

#### ASX ANNOUNCEMENT

#### Actinogen updated investor presentation

**Sydney 21 March 2019: Actinogen Medical (ASX: ACW, 'the Company')** is pleased to release an updated Investor Presentation. The presentation will be used to update shareholders, investors and brokers as part of a non-deal roadshow across Australia. The presentation outlines Actinogen's key investment highlights, clinical progress and outlook.

The investor presentation includes further insights into the clinical efficacy endpoints used in the Phase II XanADu clinical trial (refer to slides 16-20). The seven efficacy endpoints are used in the trial to identify the cognitive domains most sensitive to Xanamem's potential efficacy. The endpoints are validated cognitive outcome assessments used in Alzheimer's disease research globally and are recognised and accepted by global regulators. Multiple endpoints de-risk development and there is no reliance on achieving any one individual endpoint to progress clinical development. The totality of the XanADu and additional studies' results, expected by mid-year 2019 (refer to slide 6), will inform the optimal clinical development pathway for Xanamem going forward.

#### Key Investment Highlights

- **Novel compound:** Actinogen's lead compound Xanamem has a novel mechanism of action targeting excess cortisol production in the brain. This cortisol hypothesis and its potential role in Alzheimer's disease has been validated by multiple independent research.
- **Targeted strategic market focus:** Alzheimer's disease addressable market worth >US\$7.5bn with unmet needs and potential upside.
- Advanced clinical stage asset: Fully funded advanced clinical stage program with reported positive safety interim analysis of the XanADu Phase II Alzheimer's study, which has completed patient enrolment and is on track for results read-out in 2Q CY2019.
- **Potential value upside:** Well positioned to unlock further value in Alzheimer's disease and other indications, supported by significant big pharma interest.
- **De-risked opportunity:** Initiated nine additional Xanamem-related studies all studies fully funded and value-adding to Xanamem data-base. Further pipeline development opportunities under evaluation.
- **Experienced leadership and advisors:** Significant drug development and biotech investment experience guided by key opinion leading clinicians and drug discovery teams.

#### ENDS

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#### **About Actinogen Medical**

Actinogen Medical (ASX: ACW) is an ASX-listed biotech company focused on innovative approaches to treating cognitive decline that occurs in chronic neurodegenerative and metabolic diseases. Actinogen Medical is developing its lead compound Xanamem, as a promising new therapy for Alzheimer's disease, a condition with a multibillion-dollar market potential. In the US alone, the cost of managing Alzheimer's disease is estimated to be US\$250bn and is set 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.

#### 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  $11\beta$ -HSD1 enzyme in the brain. This enzyme is highly concentrated in the hippocampus and frontal cortex, the areas of the brain most affected by Alzheimer's disease. There is a strong association between chronic stress and excess cortisol that leads to changes in the brain affecting memory, and to the development of amyloid plaques and neural death – all hallmarks of Alzheimer's disease.

#### 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<sup>™</sup> 20mg & 30mg once daily in healthy elderly volunteers. Changes in cognitive performance from baseline to end-of-treatment will be measured as an exploratory efficacy outcome.

#### About XanADu

XanADu is a Phase II double-blind, 12-week, randomised, placebo-controlled study to assess the safety, tolerability and efficacy of Xanamem 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. Results are expected in Q2 2019. 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.

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

## **Investor Presentation**

A novel approach to treating cognitive impairment and Alzheimer's disease Dr. Bill Ketelbey: CEO & MD March 2019



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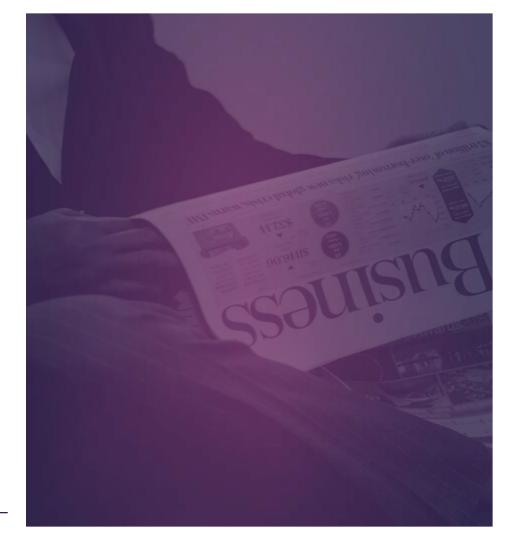
Xanamem

XanADu

Development pipeline

Outlook

Appendix



# **Executive summary**

Key investment highlights

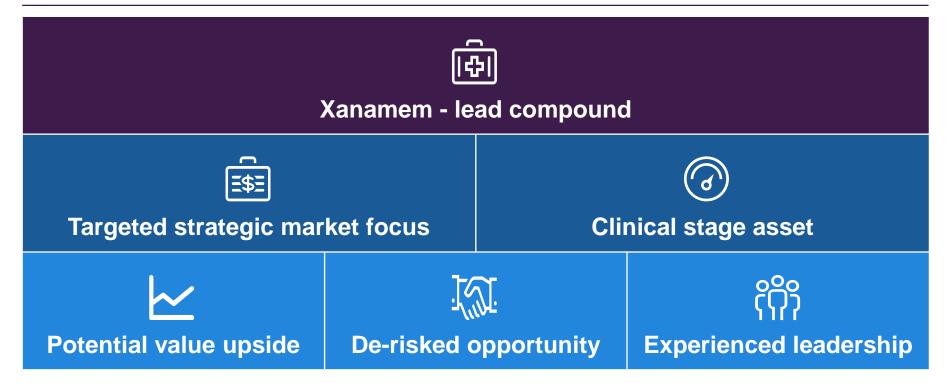
What is Xanamem

Development pipeline

## Key investment highlights



Actinogen is developing innovative treatments for cognitive impairment associated with neurodegenerative and metabolic diseases with an initial focus on Alzheimer's disease



### Xanamem



Actinogen's lead compound, Xanamem, is a novel drug designed to inhibit the production of cortisol in the brain with the potential to treat cognitive impairment and Alzheimer's disease



#### Well researched

In clinical stage development, with over 15 years of R&D completed, and A\$40m invested to date



#### Well tolerated

Dosed >150 patients with acceptable clinical safety, toxicity and PK /  $PD^1$  profile

#### ×>0 Differentiated mechanism of action

 $6 \times$  Highly selective inhibitor of the 11 $\beta$ HSD1 enzyme in the brain which reduces excess cortisol production



#### Validated

Symptomatic and disease modifying effects (in vivo) and effective demonstration of cortisol hypothesis (in humans)

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#### Well protected

Composition of matter IP coverage  $\geq$  2031, patents granted in all major markets



#### Xanamem is a novel, first-in-class, potent, orally bioavailable and brain-penetrant 11βHSD1 inhibitor

PK / PD: pharmacokinetic / pharmacodynamic

### **Clinical development and milestones**



Well progressed Phase II clinical trial (XanADu) underpinned by additional value-adding studies and an exciting Xanamem pipeline for other potential indications

Studies	4Q CY2018	1Q CY2019	2Q CY2019	
XanADu	Phase II study for Alzhe Results expected by mid			Key focus
Target Occupancy studies	Studies to demonstrate Results expected by mid	<b>enzyme binding at differe</b> CY2019	nt doses	
XanaHES		<b>es - safety study</b> ected by mid CY2019		Enhances Xanamem data set
Additional toxicology studies	Additional pre-clinical s Initial results expected by	<b>afety and toxicology studi</b> mid CY2019	ies	
Assessment of other indications e.g. diabetes, Parkinson's disease, depression, schizophrenia, amongst others	<b>Evaluating target indica</b> Preliminary decision expe		Results expected by mid CY2019	upside potential

## Xanamem

The cortisol hypothesis Validation of the cortisol hypothesis Mechanism of action Xanamem research and development

Xanamem has been developed in response to evidence that there is a strong association between chronically raised cortisol levels in the blood and in the brain, and the development and progression of Alzheimer's disease

Xanamem is underpinned by over 15 years of R&D with A\$40m invested in development

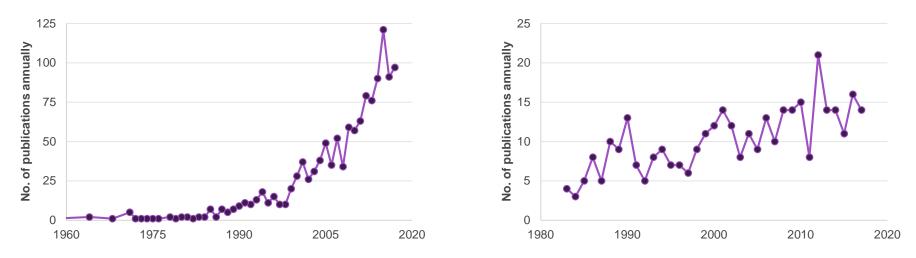
## The cortisol hypothesis



A growing body of literature showing an association between cortisol and cognitive impairment

#### Medical publications: "Cortisol and Cognition"<sup>1</sup>

#### Medical publications: "Cortisol and Alzheimer's"<sup>1</sup>

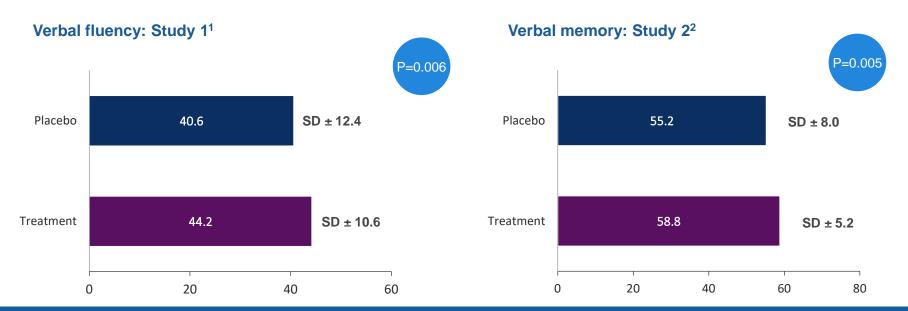


#### Actinogen is well positioned to leverage the growing significance of the relationship between cortisol and cognition

## Human pilot studies validate the cortisol hypothesis



Two pilot studies indicated inhibiting cortisol production in the brain improves cognitive function in healthy elderly men and subjects with Type 2 diabetes (11β-HSD1 inhibition with carbenoxolone – no longer commercially available)<sup>1,2</sup>



#### Significant improvement in verbal fluency and verbal memory after only 4 and 6 weeks of treatment<sup>1,2</sup>

Source: 11β-Hydroxysteroid dehydrogenase inhibition improves cognition function in healthy elderly men and type 2 diabetics Sandeep et al., 2004 PNAS (vol. 101, no. 17) 6734-6739

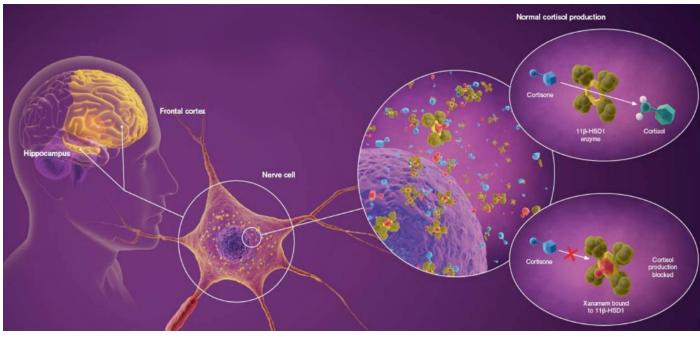
- 1. Study 1: 10 healthy subjects Age 55-75 (Mean Age = 65.5 ± 5.5) receiving 100mg carbenoxolone 3 times daily compared to placebo for 4 weeks, in a double-blind randomised crossover study
- 2. Study 2: 12 type 2 diabetics (m=9; f=3) Age 52-70 (Mean Age = 60 ± 4.9) receiving 100mg carbenoxolone 3 times daily compared to placebo for 6 weeks, in a double-blind randomised crossover study.

### **Mechanism of action**



Xanamem inhibits the activity of the 11βHSD1 enzyme, reducing the production of cortisol in the brain

#### **Overview**



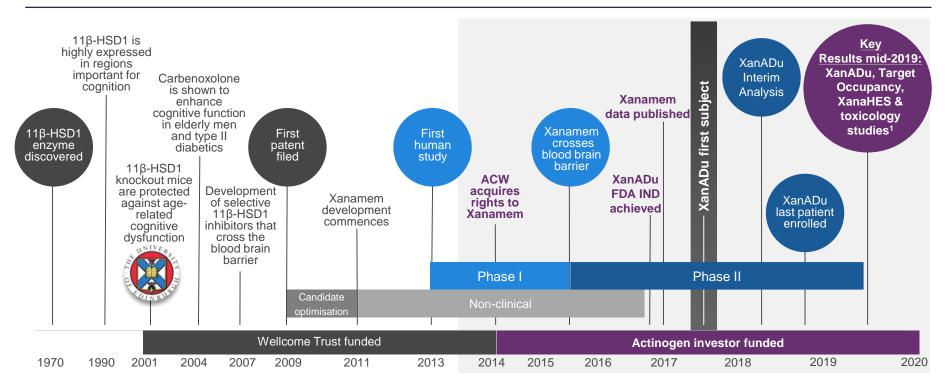
Xanamem has potential in other diseases with possible cortisol induced cognitive impairment

- Alzheimer's disease (key focus)
- Diabetes
- Depression
- Schizophrenia
- Parkinson's disease
- Down syndrome
- And more...

### Xanamem research and development



Xanamem is underpinned by significant R&D investment and clinical progress over the last 15 years



Estimated timing of key milestones

# XanADu

Efficacy considerations XanADu Phase II clinical trial and milestones Interim analysis Favourable market dynamics Competitive landscape Big Pharma interest XanADu is a global Phase II double-blind, randomised, placebo-controlled study asessing the efficacy and safety of Xanamem in patients with mild Alzheimer's disease

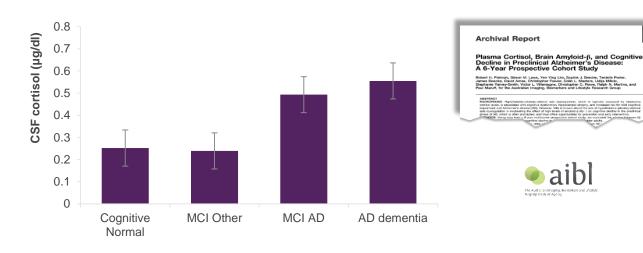
Enrolment complete with results expected in 2Q CY2019

# 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





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

This study<sup>3</sup> also demonstrated **that** 50% of those aged 65+ have raised cortisol levels

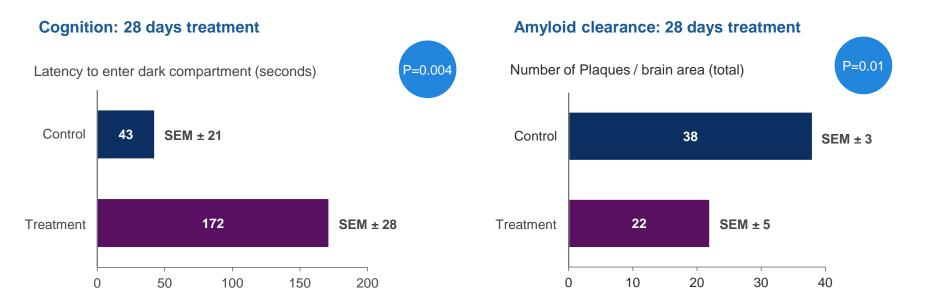
#### Research suggests that lowering cortisol levels may prevent the development / progression of Alzheimer's disease

- 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

## Efficacy underpinned by animal model



Significant and rapid symptomatic and disease modifying effects demonstrated with significant improvement in cognition within one month, continuing out to 41 weeks



#### Results from the animal model studies underpin the significant potential of the Xanamem in Alzheimer's

Source: UE2316 in Tg2576 rodent model of Alzheimer's disease. Sooy, et al., 2015. Endocrinology 156 (12) 4592-4603 SEM: Standard Error of the Mean

### 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<sup>1</sup>



Xanamem treatment course **12 weeks** 



**186** patients with mild Alzheimer's disease (enrolment complete)<sup>2</sup>





Trial conducted at 25 sites in AUS, USA and UK

Fully funded study, fully enrolled with results due in 2Q CY2019

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

### XanADu endpoints



XanADu's primary and secondary efficacy endpoints are validated cognitive outcome measures used in Alzheimer's disease research globally and accepted by all major regulatory bodies globally (including the FDA)

### ADAS-ADCOMS COG14 CDR-**MMSE** SOB Xan RAVLT **NTB** Primary NP Secondary

XanADu: primary and secondary efficacy endpoints<sup>1</sup>

#### Efficacy endpoints are **standard assessments used in Alzheimer's disease studies globally**

While overlapping in many areas, each endpoint measures **discrete** domains and function of cognition

XanADu is designed to **identify the cognitive domains most sensitive** to Xanamem's potential efficacy

Multiple endpoints de-risks development as it enables deep insight into the potential treatment outcomes with Xanamem

There is **no reliance on achieving any one individual efficacy endpoint** to progress Xanamem clinical development

A positive signal from any of the **major efficacy endpoints**<sup>2</sup> could be **considered a positive result** 

#### XanADu's results will inform future clinical development

1. ADAS-COG14: Alzheimer's Disease Assessment Scales – Cognitive Subscale Score (version 14); ADCOMs: AD COMposite Scores (composite data derived from ADAS-COG14, CDR-SOB and MMSE); CDR-SOB: Clinical Dementia Rating Scale – Sum of Boxes; RAVLT: Rey Auditory Verbal Learning Test; MMSE: Mini-Mental Status Examination; NTB: Neuropsychological Test Batteries; NPI: Neuropsychiatric Inventory 2. Major efficacy endpoints include: ADAS-COG14, ADCOMS, CDR-SOB, MMSE

### Key takeaways for XanADu efficacy endpoints<sup>1</sup>



- 1. Actinogen believes there are no safety concerns with 10mg Xanamem daily in mild Alzheimer's patients following 2 successful DSMB interim reviews and ongoing surveillance of all safety data
- 2. Results from XanADu and the additional studies initiated since mid-2018

## XanADu primary efficacy endpoints



A primary endpoint is the endpoint to which a clinical trial is powered for statistical purposes<sup>1</sup>; XanADu is powered to ADAS-COG14 (ADCOMS is a co-primary endpoint)

### ADAS-COG14

### AD Assessment Scale Cognition (version 14)

- One of the most frequently used tests to measure cognition status and commonly used in Alzheimer's disease drug development
- Considered a "gold standard" endpoint in Alzheimer's disease research globally
- Widely accepted by global regulators, academics and potential strategic partners
- XanADu is statically designed around this endpoint





Memory

### ADCOMS AD Composite Score

- Composite of most sensitive domains of ADAS-COG, CDR-SOB and MMSE
- A statistically positive result would likely indicate a positive trend in many or all of the above domains<sup>2</sup>
- Breakthrough instrument that is expected to be a routine test to investigate treatment of mild Alzheimer's disease
- Adequately powered for XanADu given sensitivity

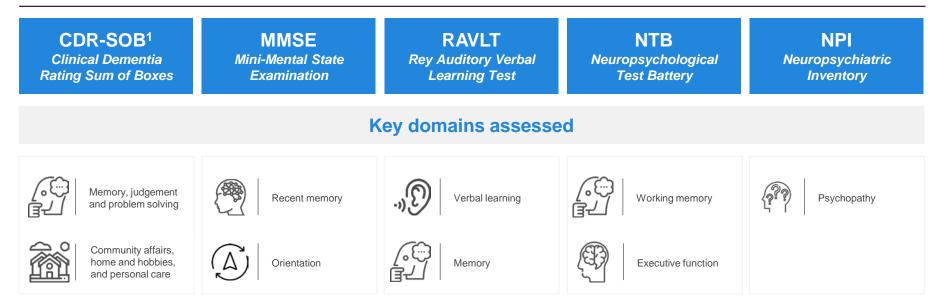


- 1. Defines how many patients are needed to achieve statistical significance
- 2. If a statistically positive result is not achieved in ADAS-COG, CDR-SOB, or MMSE, or only a trend towards a positive outcome is achieved, it is still possible that there could be a statistically significant outcome with ADCOMS as ADCOMS selects for the most sensitive outcome domains in mild cases of Alzheimer's disease

## XanADu secondary efficacy endpoints



XanADu's secondary efficacy endpoints complement the primary endpoints and provide additional information about the therapeutic efficacy of the drug candidate to inform further clinical development



#### Of these endpoints: CDR-SOB, MMSE and RAVLT results are expected to be most valued by potential strategic partners

1. CDR-SOB, while also considered a "gold standard" endpoint in Alzheimer's disease research, was not selected as a primary endpoint to avoid duplication, as it constitutes about half the ADCOMS score weighting

## Validity of XanADu's endpoints



XanADu endpoints are validated cognitive outcome measures and results will be highly valued by clinicians and potential strategic partners alike

#### Endpoints are validated and accepted by global regulatory bodies, academics and potential strategic partners



✓ FDA recognises and accepts all the XanADu endpoints, and does not require an endpoint biomarker



 $\checkmark$  ADAS-COG14 and CDR-SOB are considered the "gold standard" endpoints



✓ Potential strategic partners will find **ADCOMS result interesting** as it is derived from well-established endpoints



✓ Potential strategic partners have expressed strong interest to learn more about XanADu and Xanamem

Multiple strategic partners are currently interested to review and consider the XanADu results and data. Actinogen is well positioned to commence strategic discussions for further clinical development

### **Interim analysis**



Positive recommendations from the DSMB<sup>1</sup> reflect confidence in the safety of the drug and the design of the XanADu study. Supports the broader development of Xanamem



# First DSMB review (23 May 2018)

- Evaluation of 50 patients' safety and efficacy data reviewed by an independent DSMB<sup>2</sup>
- Recommendation by DSMB to continue XanADu without modification

# Second DSMB review (22 August 2018)

- Evaluation of 125 patients' safety data
- Reaffirmed continuation of XanADu without modification

#### **Third DSMB review**

 Expected to be completed in early CY2019



#### Positive DSMB recommendations underpin the XanADu study and further development of Xanamem in other indications

- 1. DSMB: Data Safety Monitoring Board
- 2. Evaluable patients to have completed the study note: an additional 37 patients' safety data was also included in the analysis (data was from patients still ongoing in the study)

### Market dynamics of Alzheimer's disease

Actinogen Medical

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
<b>~25.0m</b> (50% over 65 yrs)	~4.0m	~1.5m	~1.7m	~2.5m

Upside potential for earlier use Key focus



#### 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)



### **Development pipeline of other cognitive enhancers**



Xanamem is one of the most advanced cognitive enhancers currently in development<sup>1</sup>

Company	Drug candidate	Mechanism	Phase (status)	Primary endpoint(s)	Upcoming milestones <sup>2</sup>			
Actinogen Medical	Xanamem	11βHSD1 inhibitor	ll (ongoing)	ADAS-Cog14, ADCOMS	April 2019		ble by mid CY2019 ary completion April 2019	
	SUVN-502	5HT6 antagonist	ll (ongoing*)	ADAS-Cog11	April 2019 Estimated primary completion *Target to complete patient recruitment by end CY2018		end CY2018	
	Neflamapimod	p38 MAPK inhibitor	ll (ongoing)	HVLT-R <sup>4</sup>	June 2019	Estima	ated primary completion	
	Bryostatin 1	Protein Kinase C Epsilon activator	II <sup>3</sup> (ongoing)	SIB <sup>4</sup>	July 2019	E	stimated primary completion	3
biohaven	BHV4157	Na+ channel blocker	II / III (ongoing)	ADAS-Cog11	Jai	nuary 2020	Estimated prima	ry completion
Boehringer Ingelheim	BI425809	Glycine transport inhibitor	ll (ongoing)	ADAS-Cog11	I	February 2020	Estimated	primary completion
AGENEBIO	AGB101	SV2A	III (ongoing)	CDR-SOB			November 2021	Estimated primary completion
GreenValley	GV-971	Unknown	**	ADAS-Cog12	**Phase III trial conducted in China successfully completed September 2018 /international trial planned			al trial planned
	Anavex 2-73	SIGMAR1 agonist	lla	MTD <sup>4</sup>	- Initiation of Phase IIb / III announced in August 2018 – no evidence in clinical trial registries			ies
Allergan.	HTL0018318	M1 agonist	***	N/A***	***Phase II trial put on hold in September	2018 prior to initia	tion due to unexpected prim	ate toxicology

1. Some programs that may be relevant are not included due to lack of development (e.g. Sinphar Pharmaceuticals: STA-1; Allergan: CPC-201) or because they are more commonly referred to as disease modifying therapies (e.g. Cognition Therapeutics: CT1812; Daehwa Pharma: DHP1401; Agene Bio: AGB101)

2. Estimated primary completion based on clinicaltrials.gov information - unless additional information is available

3. Completed Phase II in May 2017 with equivocal results. New Phase II initiated in June 2018 with primary completion expected in July 2019

4. HVLT-R: Hopkins Verbal Learning Test – Revised; SIB: Severe Impairment Battery; MTD: Maximum Tolerated Dose

### **Comparison of Alzheimer's disease treatments**



Actinogen's novel treatment for Alzheimer's disease is clearly differentiated and may be used in combination with existing cognitive enhancers and potential anti-amyloid drugs (currently in development)

#### Overview

	Xanamem	Cognitive enhancers	Anti-amyloid drugs
Status	In development	In market <sup>1</sup>	In development
Mechanism of action	Targets cortisol	AChE <sup>2</sup> inhibitors, NMDA <sup>2</sup> receptor antagonist	Anti-amyloid
Administration	Oral (small molecule)	Oral (small molecule)	Injectable IV / SC <sup>3</sup> (biologics)
Evidence of disease modification	✓ 4	×	$\checkmark$
Duration of effect (>8 months)	✓ 4	?	✓
Potential to treat 'at risk' patients	$\checkmark$	×	✓
Applicable to other cognitive disorders	$\checkmark$	×	×
No SAEs identified	$\checkmark$	×	×
No biomarker required	$\checkmark$	✓	×
Low cost of goods	$\checkmark$	$\checkmark$	×

Xanamem may support potential combination therapy, with existing treatments and other drugs currently in development, to improve patient outcomes

- Approved cognitive enhancers have different mechanism of action and varying degrees of benefit and duration
- Despite promising data, antiamyloid therapy has high costs, compliance challenges and requires IV / SC administration

1. Analysis excludes other cognitive enhancers currently in development

2. AChE: acetylcholinesterase; NMDA: N-methyl-D-aspartate

IV: intravenous; SC: subcutaneous

4. Evidence of disease modification and duration based on animal model studies

## Significant headwinds for BACE inhibitor development



Significant opportunity for Xanamem development, with recent study data indicating that anti-amyloid may not be efficacious as initially expected

### **Overview**<sup>1</sup>

- Results indicate
  potent anti amyloid activity
  has not translated
  to substantial
  cognitive benefit
- Trending / actual cognitive worsening was observed across multiple compounds

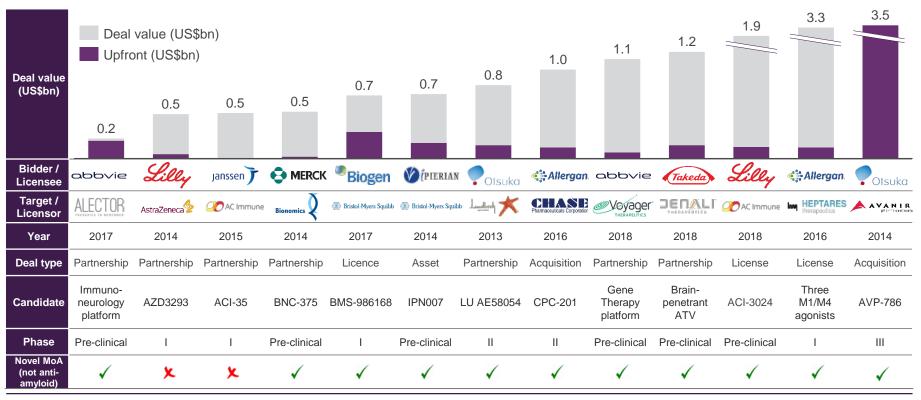
Company	Compound (Phase) Status	Population	CSF Aβ lowering range	Cognition comments	
	Verubecestat (III)	Mild moderate	60% - 80%	Early: Trend for cognitive worsening Overall: No difference	
	Stopped for futility	Prodromal	60% - 80%	Early: Cognitive worsening Overall: Cognitive worsening	
Lilly	Lanabecestat (III)	Prodromal – mild	55% - 75%	Early: Trend for cognitive worsening	
AstraZeneca	Stopped for futility	Mild	55% - 75%	Overall: Data not locked	
Johnson&Johnson	Atabecestat (III) Stopped for hepatic safety	Cognitively unimpaired	50% - 82%	Early: Trend for cognitive worsening - Cognitive worsenin Overall: Dosing discontinued	
Lilly	LY3202626 (II) Stopped for futility	Mild dementia	70% - 90%	<b>Early:</b> Trend for cognitive worsening - Equivocal <b>Overall:</b> Dosing discontinued	
Eisal Biogen	Elenbecestat (III) Ongoing	Mild moderate	~60%	Early: Trends for improvement Overall: General trends for improvement	
	CNP520 (II/III) Ongoing	Cognitively unimpaired	20% - 90%	Early: Not applicable Overall: No difference	

1. Information presented at CTAD (Clinical Trials on Alzheimer's Disease) Conference held in Barcelona in October 2018

## **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



# **Development pipeline**

Additional Xanamem studies

Other potential indications

## **Additional value-adding Xanamem studies**



Actinogen is focused on completing nine key additional studies to enhance the Xanamem data set, which can also be potentially leveraged into other indications



Actinogen is fully funded to complete these additional Xanamem studies

### **Other potential indications**

Actinogen is also focused on developing Xanamem in other indications to optimise shareholder value

#### **Overview**

Multiple potential target indications beyond
 Alzheimer's represent significant market
 expansion opportunities



Growing literature on cortisol-induced cognitive impairment associated with many conditions



Actinogen undertaking a detailed review to identify best additional target indications

Development program leverages existing data from earlier clinical programs

#### Possible target indications

Depression	Diabetes	
Schizophrenia	Parkinson's disease	
POCD & TBI <sup>1</sup>	Post-MI, PVD Stroke & HT <sup>2</sup>	
Down syndrome	And more	

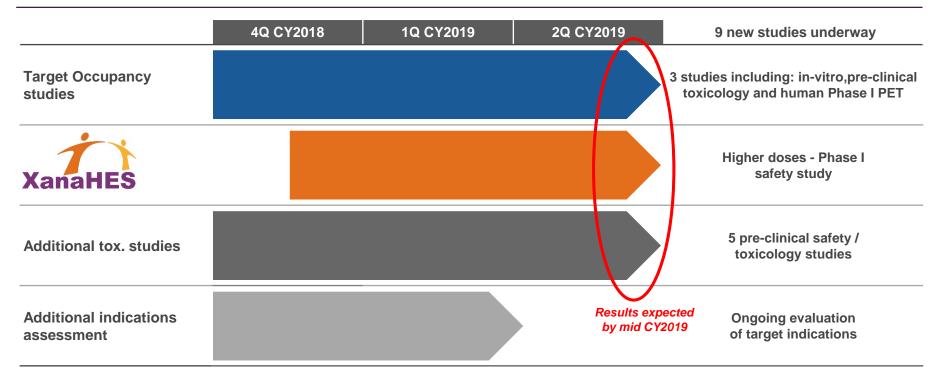
#### Preliminary assessment currently underway to identify high priority indications for development

- 1. Post-operative cognitive decline & Traumatic brain injury
- 2. Post-myocardial infarction, Peripheral vascular disease & Hypertension (peripheral & intra-cranial)

### **Development pipeline**



Multiple studies are currently underway to enhance the Xanamem data set, with results expected in 2Q CY2019, and preliminary decision on assessment of other indications planned for 1Q CY2019



# Outlook

Upcoming catalysts Key investment highlights

### **Development and commercialisation strategy**



Actinogen is focused on progressing Xanamem clinical development, while continually assessing potential value accretive opportunities to optimise shareholder value



#### Xanamem clinical development

Progress Xanamem development in Alzheimer's disease and potential studies into other target indications<sup>1</sup>

Fully funded to complete XanADu and all new studies underway, including target occupancy and XanaHES, that will inform the next stage of development



#### License / partnering

Proactive and strategic engagement with prospective development and commercialisation partners to advance Xanamem development

Discussions currently underway with many major companies and leading developers of drugs for Alzheimer's disease

#### Actinogen is well positioned to deliver significant potential value uplift to shareholders

## **Upcoming catalysts**



Significant upcoming milestones across first half 2019

Studies	1Q CY2019	2Q CY2019	3Q CY2019	4Q CY2019	Key catalysts
XanADu			Next stage of de	velopment will	Results expected to be available by mid CY2019
Target occupancy studies			be informed by results. Further of conjunction with a	levelopment in	Results expected to be available by mid CY2019
XanaHES			and key regulatory bodies		Results expected to be available by mid CY2019
Additional tox. studies			/		Initial results expected by mid CY2019
Additional indications assessment		Results exp by mid CY			Preliminary decision expected by 2Q CY2019
Strategic discussions					Ongoing discussions with potential commercial and strategic partners

#### Actinogen is fully funded to complete XanADu and other key studies

## Key investment highlights

Actinogen is developing innovative treatments for cognitive impairment associated with neurodegenerative and metabolic diseases with an initial focus on Alzheimer's disease



#### Xanamem - lead compound

Differentiated with a novel mechanism of action First-in-class, brain penetrant, orally active, small molecule, inhibitor of 11βHSD1 enzyme Xanamem mechanism of action validated by independent research on the cortisol hypothesis



#### Targeted strategic market focus

Initially focused on developing a treatment for Alzheimer's disease Addressable market worth >US\$7.5bn with unmet needs and potential upside Target indication underpinned by efficacy results from animal model studies



#### **Clinical stage asset**

Advanced clinical stage program assessing Xanamem in Alzheimer's disease XanADu clinical trial fully enrolled, with results expected Q2 CY2019 Positive safety interim analysis reported in XanADu



#### Potential value upside

Well positioned to unlock further value Multiple potential indications Significant Big Pharma interest



#### **De-risked opportunity**

Fully funded programs Additional Xanamem-related studies initiated Additional pipeline opportunities under evaluation



#### **Experienced leadership**

Board and Management with significant drug development and corporate experience, supported by key opinion leaders and Xanamem discovery team

# Appendix

Corporate overview Senior leadership Advisory boards IP protection

### **Corporate overview**



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

#### **Overview**

- Actinogen is developing Xanamem, a novel therapy for Alzheimer's disease with significant market potential
- Actinogen is completing a Phase II double-blind, 12 week, randomised, placebo-controlled study (XanADu) in Alzheimer's disease
- XanADu is designed to assess the safety, tolerability and efficacy of Xanamem in subjects with mild Alzheimer's disease

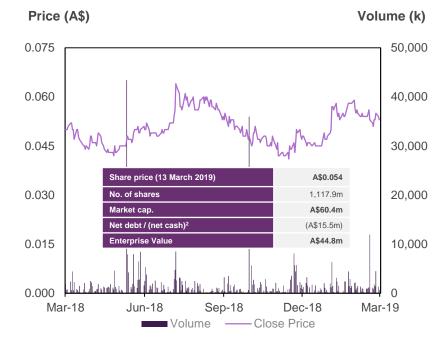
### Key shareholding metrics



1. FIL Investment Management (Hong Kong) Limited and FIL Pensions Management

2. Net cash as at 31 Dec 2018

#### LTM share price performance and trading metrics



### Substantial Institutional investment in Actinogen\*



Recognises potential and endorses strategy

Positive interim analysis catalyses significant \$15M investment through Placement

Leading investors enter register:

- USA specialist biotech investor **Biotechnology Value Fund L.P.**
- Australian institutions Platinum Investments Management and Australian Ethical Investment

Strong endorsement - Placement price represents a **13.4% premium** to the 5-day VWAP

BVF cornerstones Placement - largest shareholder with a 19.97% holding

Funding to advance the development plan through additional Xanamem studies.



### **Board of Directors**



Commercially experienced and globally recognised leadership team with decades of experience in drug development and biotech investment



Dr. Geoff Brooke *Chairman* 

- **30+ years experience** in the healthcare investment industry
- Founder and MD of Medvest Inc and GBS Venture Partners
- Significant expertise in biotech: development strategy, capital raising and investments
- MBBS (University of Melbourne); MBA (IMEDE, Switzerland)





Dr. Bill Ketelbey CEO & MD

- 30+ years experience in healthcare, biotech and pharmaceutical industries
- Formerly senior international roles at Pfizer; Director at the Westmead Institute of Medical Research
- Involved in clinical development and commercialisation of Aricept<sup>TM</sup>
- MBBCh (University of Witwatersrand); FFPM; MBA (Macquarie); GAICD





Dr. George Morstyn

Non-executive director

- 25+ years experience in biotechnology investment and drug development
- Board member of Cancer Therapeutics, Symbio and Biomedvic; Former Senior VP and SMO at Amgen
- Global responsibility for Amgen's drug development in all therapeutic areas
- MBBS (Monash University); PhD (Walter and Eliza Hall Institute); FRACP; MAICD



### **Advisory Boards**



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

#### Xanamem<sup>™</sup> Clinical Advisory Board

Positions Xanamem at the forefront of Alzheimer's drug development

### **Scientific Advisory Board**

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



### **Proactive strategic business development**

Continued strategic engagement with prospective development and commercial partners in the lead up to XanADu results

Progressing collaboration and commercial discussions with prospective big pharma partners, and presenting to, and educating the scientific community

#### Planned H1 CY2019 Partnering and Investment Conference Attendance

JP Morgan Healthcare Conference | January, San Francisco SACHS Neuroscience | January, San Francisco | Oral Presentation BIO-Europe Spring 2019 | March, Vienna BIO 2019 | June, Philadelphia

#### Planned CY2019 Scientific Conference Attendance

AD/PD 2019 | March, Lisbon AAIC 2019 | July, Los Angeles CTAD 2019 | December, San Diego





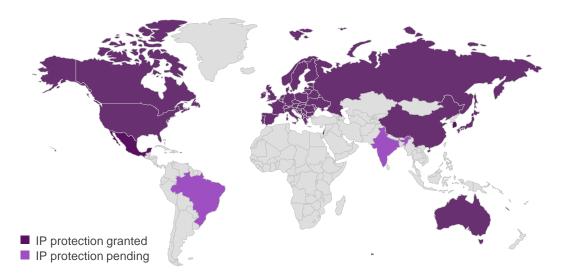


### **IP** protection



Actinogen maintains a broad granted composition of matter patent estate, extending to at least 2031, 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
- Actinogen's patent portfolio extends to at least 2031

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

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