

ASX ANNOUNCEMENT**Actinogen updated Investor Presentation**

Sydney 1 May 2019: Actinogen Medical (ASX: ACW, 'the Company') is pleased to release an updated Investor Presentation. This presentation will be used to update investors and potential strategic partners following the recent expansion of the Xanamem clinical development program, announced on 10 April 2019.

The presentation includes further insights (slides 30 to 33) into cognitive impairment in mood disorders (including depression and bipolar disorder) and schizophrenia, which are the new indications selected for further clinical development of Xanamem. Selection of these new indications follows significant clinical interest in evaluating Xanamem in a range of medical conditions associated with raised cortisol. There are currently limited or no therapeutic options available to clinicians and their patients for treating these conditions and they therefore represent major unmet medical needs and substantial market opportunities. A specialist Advisory Board is currently being established to assist Actinogen with the design of the most appropriate clinical development plan to effectively demonstrate the Xanamem's potential in these indications.

Further, the presentation expands on the XanADu Alzheimer's disease study endpoints and articulates how the totality of the results from XanADu (expected within the next 2 months, as previously announced) and the additional studies initiated in mid-2018, will inform on the overall optimal clinical development pathway for Xanamem's future development (slides 16 to 21).

Key Investment Highlights

- **Novel compound:** Actinogen's lead compound Xanamem has a mechanism of action targeting excess cortisol production in the brain. This cortisol hypothesis and its potential role in the treatment of Alzheimer's disease has been validated by 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 development program with XanADu results on track for read-out within the next two months.
- **Potential value upside:** Well positioned to unlock further value in Alzheimer's and other neurological indications, including mood disorders and schizophrenia, supported by significant big pharma interest.
- **De-risked opportunity:** Initiated nine additional Xanamem-related studies in mid-2018 – all studies fully funded and value-adding to Xanamem database. Further pipeline development opportunities in mood disorders and schizophrenia recently announced.
- **Experienced leadership and advisors:** Significant drug development, biotech investment and transactional experience guided by Board, management, key opinion leading clinicians and drug discovery teams.

ENDS**Actinogen Medical**

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 @BillKetelbey **About Actinogen Medical****Investor and Media Enquiries**

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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 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.

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 & 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.

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

Dr. Bill Ketelbey: CEO & MD

May 2019



Actinogen
Medical

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Executive summary

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What is Xanamem

Development pipeline



Key investment highlights

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



Xanamem - lead compound



Targeted strategic market focus



Clinical stage asset



Potential value upside



De-risked opportunity



Experienced leadership

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



Well researched

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



Well tolerated

Dosed >200 patients with acceptable clinical safety, toxicity and PK / PD¹ profile



Differentiated mechanism of action

Highly selective inhibitor of the 11 β HSD1 enzyme in the brain which reduces excess cortisol production



Validated in Alzheimer's disease

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



Well protected

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

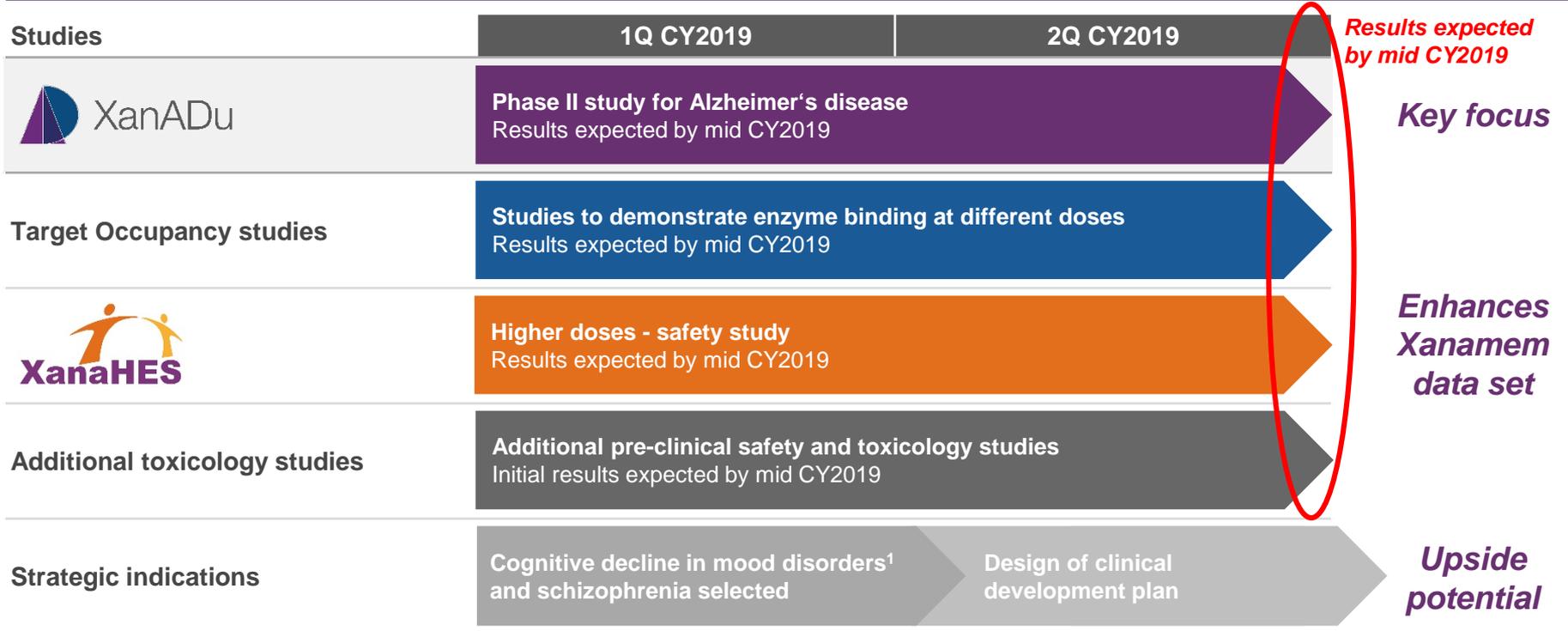


Xanamem is a novel, first-in-class, potent, orally bioavailable and brain-penetrant 11 β HSD1 inhibitor

1. 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 in mood disorders and schizophrenia



1. Including depression and bipolar disorder

Xanamem

The cortisol hypothesis

Validation of the cortisol hypothesis

Mechanism of action

Xanamem research and development

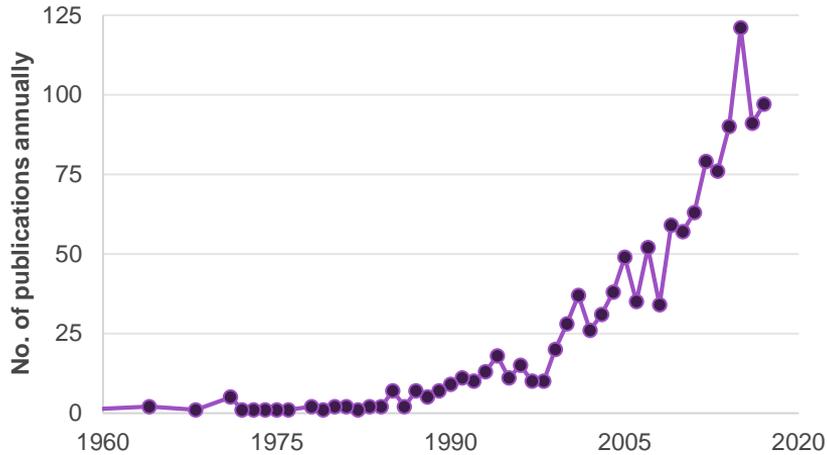
Xanamem has been developed in response to evidence that there is a strong association between chronically raised cortisol levels in the blood and in the brain, and the development and progression of cognitive impairment, including in Alzheimer's disease

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

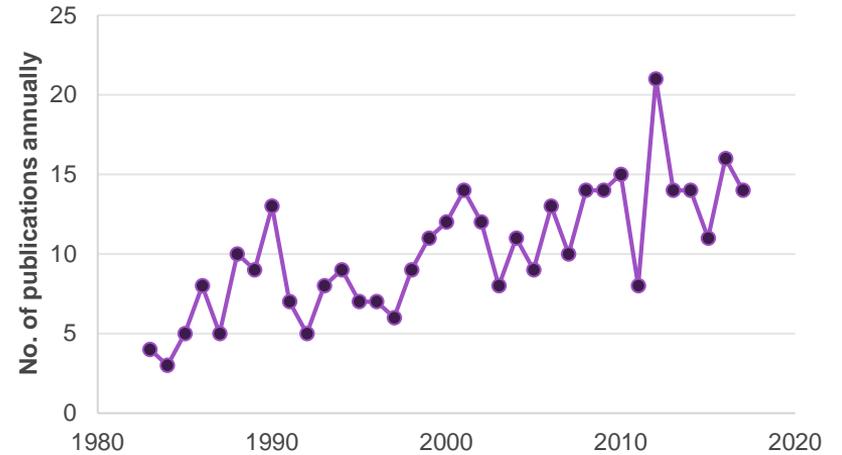
The cortisol hypothesis

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

Medical publications: “Cortisol and Cognition”¹



Medical publications: “Cortisol and Alzheimer’s”¹



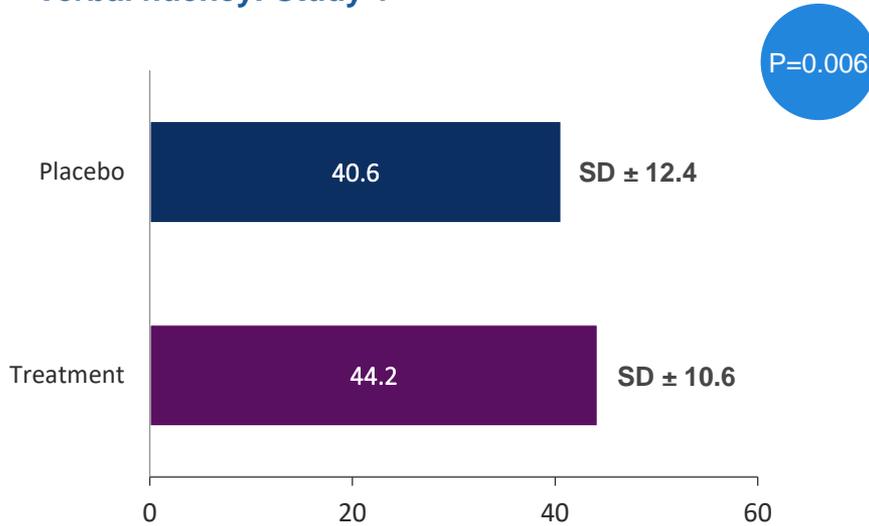
Actinogen is well positioned to leverage the growing significance of the relationship between cortisol and cognition

1. PubMed keyword search

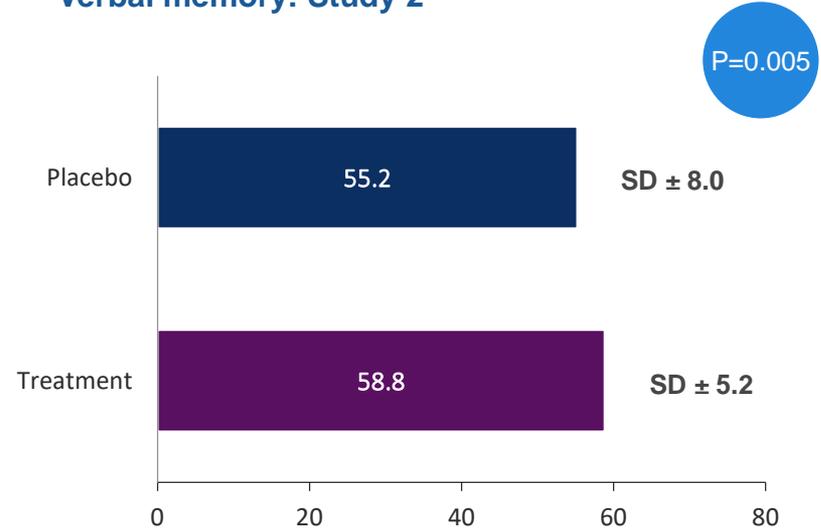
Human pilot studies validate the cortisol hypothesis

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

Verbal fluency: Study 1¹



Verbal memory: Study 2²



Significant improvement in verbal fluency and verbal memory after only 4 and 6 weeks of treatment^{1,2}

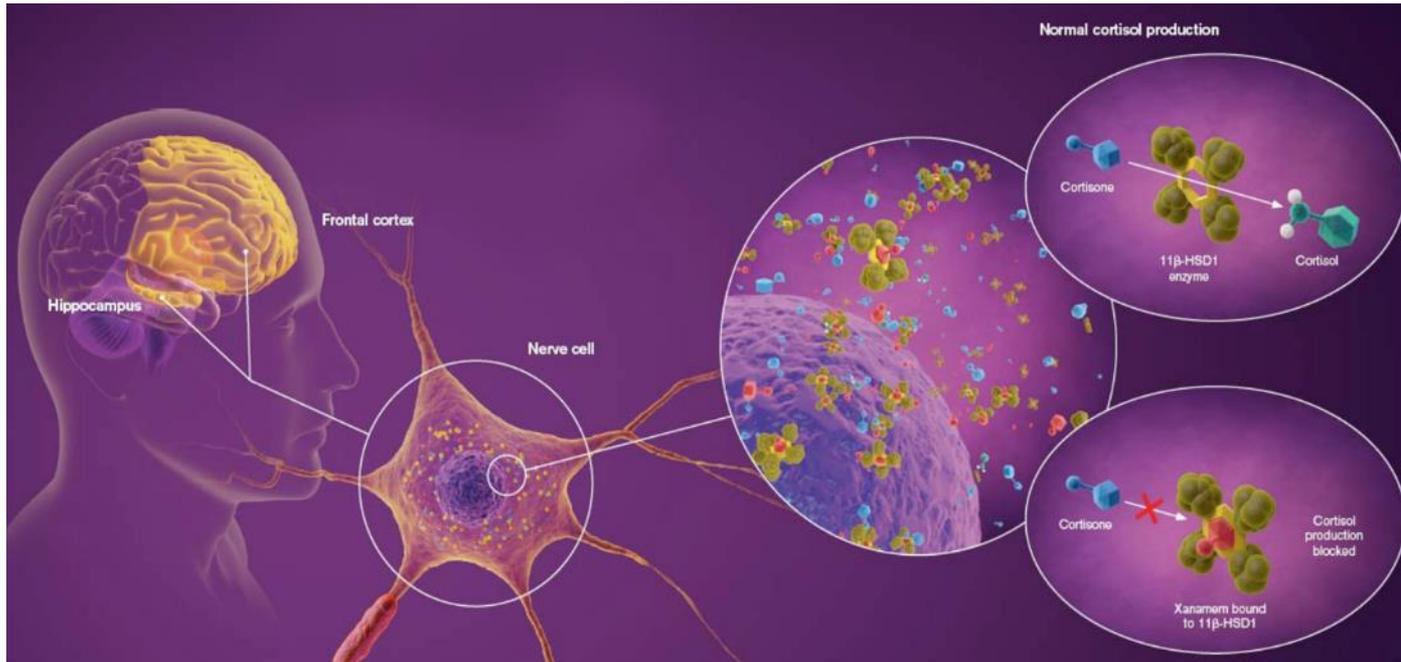
Source: 11 β -Hydroxysteroid dehydrogenase inhibition improves cognition function in healthy elderly men and type 2 diabetics Sandeep et al., 2004 PNAS (vol. 101, no. 17) 6734-6739

1. Study 1: 10 healthy subjects Age 55-75 (Mean Age = 65.5 \pm 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 \pm 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 11β HSD1 enzyme, reducing the production of cortisol in the brain

Overview

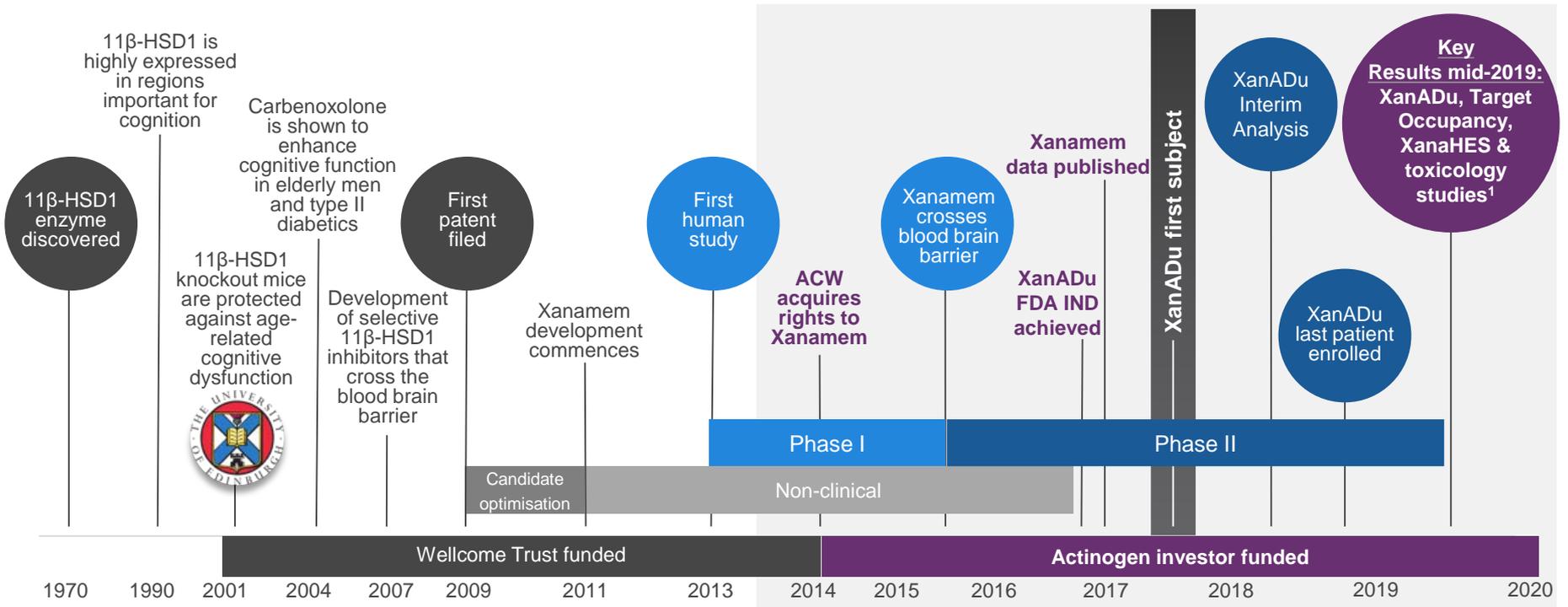


Xanamem has potential in other diseases with possible cortisol induced cognitive impairment

- **Alzheimer's disease (key focus)**
- **Mood disorders and schizophrenia (secondary focus)**
- **And more...**

Xanamem research and development

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



1. Estimated timing of key milestones

XanADu

Efficacy considerations

Phase II clinical trial design and endpoints

Interim analysis

Favourable market dynamics

Competitive landscape

Big Pharma interest

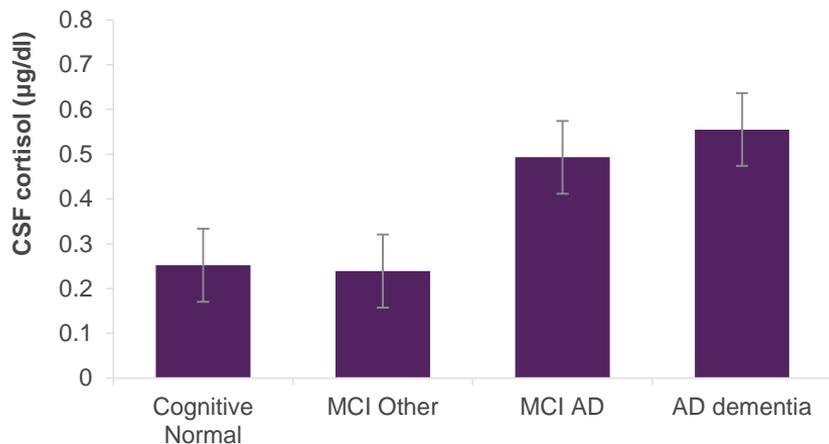
XanADu is a global Phase II double-blind, randomised, placebo-controlled study assessing the efficacy and safety of Xanomem in patients with mild Alzheimer's disease

Enrolment complete with results expected in 2Q CY2019

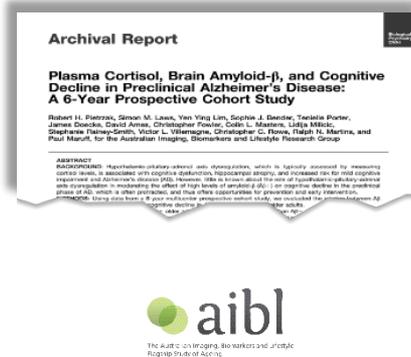
Alzheimer's strategic focus underpinned by medical research

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

Raised cortisol associated with Alzheimer's disease¹



Supported by growing body of medical literature



Many studies support the association between **cortisol and Alzheimer's disease development and progression²**

A recent AIBL³ study provided compelling evidence that elderly subjects with **higher plasma cortisol levels are at much greater risk of developing Alzheimer's disease**

This study³ 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

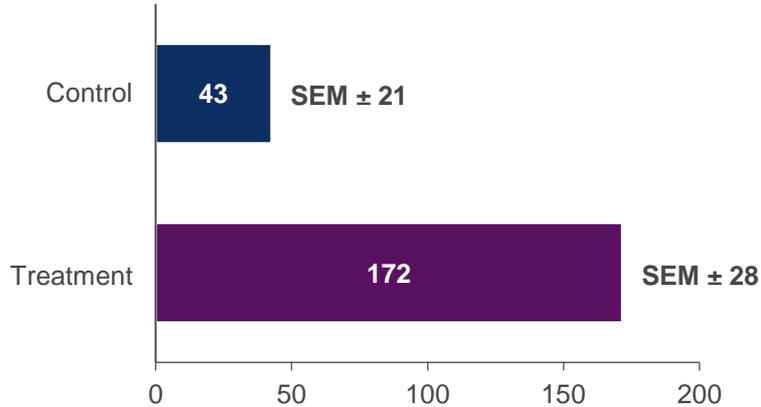
Efficacy underpinned by animal model

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

Cognition: 28 days treatment

Latency to enter dark compartment (seconds)

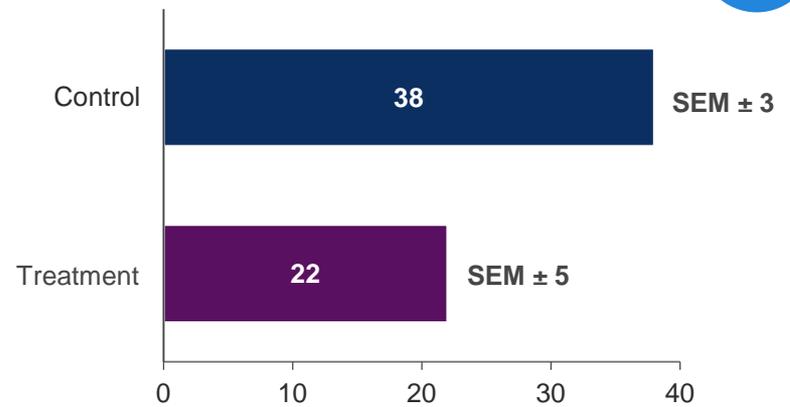
P=0.004



Amyloid clearance: 28 days treatment

Number of Plaques / brain area (total)

P=0.01



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

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 disease¹



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

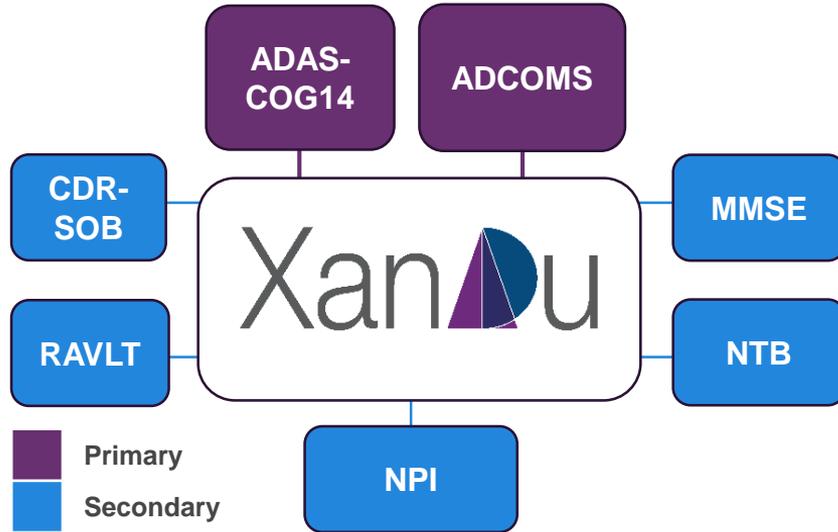
Fully funded study, fully enrolled with results due in 2Q CY2019

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)

XanADu: primary and secondary efficacy endpoints¹



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

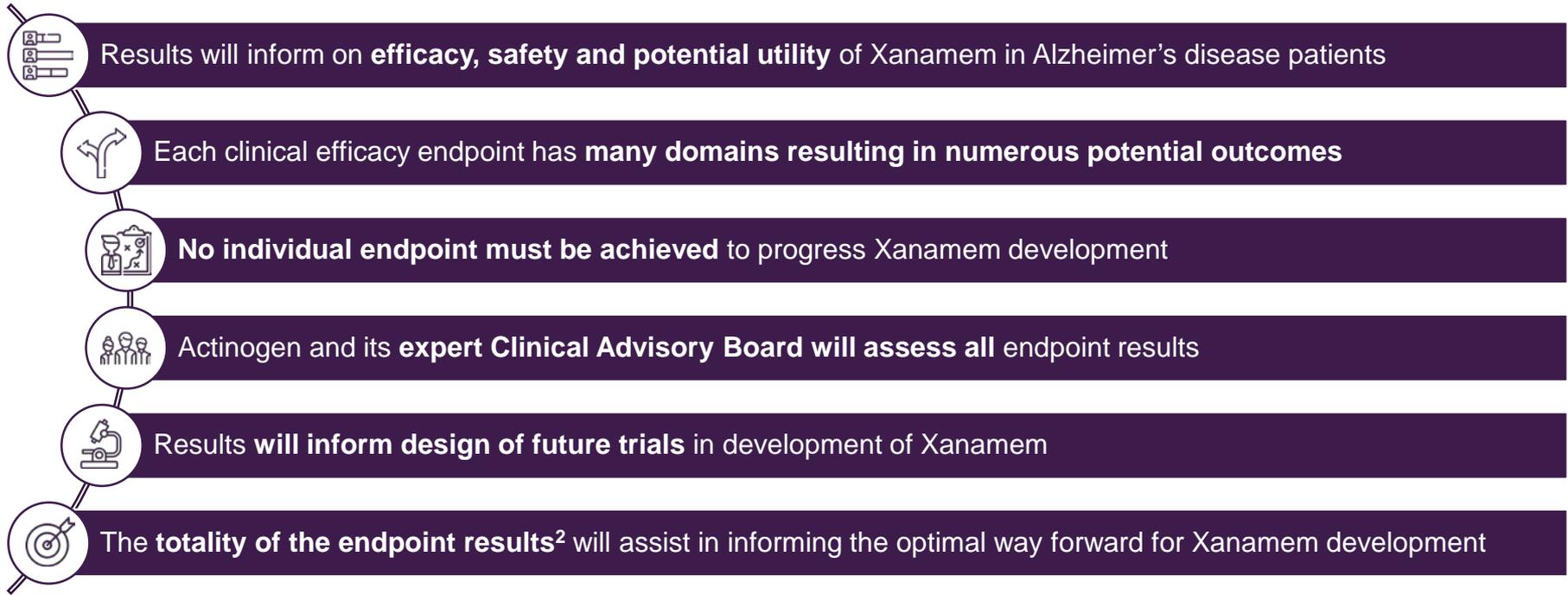
There is **no reliance on achieving any one individual efficacy endpoint** to progress Xanamem clinical development

A positive signal from any of the **major efficacy endpoints²** 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 endpoints¹



1. Actinogen believes there are no safety concerns with 10mg Xanamem daily in mild Alzheimer's patients – following 3 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 purposes¹; 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**



Language



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 domains²
- Breakthrough instrument that is **expected to be a routine test** to investigate treatment of mild Alzheimer's disease
- **Adequately powered for XanADu** given sensitivity



Language



Orientation, time



Memory, judgement and problem solving



Community affairs, home & hobbies, and personal care

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

CDR-SOB¹ <i>Clinical Dementia Rating Sum of Boxes</i>	MMSE <i>Mini-Mental State Examination</i>	RAVLT <i>Rey Auditory Verbal Learning Test</i>	NTB <i>Neuropsychological Test Battery</i>	NPI <i>Neuropsychiatric Inventory</i>
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Key domains assessed

 <p>Memory, judgement and problem solving</p>  <p>Community affairs, home and hobbies, and personal care</p>	 <p>Recent memory</p>  <p>Orientation</p>	 <p>Verbal learning</p>  <p>Memory</p>	 <p>Working memory</p>  <p>Executive function</p>	 <p>Psychopathy</p>
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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

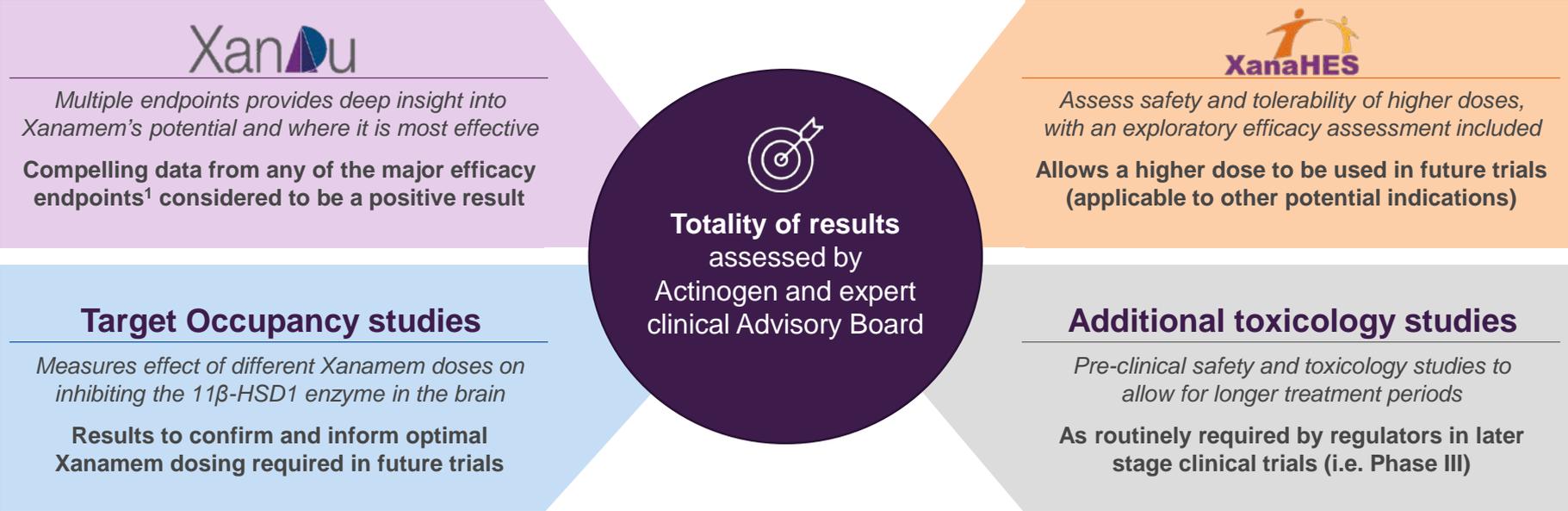
Endpoints are validated and accepted by global regulatory bodies, academics and potential strategic partners

-  ✓ **FDA recognises and accepts all the XanADu endpoints**, and does not require an endpoint biomarker
-  ✓ ADAS-COG14 and CDR-SOB are considered the “**gold standard**” endpoints
-  ✓ Potential strategic partners will find **ADCOMS 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

Comprehensive assessment process

The comprehensive review of the data and results from XanADu and the additional studies will underpin the optimal clinical development pathway forward



The totality of results will underpin further Xanamem development (independently / partnership)

1. Major XanADu efficacy endpoints: ADAS-COG14, ADCOMS, CDR-SOB, and MMSE

Interim analysis

Positive recommendations from the DSMB¹ 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 DSMB²
- **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 (26 March 2019)

- Evaluation of 162 patients' safety data
- **Reaffirmed continuation of XanADu without modification**



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

Presents a compelling commercial opportunity for Actinogen to target initially

Substantial target market with significant upside¹

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

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

Development pipeline of other cognitive enhancers

Xanamem is one of the most advanced cognitive enhancers currently in development¹

Company	Drug candidate	Mechanism	Phase (status)	Primary endpoint(s)	Upcoming milestones ²	
 Actinogen Medical	Xanamem	11 β HSD1 inhibitor	II (ongoing)	ADAS-Cog14, ADCOMS	April 2019	Results available by mid CY2019 Estimated primary completion April 2019
 SUVEN	SUVN-502	5HT6 antagonist	II (ongoing*)	ADAS-Cog11	April 2019	Estimated primary completion *Target to complete patient recruitment by end CY2018
 EIP	Neflamapimod	p38 MAPK inhibitor	II (ongoing)	HVLT-R ⁴	June 2019	Estimated primary completion
 Neurotrope BioScience	Bryostatin 1	Protein Kinase C Epsilon activator	II ³ (ongoing)	SIB ⁴	July 2019	Estimated primary completion ³
 biohaven	BHV4157	Na ⁺ channel blocker	II / III (ongoing)	ADAS-Cog11	January 2020	Estimated primary completion
 Boehringer Ingelheim	BI425809	Glycine transport inhibitor	II (ongoing)	ADAS-Cog11	February 2020	Estimated primary completion
 AGENE BIO	AGB101	SV2A	III (ongoing)	CDR-SOB	November 2021	Estimated primary completion
 GreenValley	GV-971	Unknown	III**	ADAS-Cog12	**Phase III trial conducted in China successfully completed September 2018 /international trial planned	
 anavex	Anavex 2-73	SIGMAR1 agonist	IIa	MTD ⁴	Initiation of Phase IIb / III announced in August 2018 – no evidence in clinical trial registries	
 Allergan	HTL0018318	M1 agonist	II***	N/A***	***Phase II trial put on hold in September 2018 prior to initiation due to unexpected primate toxicology	

- 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)
- Estimated primary completion based on clinicaltrials.gov information – unless additional information is available
- Completed Phase II in May 2017 with equivocal results. New Phase II initiated in June 2018 with primary completion expected in July 2019
- 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 ¹	In development
Mechanism of action	Targets cortisol	AChE ² inhibitors, NMDA ² receptor antagonist	Anti-amyloid
Administration	Oral (small molecule)	Oral (small molecule)	Injectable IV / SC ³ (biologics)
Evidence of disease modification	✓ ⁴	✗	✓
Duration of effect (>8 months)	✓ ⁴	?	✓
Potential to treat 'at risk' patients	✓	✗	✓
Applicable to other cognitive disorders	✓	✗	✗
No SAEs identified	✓	✗	✗
No biomarker required	✓	✓	✗
Low cost of goods	✓	✓	✗

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, anti-amyloid 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
 3. 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 Xanomem development, with recent study data indicating that anti-amyloid may not be efficacious as initially expected

Overview¹

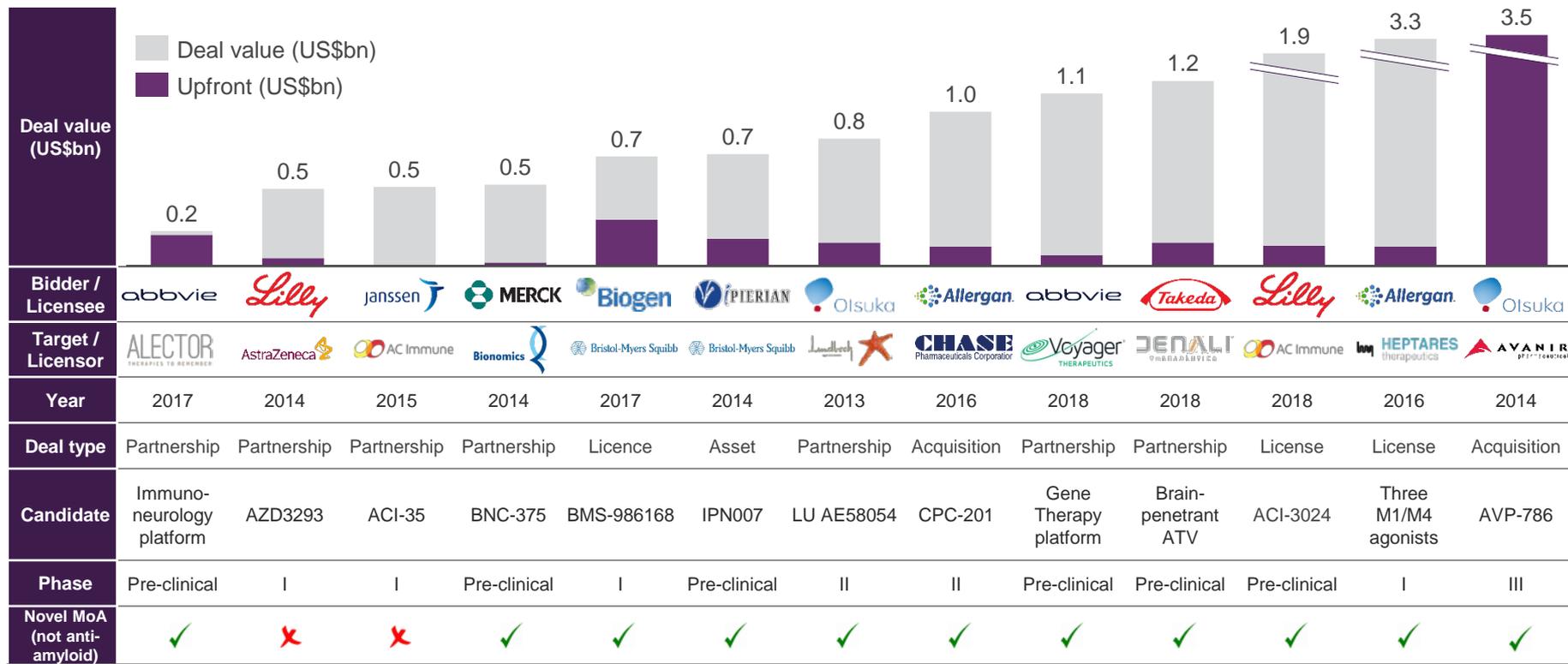
- Results indicate **potent anti-amyloid activity has not translated to substantial cognitive benefit**
- Trending / actual cognitive worsening was observed** across multiple compounds

Company	Compound (Phase) Status	Population	CSF A β lowering range	Cognition comments
	Verubecestat (III) Stopped for futility	Mild moderate	60% - 80%	Early: Trend for cognitive worsening Overall: No difference
		Prodromal	60% - 80%	Early: Cognitive worsening Overall: Cognitive worsening
 	Lanabecestat (III) Stopped for futility	Prodromal – mild	55% - 75%	Early: Trend for cognitive worsening Overall: Data not locked
		Mild	55% - 75%	
	Atabecestat (III) Stopped for hepatic safety	Cognitively unimpaired	50% - 82%	Early: Trend for cognitive worsening - Cognitive worsening Overall: Dosing discontinued
	LY3202626 (II) Stopped for futility	Mild dementia	70% - 90%	Early: Trend for cognitive worsening - Equivocal Overall: Dosing discontinued
 	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

Strategic 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



Target occupancy studies

Aims to accurately demonstrate the effect different doses of Xanamem has on inhibiting the 11β -HSD1 enzyme in the human brain and to optimise Xanamem dosing

Currently underway with **results expected in 2Q CY2019**



Higher dose safety study

To expand the safety data-set for Xanamem and explore potential for higher doses of the drug to be used in Alzheimer's and other indications

XanaHES study initiated with **initial results expected in 2Q CY2019**



Further safety / toxicology studies

To allow for longer treatment periods, as routinely required by global regulatory authorities in the development of any drug

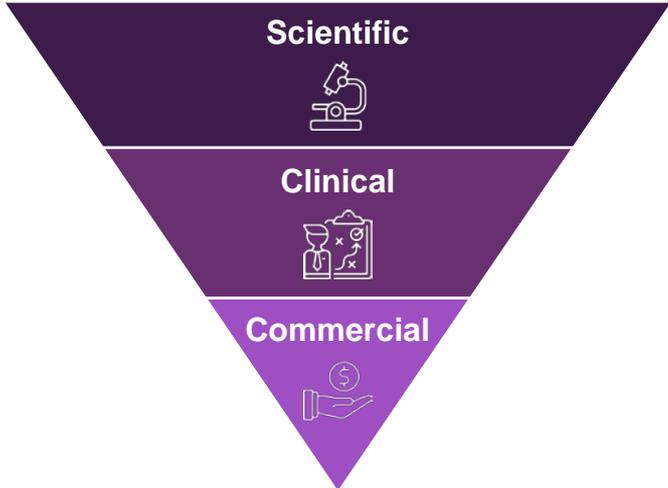
Additional studies initiated with **results expected in 6-12 months**

Actinogen is fully funded to complete these additional Xanamem studies

Assessment of new target indications completed

Following extensive scientific, clinical, and commercial review, cognitive impairment in mood disorders and schizophrenia selected as the next indications for development and commercialisation of Xanamem

12 indications assessed



- Selection follows significant clinical interest in trialling Xanamem in a range of medical conditions associated with raised cortisol
- Potential indications assessed for association between raised cortisol and cognitive impairment, and Xanamem's potential to be an effective treatment
- Key considerations are clinical development path and unmet medical need
- Market analyses reveal substantial commercial opportunities – including population size; current standard of care; pricing and competitive landscape

Cognitive impairment in mood disorders and schizophrenia

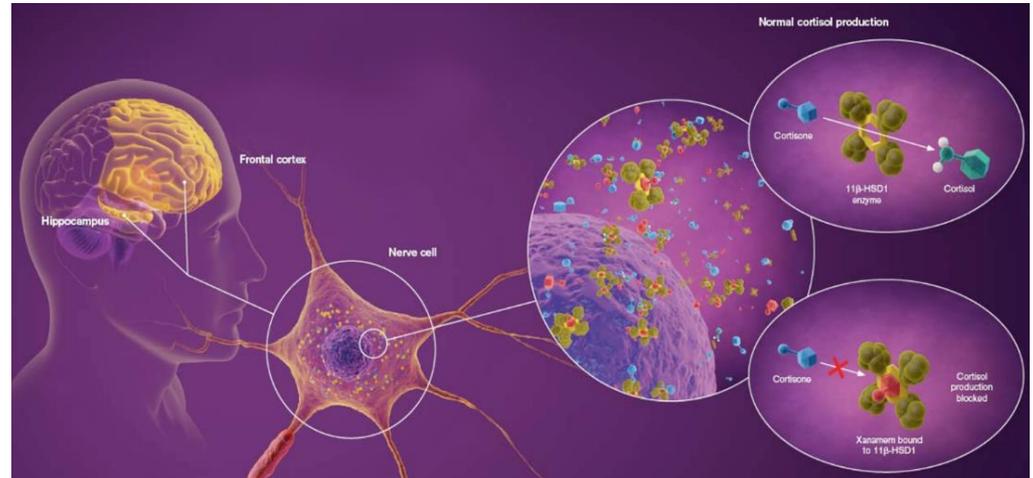
A specialist Advisory Board will assist Actinogen to design the most appropriate clinical development plan for Xanamem

Cognitive impairment in mood disorders & schizophrenia

Cognitive impairment can be a debilitating feature of mood disorders and schizophrenia, which exhibit raised cortisol levels

- High cortisol levels are found in severe mood disorders, particularly depression and bipolar disorder, and psychotic disorders (such as schizophrenia)
- Increased cortisol may cause or exacerbate cognitive impairment and depressive symptoms
- The continuum model of mood disorders provides for a broad spectrum and large population of relevant patients
- While some incumbent treatments slightly improve cognition (typically as a side effect), they do not normalise it

Xanemem's differentiated mechanism of action may improve neurocognitive functioning and attenuate depressive symptoms



New indications represent a spectrum of inter-related disorders associated with raised cortisol and cognitive impairment

Significant opportunity

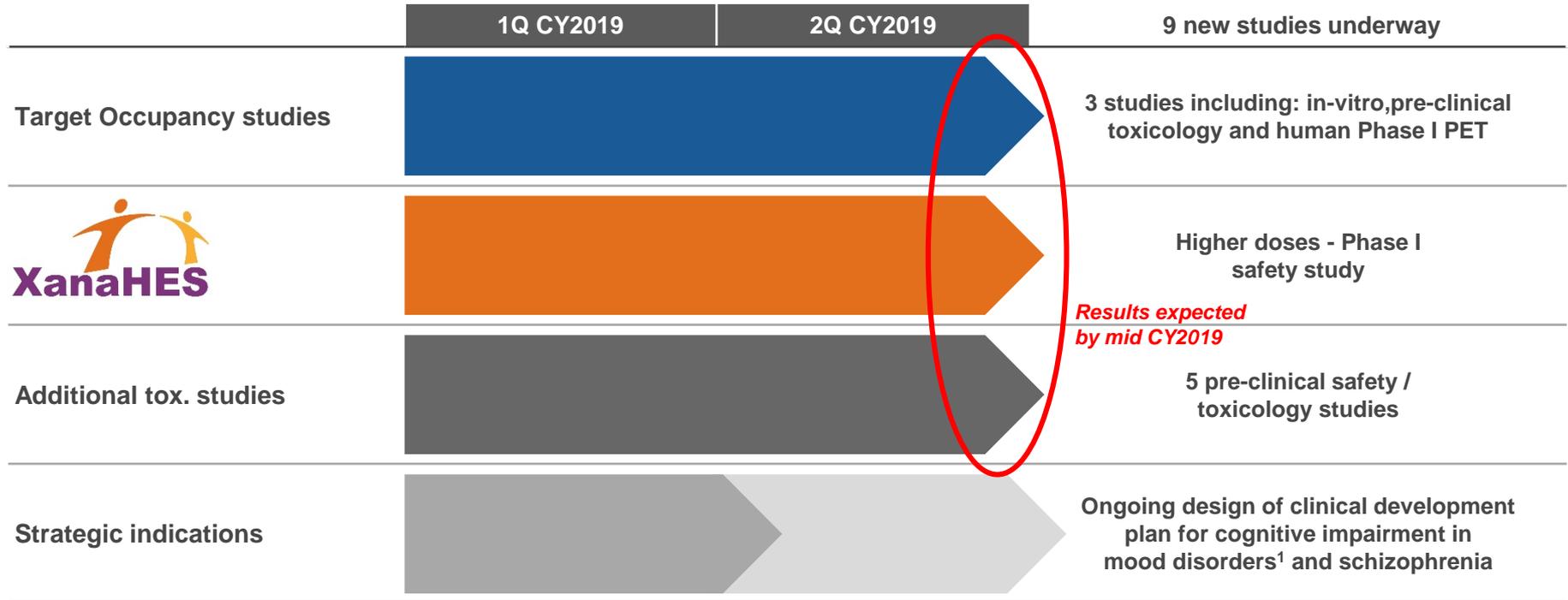
Large patient populations and economic costs suggest a high unmet need with significant market opportunity for Xanamem to be used in combination with current therapies in order to address cognitive decline

	Depression	Bipolar disorder	Schizophrenia
Prevalence in the US¹	16m	6m	2m
Estimated economic cost of disorder to the US system	~US\$200bn <i>In 2016, a 21% increase from 2005²</i>	~US\$202bn <i>In 2015 in Bipolar I disorder⁴</i>	~US\$154bn <i>In 2013⁶</i>
Global sales forecasts for disorder treatments	~US\$5.0bn in 2018 Forecast ~US\$9.5bn in 2024 ³	~US\$0.4bn+ ⁵	~US\$8.9bn sales in 2018 Forecast ~US\$10.1bn in 2024 ⁷
Cognitive issues in current patient population (prevalence)	85-95%	40-60%	75%
Currently available treatments for cognition¹	Significant treatment gap	None	None
Competitive landscape (cognitive enhancers)	One approved anti-depressant with limited efficacy and not specifically approved for cognition	No industry led trials for cognitive enhancers	Limited assets in development pipeline but none that specifically addresses raised cortisol

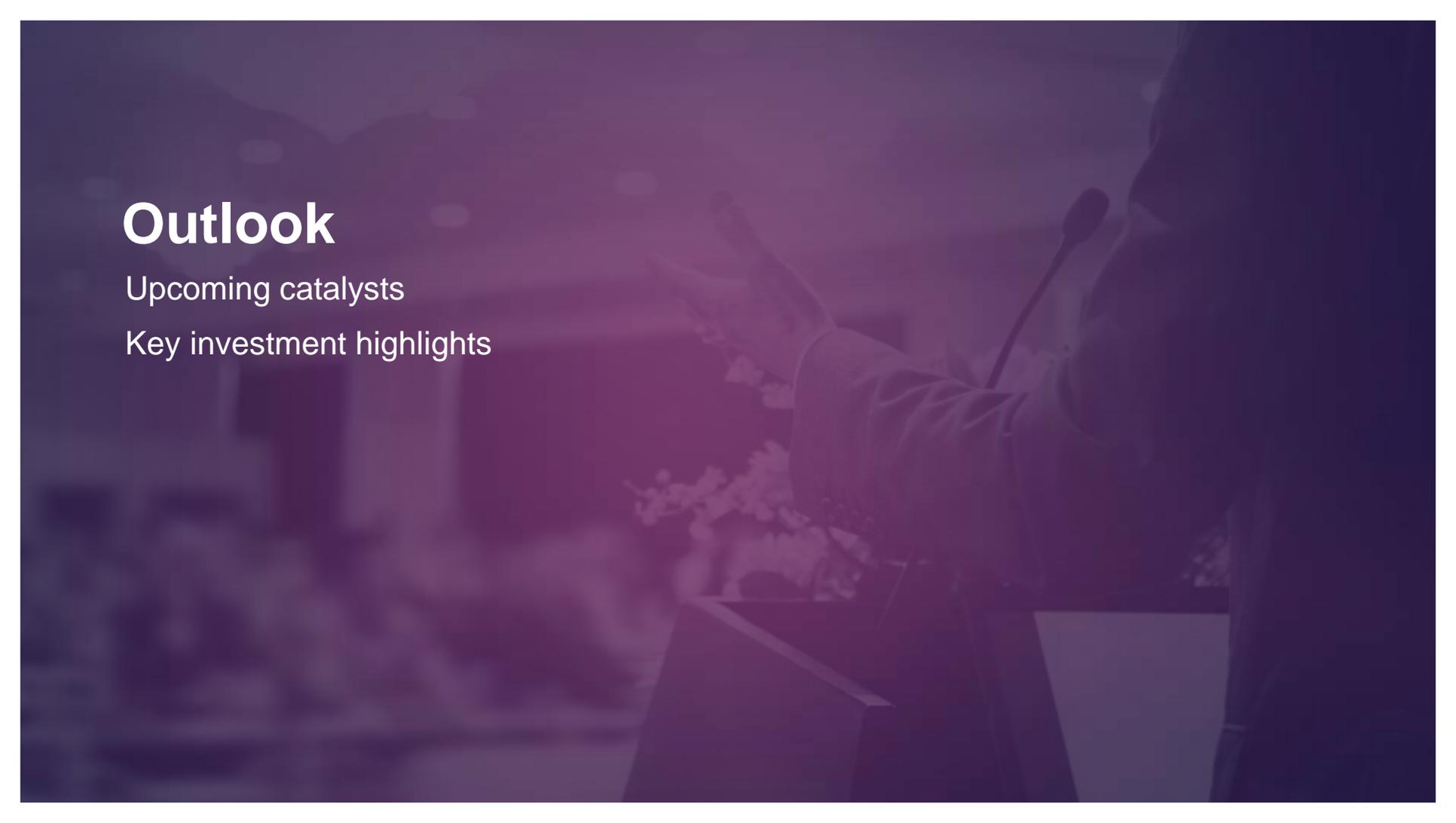
1. Bio-Link Market Analyses – Depression and Schizophrenia; 2. Greenberg PE, et al (2015) *J Clin Psychiatry*, 2015; 76(2):155–162; 3. Source: EvaluatePharma – depression, note: Trintellix (vortioxetine, Lundbeck/Takeda) only approved therapy with label supporting cognitive enhancement; 4. Cloutier, M et al (2018) *J Affective Disorders*, Volume 226, 45-51; note: this is for Bipolar I disorder, a subset of bipolar disorder. 5. EvaluatePharma – bipolar disorder; 6. Cloutier, M et al (2016) *J Clin Psychiatry*, 2016 Jun;77(6):764-71; 7. EvaluatePharma - schizophrenia

Development pipeline

Multiple studies are currently underway to enhance the Xanamem data set, with results expected in 2Q CY2019, and new indications clinical strategy initiated



1. Including depression and bipolar disorder



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 new studies into strategic indications¹

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, mood disorders and schizophrenia

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

1. Subject to data / results

Upcoming catalysts

Significant upcoming milestones across first half 2019

Studies	1Q CY2019	2Q CY2019	3Q CY2019	4Q CY2019	Key catalysts
 XanADu			<p>Results expected by mid CY2019</p> <p><i>Next stage of development will be informed by these study results. Further development in conjunction with advisory boards and key regulatory bodies</i></p>		Results expected to be available by mid CY2019
Target occupancy studies			Results expected to be available by mid CY2019		
 XanaHES			Results expected to be available by mid CY2019		
Additional tox. studies					Initial results expected by mid CY2019
Strategic indications					Design of clinical development strategy
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 neurological 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 11 β HSD1 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 analyses 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 strategic indications selected



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



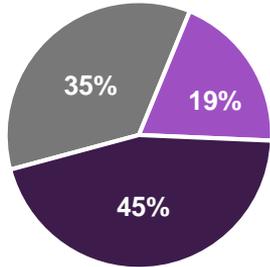
Corporate overview

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

Overview

- Actinogen is developing Xanamem, a novel therapy for Alzheimer’s disease, mood disorders and schizophrenia, 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



BVF Partners 

Top 5 (excl. BVF Partners)

Top 20 (excl. BVF Partners)

Remaining shareholders

LTM share price performance and trading metrics



1. FIL Investment Management (Hong Kong) Limited and FIL Pensions Management
 2. Net cash as at 31 Dec 2018

Substantial Institutional investment in Actinogen

Recognises potential and endorses strategy

Positive 2018 interim analysis catalyses significant A\$15m investment through Placement¹

- 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** at time of placement

Further strategy endorsement 1H 2019: institutional investment by **FIL**²



1. Announced 23 May 2018
2. FIL Investment Management (Hong Kong) Limited and FIL Pensions Management, announced 14 March 2019 and 23 April 2019

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™
- MBChB (University of Witwatersrand); FFPM; MBA (Macquarie); GAICD



Dr. George Morstyn
Non-executive director

- **25+ years experience** in biotech 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



Mr. Malcolm McComas
Non-executive director

- **25+ years experience** in the financial services industry
- Chairman of Pharmaxis and Fitzroy River Corporation; previously senior leadership roles in investment banking
- Extensive experience in corporate finance, M&A, debt and equity funding transactions across multiple sectors
- BEc, LLB (Monash University); FAICD; SF Fin



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, 11 β -HSD1 and drug discovery



Prof. Jonathan Seckl



THE UNIVERSITY
of EDINBURGH



Prof. Brian Walker



**Newcastle
University**



Prof. Scott Webster



THE UNIVERSITY
of EDINBURGH

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 2019 | June, Philadelphia

Planned CY2019

Scientific Conference Attendance

AAIC 2019 | July, Los Angeles

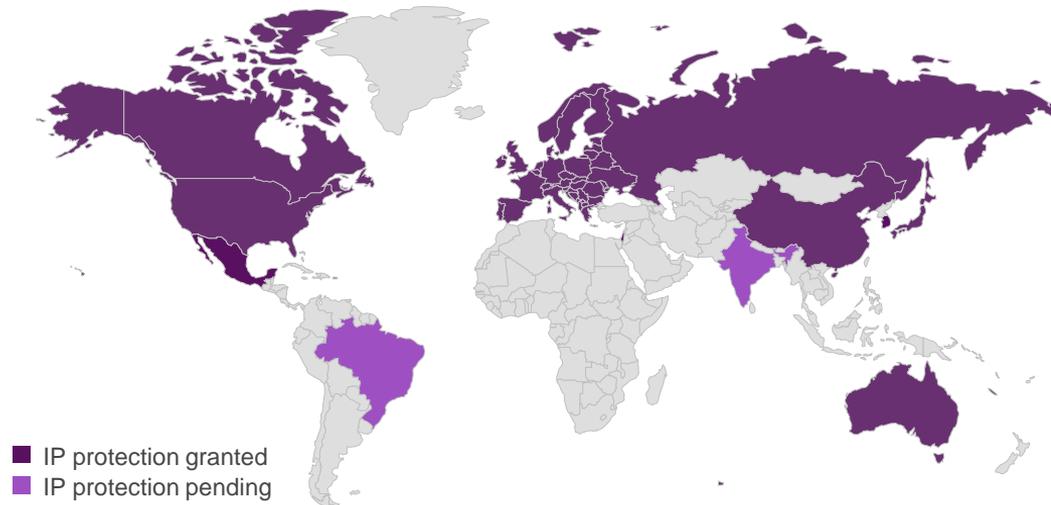
CTAD 2019 | December, San Diego



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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