dr. Bill Ketelbey: CEO & MD

25 November 2019

Actinogen Medical

2019 Highlights: Xanamem's efficacy demonstrated!

Enhancing the Xanamem dataset

Actinogen Medical

XanaHES

Efficacy shown in Phase 1 clinical trial in healthy elderly patients (20mg Xanamem daily)

✓ **Completed**

Target Occupancy & Homogenate Binding Studies

Phase 1 Target Occupancy, & Homogenate Binding Studies

✓ **Progressing on schedule**

XanADu

Phase 2 clinical trial in mild Alzheimer's disease (10mg Xanamem daily)

✓ **Completed**

Additional Toxicology Studies

Pre-clinical safety and toxicology studies to allow longer treatment periods

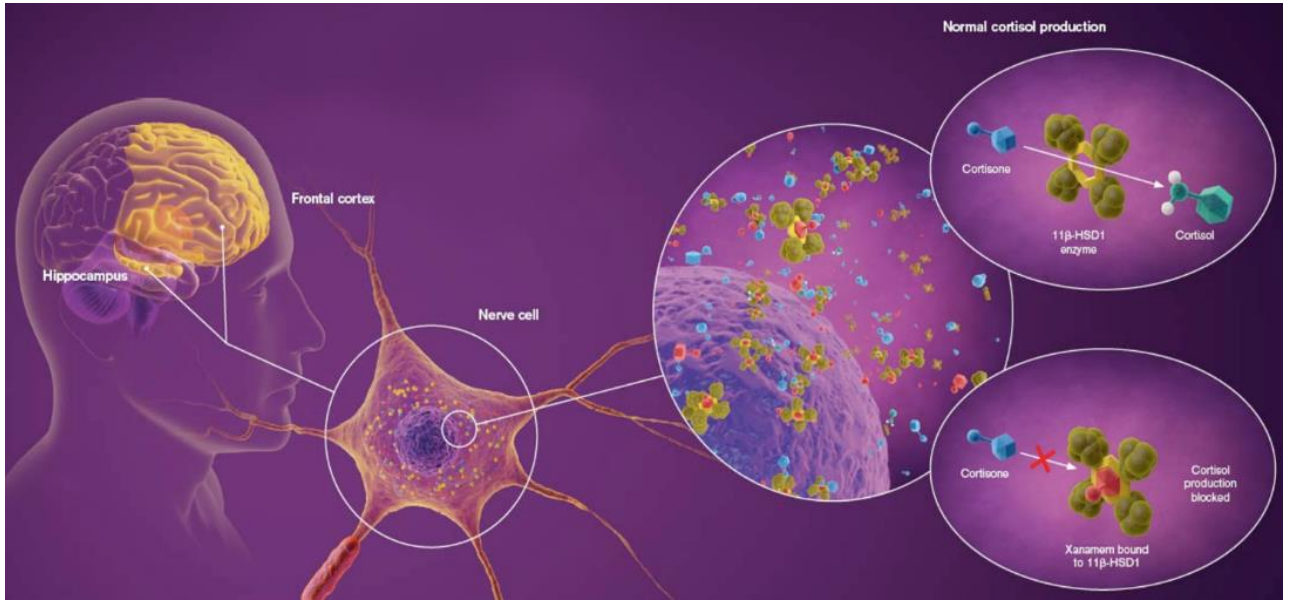
✓ **Progressing on schedule**

Rapidly increasing addressable AD market, while other drugs under development for AD, continue to fail

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 11β-HSD1 inhibitor with a strong safety profile

1. POC: proof of concept; MoA: Mechanism of Action

Significant Cognitive Efficacy Signal Achieved

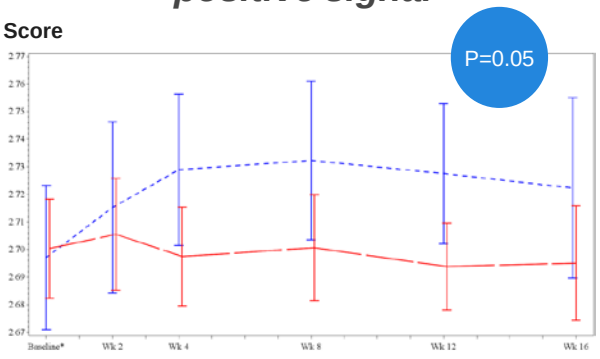
Breakthrough XanaHES results demonstrate strong statistically significant cognitive efficacy improvement in multiple cognition domains – based on Cogstate Cognitive Test Battery

Working memory (One Back Test)

Strongly statistically significant result

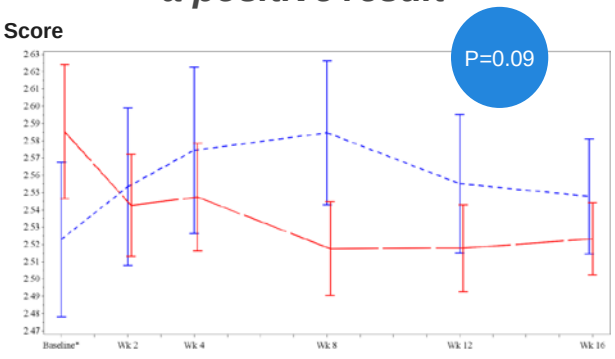
Visual attention (Identification Test)

Statistically positive signal



Psychomotor function (Detection Test)

Good trend to a positive result



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

Baseline* Mean of Observed Data

Significant Cognitive Efficacy Signal Achieved

Cogstate Cognitive Test Battery evaluated six domains. Statistically significant cognitive improvement in three domains with significant effect size demonstrated

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

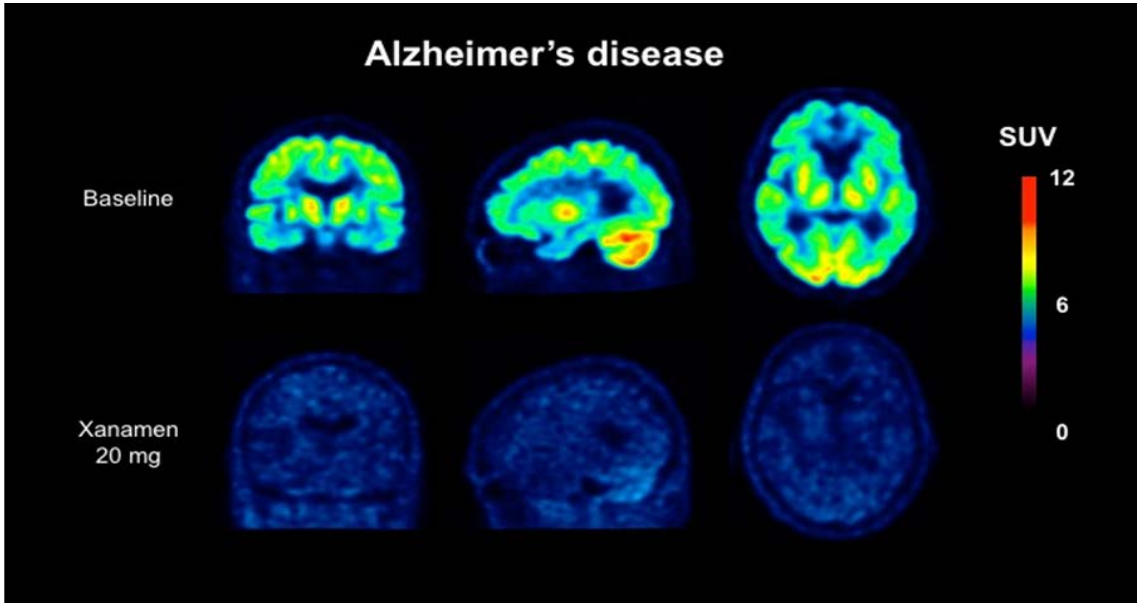
Cognitive Evaluation (Test)	p value			Treatment Effect Size: Cohen's d			
	All	Male	Female	Week 2	Week 4	Week 8	Week 12
Working Memory (One Back Test)	**<0.01***	**<0.01***	**0.03***	**0.64#**	**0.78#**	**0.64#**	**0.83Δ**
Visual Attention (Identification Test)	**0.05***	**0.04***	0.60	0.19	**0.67#**	**0.62#**	**0.67#**
Psychomotor Function (Detection Test)	**0.09**	0.94	0.13	0.47	**0.65#**	**1.12Δ**	**0.76#**
Paired Associate Learning (CPAL[1] Test)	0.21	0.34	0.49	**0.87Δ**	0.01	**0.66#**	0.08
Memory (CPAL[1] – 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; # 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 10-30mg Xanamem dosed for seven days significantly occupies the neuronal 11β-HSD1 enzyme throughout the brain



50% to 85% occupancy, dependent upon brain region, dosage and study subject

Further study data available in 4Q CY2019

Additional ongoing cohorts at 5mg Xanamem and 10mg with delayed PET imaging

Phase I Target Occupancy supports Xanamem as a potent, orally bioavailable and brain-penetrant 11β-HSD1 inhibitor

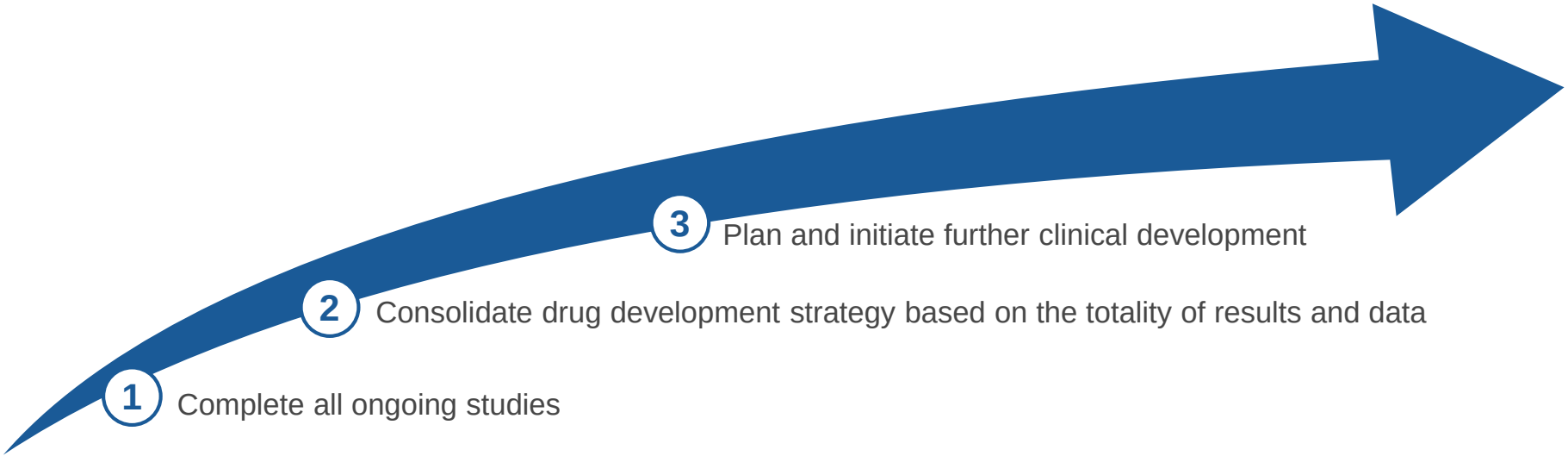
Key outcomes from Xanamem studies

Target Occupancy	Xanamem **10mg-30mg** achieves target occupancy (50-85%) of 11B-HSD1 enzyme in the brain
Cortisol inhibition	Xanamem **10mg and 20mg** inhibits cortisol production and; Xanamem **20mg** achieves statistically significant reduction in serum cortisol
Safety	Xanamem **10mg and 20mg** – no treatment related serious adverse events reported after 12 weeks therapy
Cognitive Efficacy	Xanamem **20mg** - statistically significant **cognitive improvement** in healthy volunteers after 12 weeks therapy; effect apparent after only 4 weeks, and sustained

Strategic direction and next steps

The totality of the information from all Xanamem studies are informing Actinogen's decisions on its future clinical development

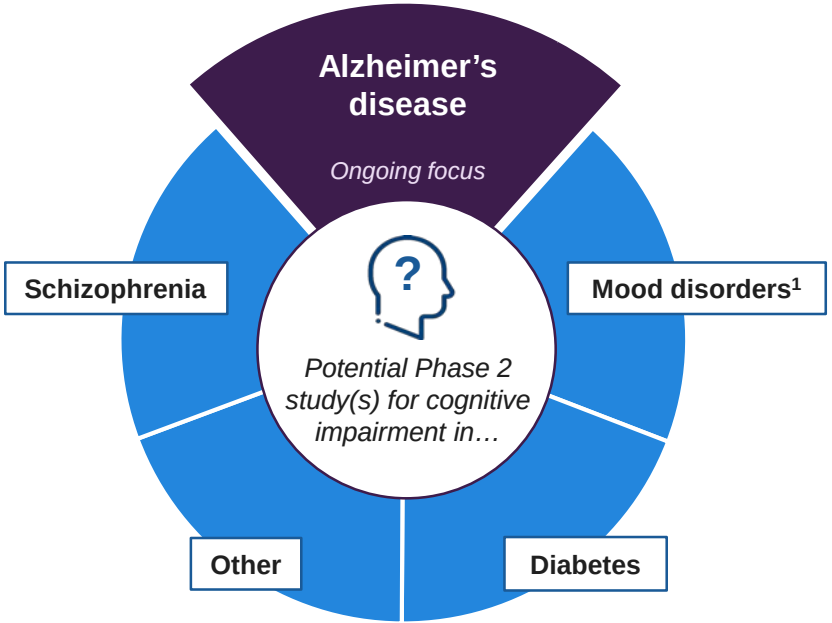
Xanamem - an **efficacious, oral, brain penetrant, selective 11β –HSD1 inhibitor with a good safety profile**



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

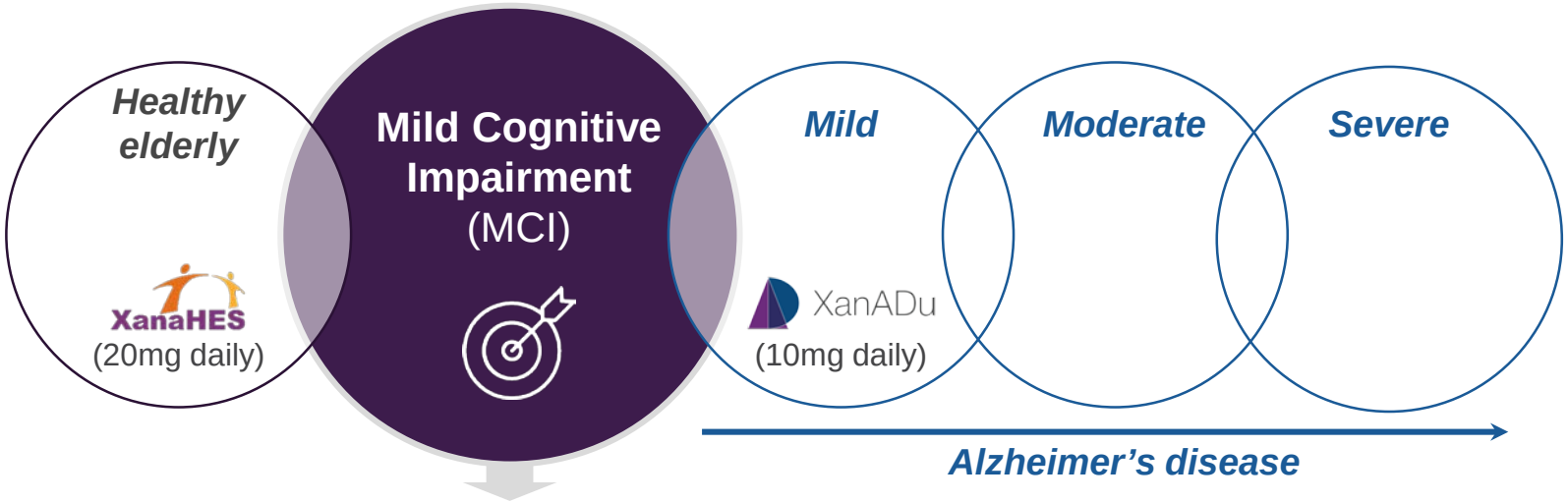
Partnerships / collaborations

Exploring potential funding opportunities with external partners (e.g. industry, academic, and government groups)

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

Alzheimer’s - 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

Actinogen - targeting a huge unmet medical need

Alzheimer's disease - the only top-ten leading fatal illness that cannot be prevented, treated or cured
Leading cause of death in Australian women and second only to CV disease in men

Huge, and growing numbers

~50 MILLION

Alzheimer's disease[1] or related dementia sufferers world-wide, doubling every 20 years

Limited treatment options

ONLY 4 DRUGS

currently available[2] providing limited symptomatic benefit, typically ~6 months

Unsustainable cost to health budgets

US$2 TRILLION

total forecast cost in US for dementia care by 2030

1. The Alzheimer's Association Facts and Figures, 2014. The World Alzheimer's Report
2. Currently available drugs: donepezil, rivastigmine, galantamine and memantine

Market dynamics of Alzheimer's disease

Presents a compelling commercial opportunity for Actinogen to target initially

Substantial target market with significant upside[1]

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)[2]

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

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

Investment summary

Actinogen - developing innovative treatments for cognitive impairment associated with neurological and metabolic diseases, with a primary focus on Alzheimer's disease

- ✓ Xanamem – our **differentiated lead compound** (efficacious, oral, brain penetrant, selective 11β-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 clinical development expected to **target patients with Mild Cognitive Impairment (MCI)** – based on recently completed XanaHES results
- ✓ Leverage platform technology across **multiple other indications**, including cognitive impairment associated with schizophrenia, bipolar and diabetes
- ✓ Future **study parameters optimised, including dose** following latest trial results, and exploring potential **partnership and collaboration funding** opportunities
- ✓ Xanamem development targeting **huge unmet medical needs** with **unsustainable healthcare costs**

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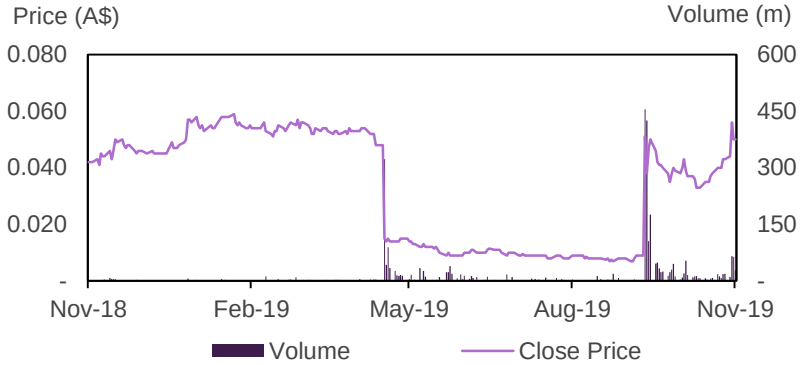
Appendix:
Background information

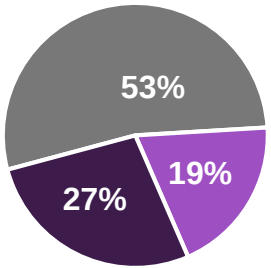
Corporate overview ASX:ACW

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



BVF Partners

Top 20
(excl. BVF Partners)

Remaining shareholders

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 UNIVERSITY OF MELBOURNE

The Royal Melbourne Hospital

THE FLOREY INSTITUTE OF NEUROSCIENCE & MENTAL HEALTH

Prof. Jeffrey Cummings

Cleveland Clinic

Scientific Advisory Board

Combining deep understanding of cortisol, 11β-HSD1 and drug discovery

Prof. Jonathan Seckl

THE UNIVERSITY of EDINBURGH

Prof. Brian Walker

Newcastle University

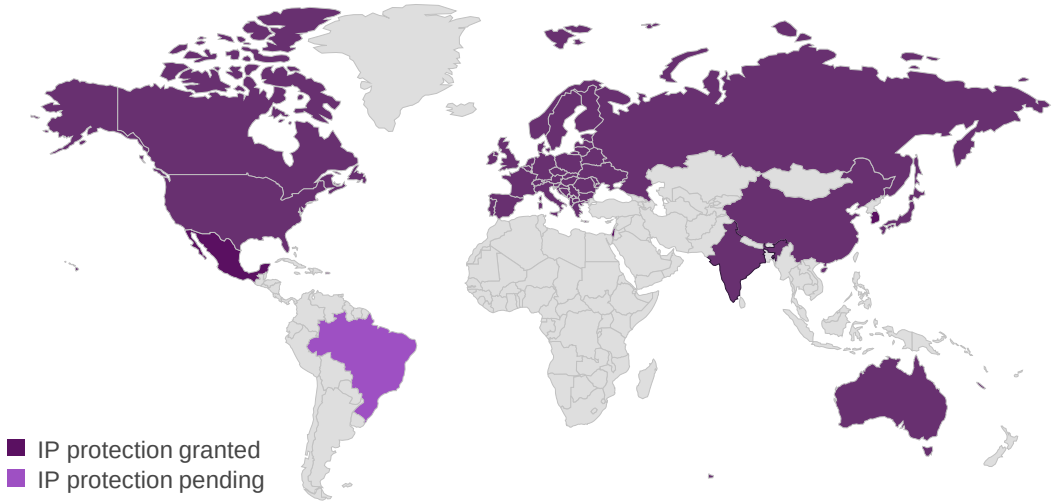
Prof. Scott Webster

THE UNIVERSITY of EDINBURGH

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
- Xanamem **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

Xanamem

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

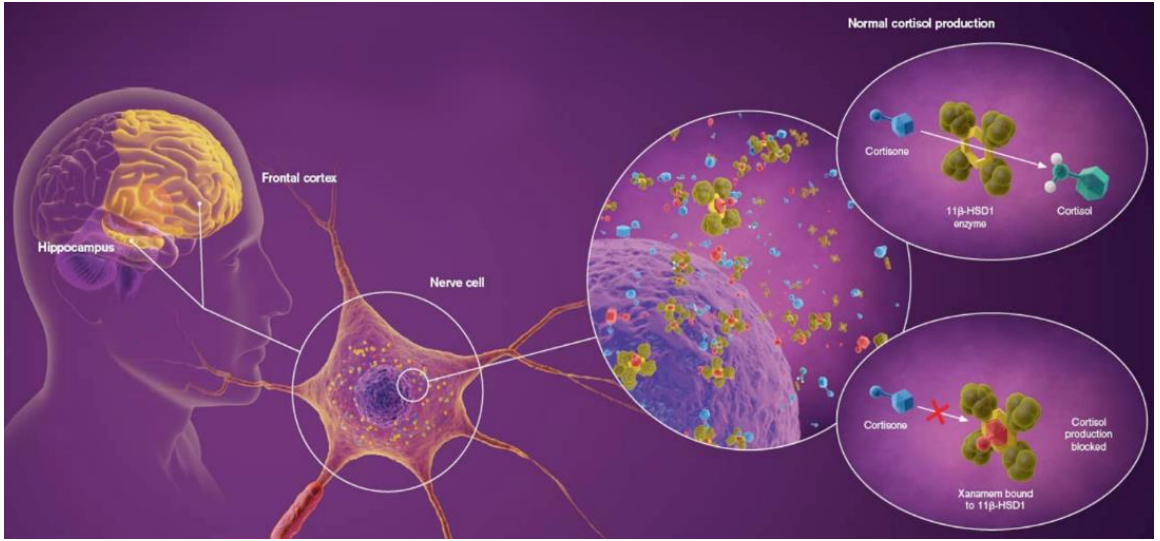
Well tolerated
Dosed >200 patients with acceptable clinical safety, toxicity & PK / PD[1] profile

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

Validated in Alzheimer's disease
Symptomatic and disease modifying effects (in vivo) and demonstrated effect of cortisol hypothesis (in humans)

Potential in other diseases
Secondary focus on cognitive impairment in mood disorders and schizophrenia

Differentiated mechanism of action:
Highly selective 11βHSD1 inhibitor in the brain which reduces excess cortisol production



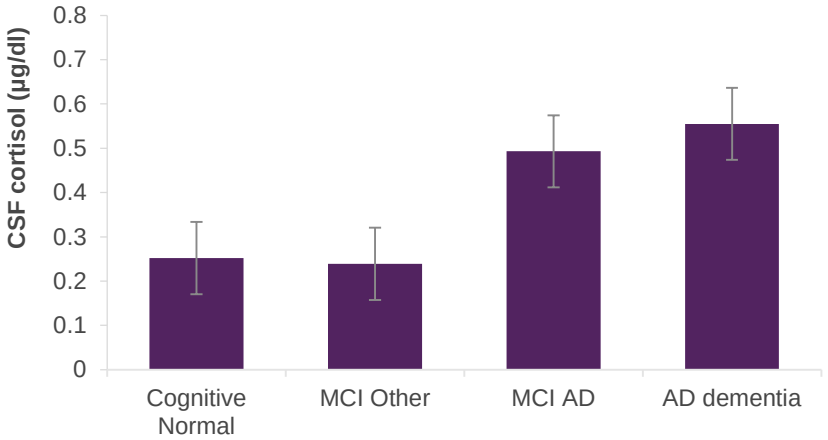
Xanamem is a novel, first-in-class, potent, orally bioavailable and brain-penetrant 11β-HSD1 inhibitor

1. PK / PD: pharmacokinetic / pharmacodynamic

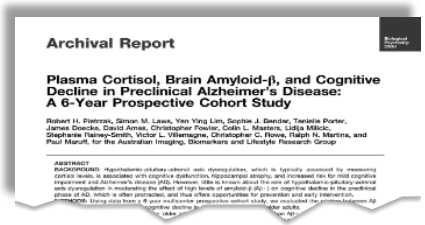
Alzheimer‘s strategic focus underpinned by medical research

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

Raised cortisol associated with Alzheimer’s disease[1]



Supported by growing body of medical literature


Archival Report

Plasma Cortisol, Brain Amyloid-β, and Cognitive Decline in Preclinical Alzheimer's Disease: A 6-Year Prospective Cohort Study

Robert H. Pietrzak, Simon M. Laws, Yen Ying Lim, Sophie J. Bender, Tenielle Porter, James Doecke, David Ames, Christopher Fowler, Colin L. Masters, Lidija Milicic, Stephanie Rainey-Smith, Victor L. Villemagne, Christopher C. Rowe, Ralph N. Martins, and Paul Maruff, for the Australian Imaging, Biomarkers and Lifestyle Research Group

ABSTRACT

BACKGROUND

aibl

The Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing

Many studies support the association between **cortisol and Alzheimer’s disease development and progression**[2]

A recent AIBL[3] study provided compelling evidence that elderly subjects with **higher plasma cortisol levels are at much greater risk of developing Alzheimer‘s disease**

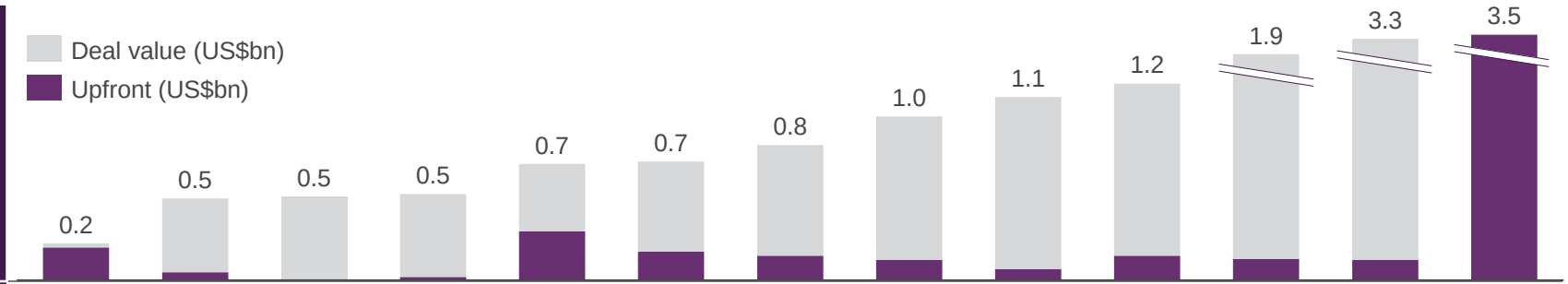
This study[3] also demonstrated **that 50% of those aged 65+ have raised cortisol levels**

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-β, 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

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



Deal value (US$bn)	0.2	0.5	0.5	0.5	0.7	0.7	0.8	1.0	1.1	1.2	1.9	3.3	3.5
Bidder / Licensee	abbvie	Lilly	janssen	MERCK	Biogen	PIERIAN	Otsuka	Allergan	abbvie	Takeda	Lilly	Allergan	Otsuka
Target / Licensor	ALECTOR	AstraZeneca	AC Immune	Bionomics	Bristol-Myers Squibb	Bristol-Myers Squibb	Lundbeck	CHASE Pharmaceuticals Corporation	Voyager THERAPEUTICS	DENALI	AC Immune	HEPTARES therapeutics	AVANIR
Year	2017	2014	2015	2014	2017	2014	2013	2016	2018	2018	2018	2016	2014
Deal type	Partnership	Partnership	Partnership	Partnership	Licence	Asset	Partnership	Acquisition	Partnership	Partnership	License	License	Acquisition
Candidate	Immuno-neurology platform	AZD3293	ACI-35	BNC-375	BMS-986168	IPN007	LU AE58054	CPC-201	Gene Therapy platform	Brain-penetrant ATV	ACI-3024	Three M1/M4 agonists	AVP-786
Phase	Pre-clinical	I	I	Pre-clinical	I	Pre-clinical	II	II	Pre-clinical	Pre-clinical	Pre-clinical	I	III
Novel MoA (not anti-amyloid)	✓	✗	✗	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Phase I clinical trial

Single blind placebo-controlled, dose escalation study to assess safety, tolerability and efficacy of Xanamem in healthy elderly subjects – full results expected in 4Q CY2019

12 weeks
Xanamem treatment course
Trial conducted at 1 site in Australia

42
Healthy elderly subjects
(no cognitive impairment)

20mg daily
Xanamem 30 subjects
Placebo 12 subjects

Cognition assessed
Through computerised efficacy tests
(Cogstate CTB[1])

Key objective to expand the Xanamem safety dataset and evaluate potential for higher dosage in future clinical trials

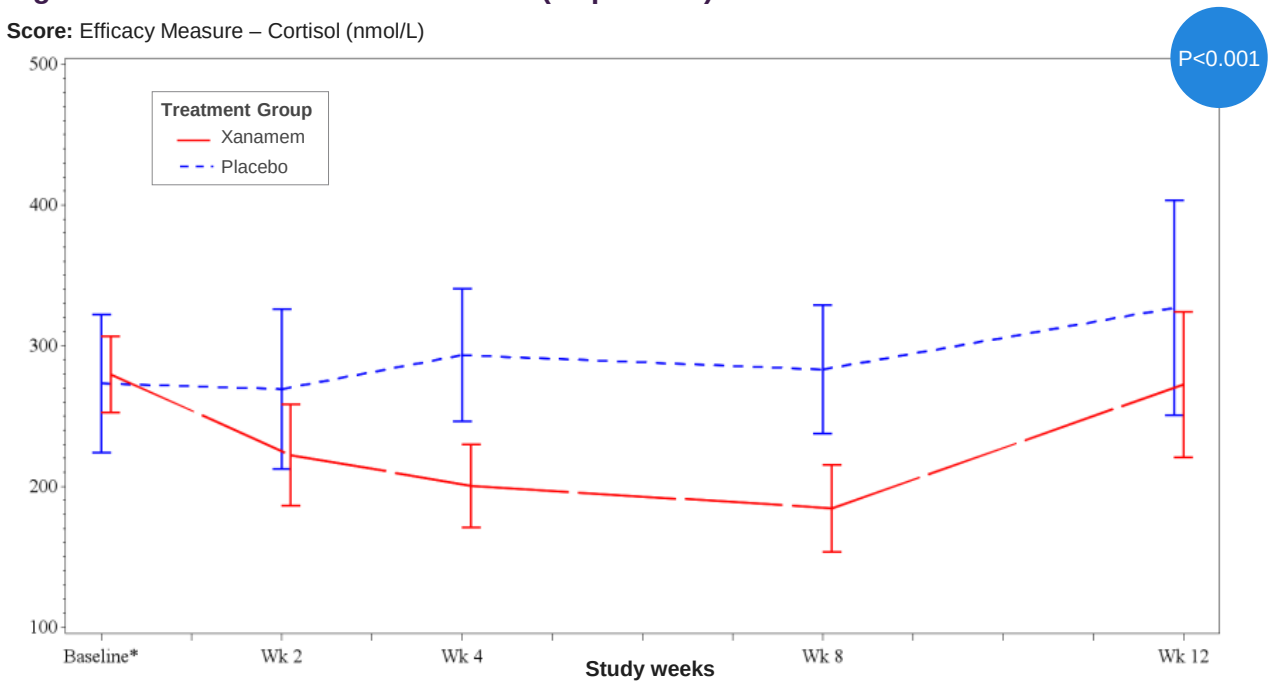
1.Cogstate Cognitive Test Battery

Cortisol Levels Reduced with Acceptable Safety

Efficacy results complemented by a statistically significant reduction in serum cortisol observed in the trial

Significant reduction in cortisol levels (all patients)

Score: Efficacy Measure – Cortisol (nmol/L)



Baseline * Mean of Observed Data

Xanamem achieved an average decrease of 73.2nmol/L vs. placebo (p<0.001)

These breakthrough results support the cortisol hypothesis that lowering persistently raised cortisol levels in the brain is expected to positively enhance cognition

Xanamem: Phase I Target Occupancy Study & Homogenate Binding Studies

To assist with confirming and optimising Xanamem dosing

Aim

To accurately demonstrate the effects different doses of Xanamem have on inhibiting the 11β-HSD1 enzyme in the human brain.

Phase I Target Occupancy studies

- Competitive binding, radio-labelled tracer PET imaging assay
- Subject cohorts tested with Xanamem at 5mg, 10mg, 20mg, and 30mg doses.
- Data available from 10-30mg dosing cohorts

In vitro Homogenate Binding Studies

- Enzyme occupancy competition studies, saturation binding studies, and enzyme activity assays in rat and human brain sections (ongoing)
- To correlate enzyme occupancy and enzyme activity at incremental doses of Xanamem

Key studies to help interpret XanADu results and support future clinical development strategy

Long-Term Safety and Toxicology Studies

Aim

Evaluate safety and toxicology in rodent (six months) and dog (nine months) studies in preparation for longer term clinical studies

- Studies **required by all regulators - FDA**
- Will allow future **clinical studies beyond 12 weeks**
- Studies **ongoing**
- **No substantive safety issues** observed to date

Key study to support future clinical development strategy

XanADu Phase II clinical trial

Double-blind, randomised, placebo-controlled study to assess the efficacy and safety of Xanamem in subjects with mild Alzheimer's disease[1]

Xanamem treatment course
12 weeks

186 patients with mild Alzheimer's disease (enrolment complete)[2]

10mg daily
Xanamem for 12 weeks (vs. placebo)

Trial conducted at 25 sites in
AUS, USA and UK

Largest AD global clinical trial run by an Australian biotech

1. Study registered on Clinicaltrials.gov: NCT02727699
2. Fully enrolled 26 November 2018