

ASX ANNOUNCEMENT**Actinogen Medical to present at BIO International 2018**

- Actinogen Medical to present at BIO International Convention, the world's largest and most prestigious biotechnology convention held in Boston USA, in early June.
- BIO International attracts the leading organisations in global biotech and facilitates networking on new opportunities and partnerships.
- BIO 2018 is the ideal forum to showcase Actinogen and Xanamem - including the excellent progress made with XanADu, the recently announced Interim Analysis outcome, the \$17M capital raising and the broader development plans for Xanamem that flow from it.

Sydney 31 May 2018. Actinogen Medical (ASX: ACW) is pleased to announce that the Company's CEO Dr. Bill Ketelbey is leading the Actinogen team, and presenting, at the BIO International Convention in Boston USA, 4-7 June 2018.

Dr Ketelbey will meet with global biotech industry leaders and prospective future business partners. This follows on from the pleasing progress made with XanADu, the Company's Phase II clinical trial of Xanamem in Alzheimer's disease, with the positive recommendation from the Data Safety Monitoring Board (DSMB) following the Interim Analysis, to continue XanADu without modification. XanADu currently has 103 of the 174 patients enrolled – 60% of the total. Concurrent with the positive Interim Analysis recommendation, the Company secured a \$15M investment by three leading institutional investors, led by leading US specialist biotech investor Biotechnology Value Fund L.P. (BVF), providing strong endorsement of the Company and its added development plans for Xanamem. Additionally, a Share Purchase Plan has been launched to raise up to a further \$2M.

The BIO International Convention, hosted by the Biotechnology Innovation Organisation (BIO), is the largest global convention for the biotechnology industry and attracts the leading organisations in biotech to network on new opportunities and potential partnerships.

Participation at BIO International provides Actinogen unparalleled networking opportunities to showcase the Company and the quality research that supports Xanamem's development. The BIO International presentation is attached.

ENDS

Actinogen Medical

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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 Xanamem 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 β -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 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, will enrol 174 patients at 20 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.

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



Actinogen
Medical

Alzheimer's Treatment Needs a New Approach – Xanamem™

BIO International Convention – June 2018

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Actinogen Medical (ASX:ACW)

- Developing Xanamem for the treatment of Alzheimer's disease (AD) and cortisol-associated cognitive impairment
- Xanamem, a novel differentiated mechanism of action: prevents the production of excess brain cortisol
- Persistently raised cortisol in the brain is associated with the development and progression of AD
- First-in-class, brain penetrant, orally active, inhibitor of 11 β HSD1 enzyme, reducing conversion of cortisone to cortisol
- Experienced board and management; expert clinical and scientific advisory boards

Largest holders

Pending completion of the Placement of 300,000,000 shares (Tranche 1 and 2) and the Share Purchase Plan (SPP)*

- **Biotechnology Value Fund, L.P.**
- **Platinum Investment Management Limited**
- **Edinburgh Technology Fund Limited**
- **Australian Ethical Investment**
- JK Nominees
- Sunset Capital Management
- Warambi Sarl
- BNP Paribas Nominees



* Announced 23 May 2018

Interim analysis – DSMB recommendation to continue trial without modification*



- Interim Analysis undertaken by independent Data Safety Monitoring Board (DSMB)
- Safety and efficacy data reviewed
- Conducted on data from first 50 evaluable XanADu trial patients. Additional 37 patients' safety data included in the analysis
- No treatment related serious adverse events
- Recommendation affirms the positive benefit-risk safety profile of Xanamem 10mg daily
- Supports progression of study as planned
- Underpins further development in other indications

XanADu

* Announced 23 May 2018

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 an 13.4% premium to the 5-day VWAP
- BVF cornerstones Placement to become the largest shareholder with a 19.9% holding
- Funding to advance Company's development plan through additional Xanamem studies. Focus on enhancing the data-set for Xanamem, adding substantial value to ongoing partnering discussions



* Announced 23 May 2018

New Xanamem studies – funded through May '18 capital raising

Enhancing value, broadening scope, strengthening data-set

- New funding to advance Company's development plan
- Focus on enhancing the data-set for Xanamem, broadening scope of use and adding substantial value to asset
 - Target engagement and safety studies – to help define optimum dose
 - Additional standard toxicology studies required by regulators (positioning Xanamem for Phase III development)
 - New indications

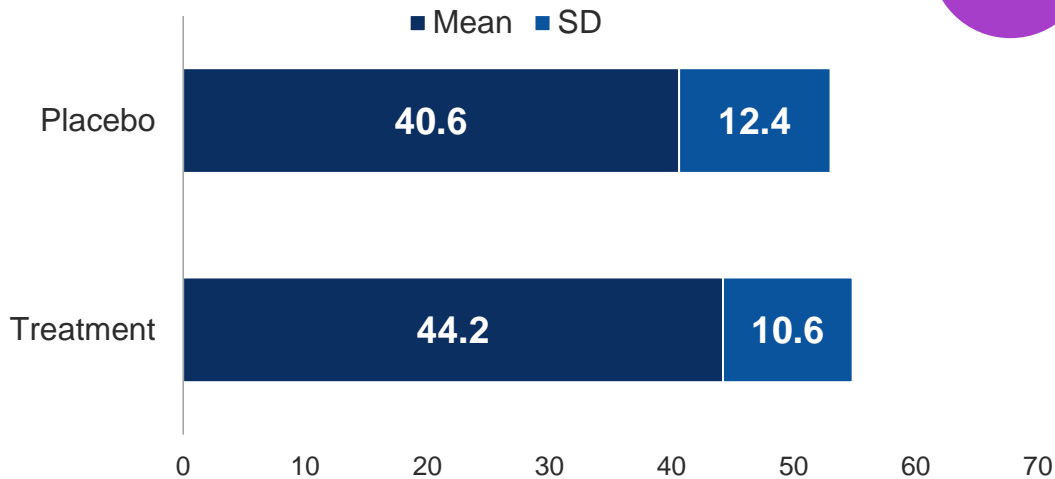


Cortisol inhibition improves cognition – key factor in 2014 acquisition

Two 2004 pilot studies concluded that inhibiting cortisol production in the brain with carbenoxolone improves cognitive function in healthy elderly men & type 2 diabetics – established Edinburgh Uni cortisol hypothesis

VERBAL FLUENCY – Study 1*

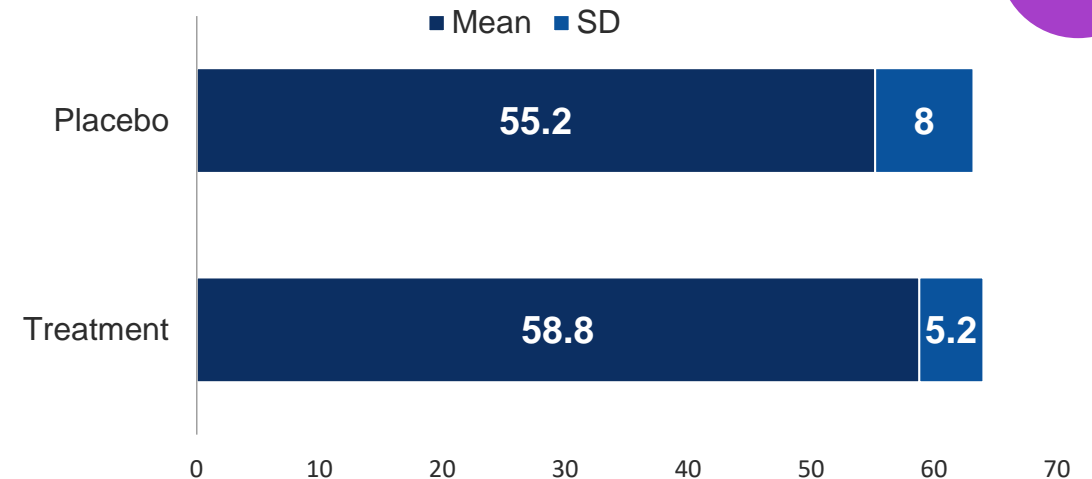
P=0.006



* 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.

VERBAL MEMORY – Study 2**

P=0.005



**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.

Significant improvement in verbal fluency and verbal memory after only 4 and 6 weeks treatment

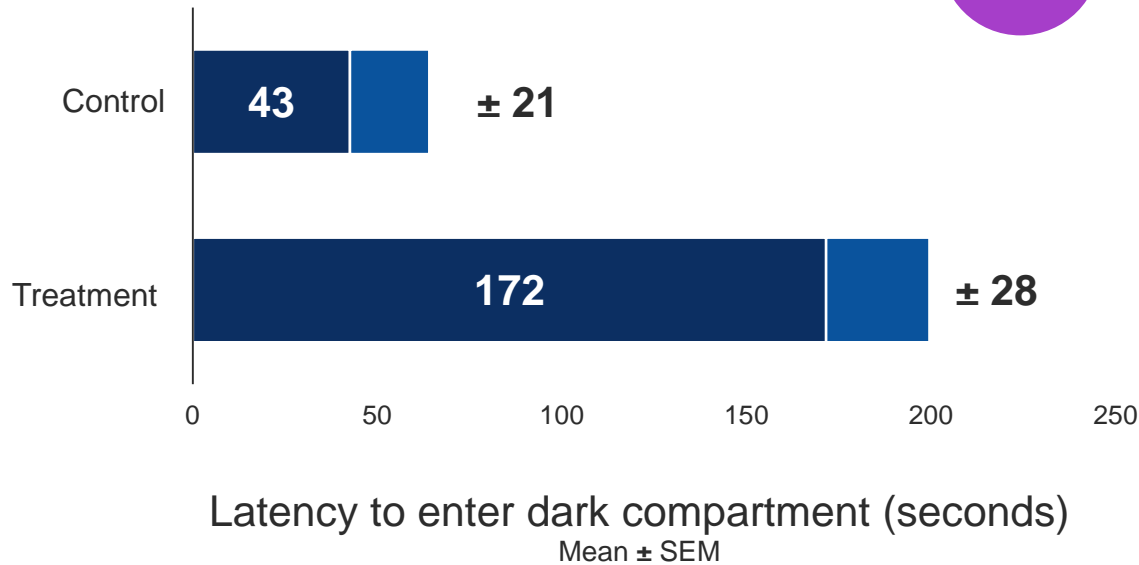
11 β -Hydroxysteroid dehydrogenase inhibition improves cognition function in healthy elderly men and type 2 diabetics
Sandeep et al., 2004 PNAS (vol. 101, no. 17) 6734-6739

Robust animal data with new candidate - key factor in 2014 acquisition

Symptomatic and disease modifying effects in mouse models – AUD \$25 million invested pre-acquisition

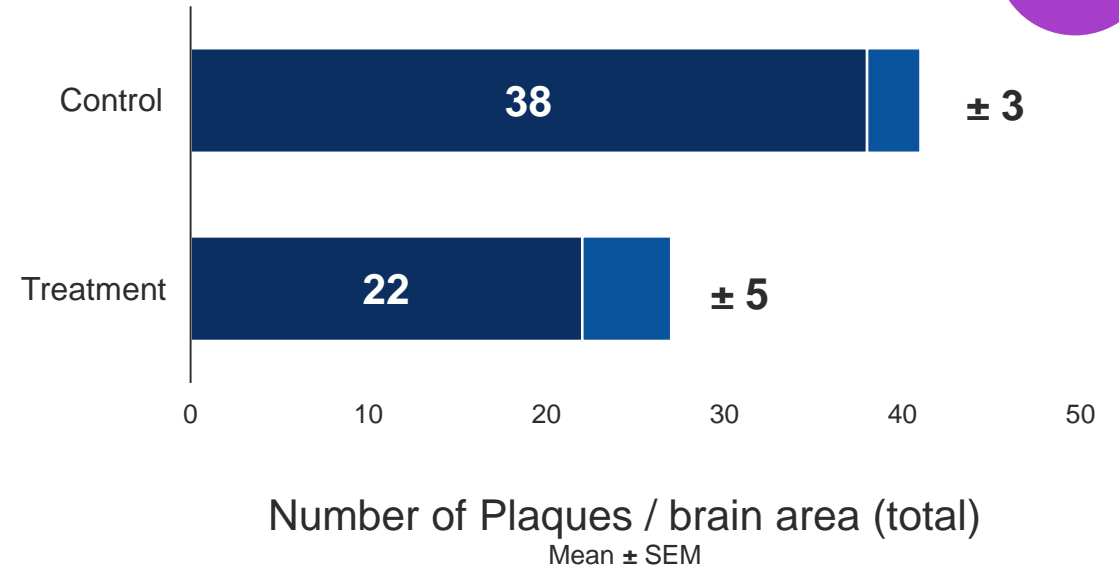
COGNITION: treatment 28 days

P=0.004



AMYLOID CLEARANCE: treatment 28 days

P=0.01



Significant improvement in cognition after only 28 days treatment, continuing out to 41 weeks

UE2316 in Tg2576 rodent model of Alzheimer's disease.
Sooy, et al., 2015. Endocrinology 156 (12) 4592-4603



Xanamem

Xanamem

- A novel, first in class, potent, orally bioavailable, brain-penetrant, 11 β HSD1 inhibitor¹
- Differentiated mechanism of action: blocking cortisol production in the brain
- Symptomatic and disease modifying effects *in vivo*¹
- Well-tolerated – dosed >100 patients/subjects: acceptable clinical safety, toxicity and PK/PD profile¹
- Effective human brain concentrations demonstrated¹
- XanADu – phase II clinical study underway, dosing subjects with mild AD dementia in USA, UK, AU
- Planning ongoing for additional clinical indications
- Composition of matter IP coverage \geq 2031, patents granted in all major markets
- XanADu Alzheimer's trial fully funded following completion of ~A\$5.3 million capital raise in November 2017
- A range of additional studies adequately funded following completion of ~\$17 million capital raising in May 2018



1. Webster *et al.*, 2017, British J Pharmacol 174:396-408

Cortisol: a validated biomarker and target for AD

Cortisol and Alzheimer's

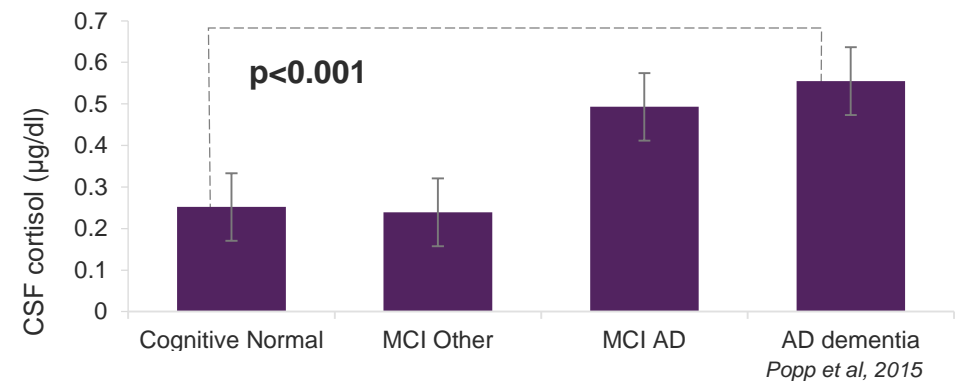
- Recent independent studies support the association between cortisol and AD development and progression¹⁻⁵
- Cognitive impairment in patients with neuroendocrine dysfunction⁶⁻⁹
- Compelling evidence provided by the Australian Imaging, Biomarker & Lifestyle Study of Ageing (AIBL) study (2017)⁵
 - Subjects with higher plasma cortisol at much greater risk of developing AD
 - Accelerated effect of A β + on decline in global cognition, episodic memory and attention

Xanmem

- Data presented at four major international medical congresses in 2016 – AAIC Toronto; CTAD San Diego; ICE Beijing; MMC Lisbon
- Pre-clinical and Phase I data published¹⁰⁻¹¹



MEAN CSF CORTISOL LEVELS



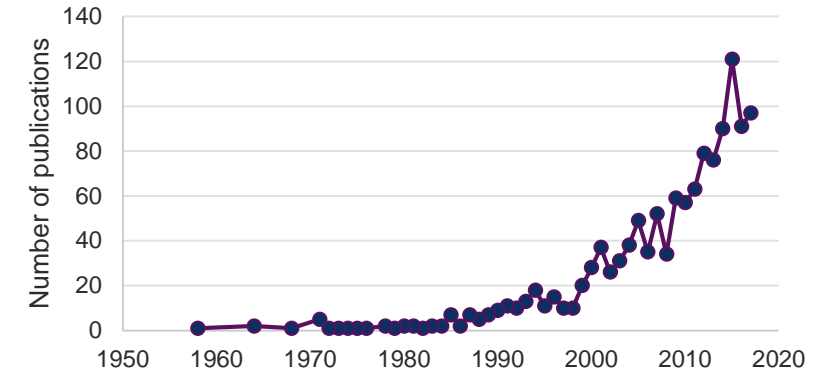
[1] Geerlings et al., 2015, Neurology 85: 1-8; [2] Lehallier et al., 2016, JAMA Neurology 73(2), 203-212; [3] Popp et al., 2015, Neurobiol. Aging 36:601–607; [4] Ennis et al., 2017, Neurology 88(4):371-378; [5] Pietrzak et al., 2017, Biol Psychiatry: Cognitive Neuroscience and Neuroimaging, 2:45-52; [6] Lupien et al., 2009, Nat Rev Neurosci 10:434–445; [7] Starkman et al., 1999, Biol Psychiatry 46: 1595–1602; [8] Lupien et al., 1998, Nat Neurosci 1:69–73; [9] MacLulich et al., 2005, Psychoneuroendocrinology 30:505–515; [10] Sooy et al., 2015, Endocrinology 156(12):4592-4603; [11] Webster et al., 2017, British J Pharmacol 174:396-408.

Cortisol, cognitive decline and AD: a growing body of literature

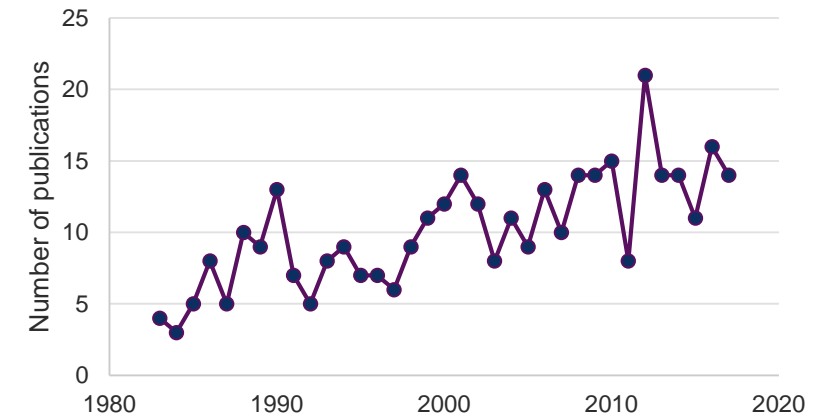
Recent relevant reviews:

- Cortisol: Mediator of association between Alzheimer's disease and diabetes mellitus? (Notarianni, 2017, *Psychoneuroendocrinology*)
- Unified theory of Alzheimer's disease (UTAD): implications for prevention and curative therapy. (Nehls 2016, *J Mol Psychiatry*)
- Is Dysregulation of the HPA-Axis a Core Pathophysiology Mediating Co-Morbid Depression in Neurodegenerative Diseases? (Du and Pang, 2015; *Front Psychiatry*)
- The impact of stress and glucocorticoids on memory. (Tatomir et al. 2014; *Clujul Med.*)
- Contribution of glucocorticoids and glucocorticoid receptors to the regulation of neurodegenerative processes. (Vyas and Maatouk, 2013; *CNS Neurol Disord Drug Targets*)
- Stress-induced cytokines and neuronal dysfunction in Alzheimer's disease. (Ricci et al., 2012; *J. Alzheimer's Dis.*)
- Local amplification of glucocorticoids in the aging brain and impaired spatial memory (Yau and Seckl, 2012; *Front. Aging Neuroscience*)

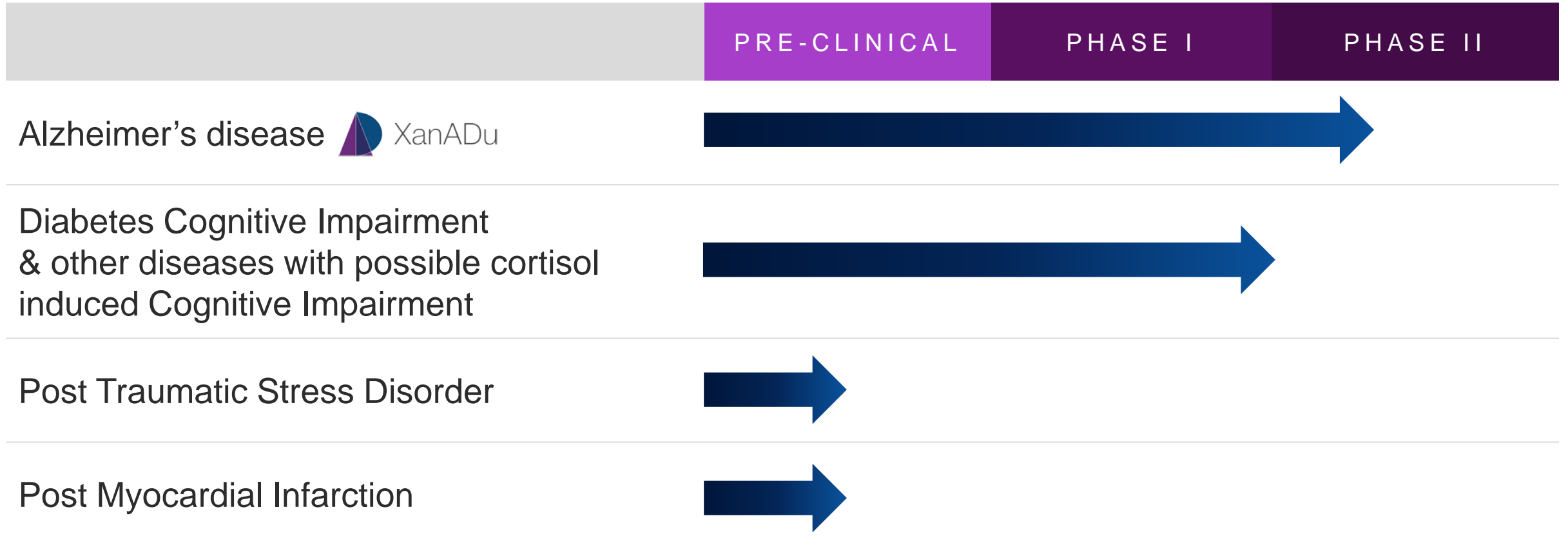
PUBMED:"CORTISOL AND COGNITION"



PUBMED: "CORTISOL AND ALZHEIMER'S"



Xanamem pipeline of indications, back-up compounds*



* Back-up compounds to Xanamem, licenced from Edinburgh University



XanADu – Phase II Trial

XanADu – Xanamem in Alzheimer's disease



Phase II double blind, randomised, placebo-controlled study to assess the efficacy and safety of Xanamem in participants with mild Alzheimer's disease*

- 103 patients enrolled (60% of total study cohort) and more than 68 patients already completed study**
- On track for last patient enrolled in Q4 2018 and top line results in Q2 2019
- Interim Analysis on first 50 evaluable patients - DSMB recommends continuing XanADu without modification



Xanamem treatment course

12 weeks



174

Mild Alzheimer's patients



Xanamem 10mg daily
for 12 weeks vs placebo



Trial conducted at 20 sites in
AUS, USA and UK

Primary and secondary endpoints are standard and experimental cognitive outcome measures used in Alzheimer's research: ADASCog14, ADCOMS, CDR-SOB, MMSE, RAVLT, NTB-ED

* Registered on Clinicaltrials.gov: NCT02727699

** As at 31 May 2018



Investment potential

Commercially experienced, globally recognised

Board of Directors



Dr. Geoff Brooke
Chairman



Dr. Bill Ketelbey
CEO & MD



Dr. Jason Loveridge
Non-Executive Director



Dr. George Morstyn
Non-Executive Director

Xanamem Clinical Advisory Board



Prof. Craig Ritchie
Chair



Prof. Colin Masters

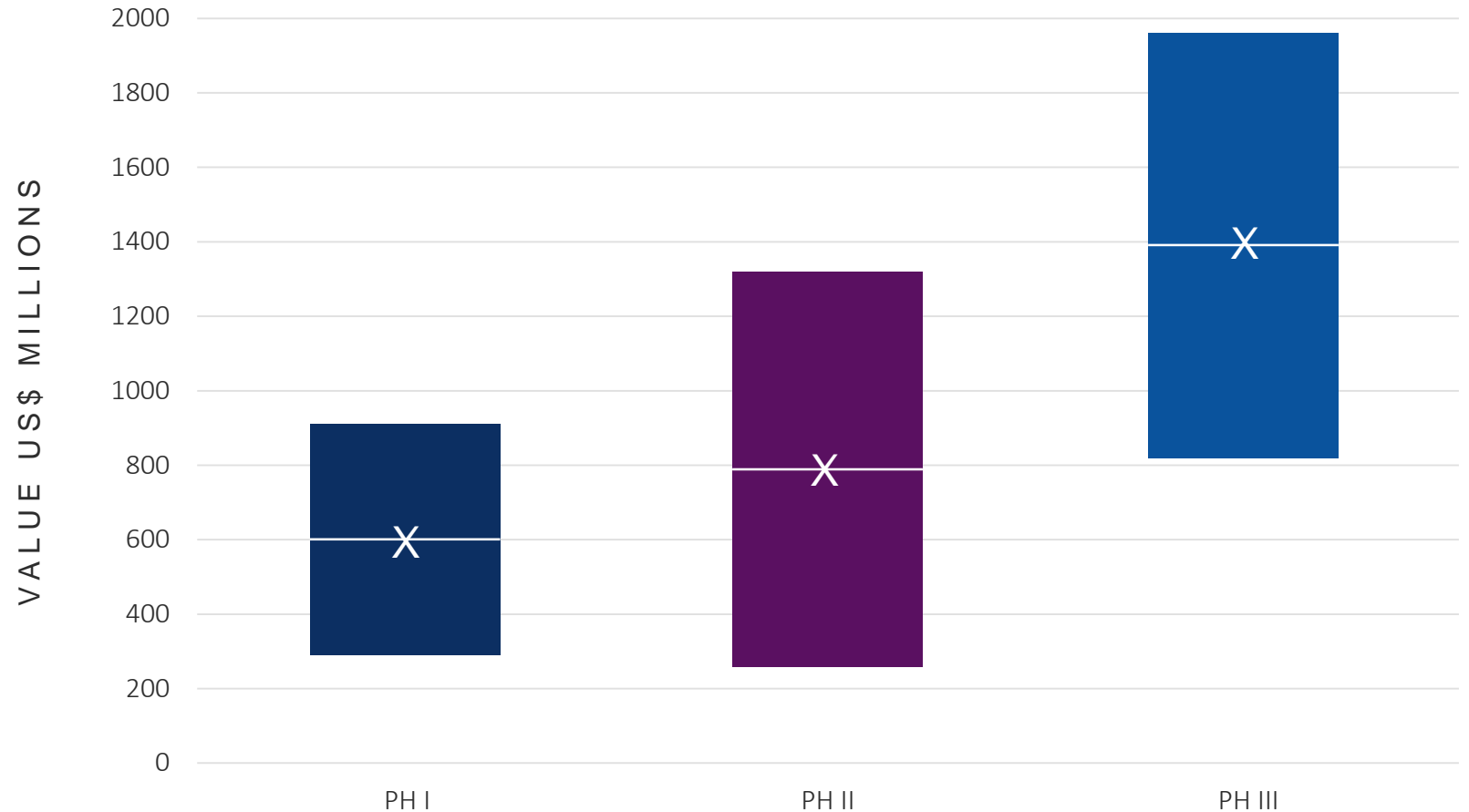


Prof. Jeffrey Cummings



Peer comparison

What big pharma companies are paying for acquisition of drug developers in the Alzheimer's space





Xanamem™ - summary

Summary



A huge market with a significant unmet medical need

Xanamem

- Differentiated, with a novel mechanism of action
- Small molecule - oral
- High quality development plan and regulatory review
- Solid IP out to at least 2031
- Potential utility in other neurological indications

XanADu

- Fully funded to completion of XanADu
- Additional studies funded with May 2018 capital raise
- Interim Analysis – continue study without modification
- On track for last patient enrolled before end 2018
- 103 patients enrolled (60% of total); 68 already completed



Substantial independent support for cortisol/Alzheimer's hypothesis



Highly experienced Board



Growing interest in Xanamem from pharma partners



A compelling investment opportunity

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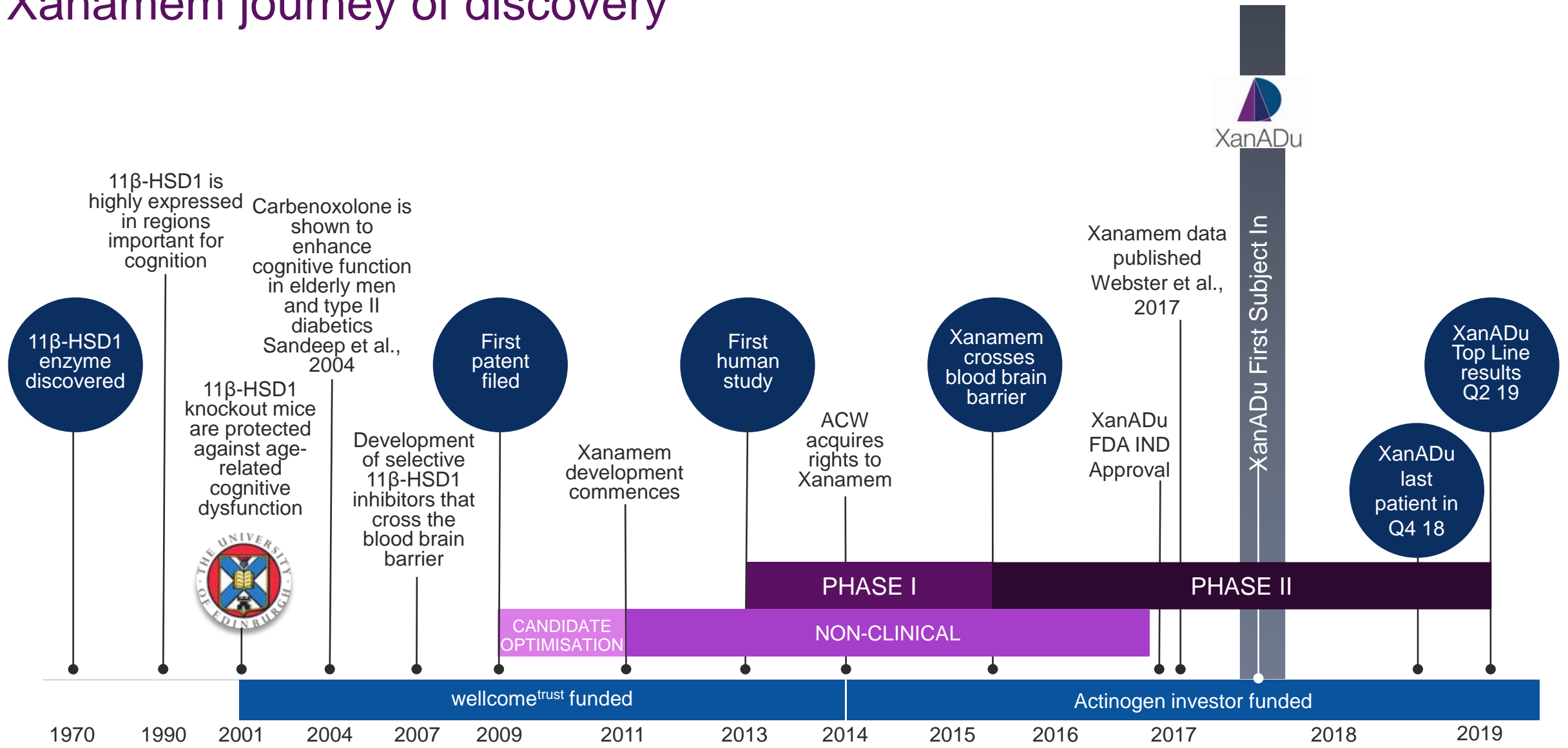


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Appendix

Xanamem journey of discovery



Recent comparable deals

Assets with Alzheimer's disease as the lead indication or key indication

Licensee/acquirer	Licensor/acquired	Year	Candidate(s)	Phase	Deal Value (US\$M)	Upfront (US\$M)
Takeda	Denali	2018	ATV platform, three programs	Pre-clinical	<u>~\$1,000</u>	\$150
AbbVie	Voyager	2017	AAV anti-tau antibodies	Pre-clinical	<u>\$1,109</u>	\$69
Biogen	BMS	2017	BMS-986168	Ph 1	<u>\$710</u>	\$300
Allergan	Heptares	2016	Three M1/M4 agonists	Ph I	<u>\$3,340</u>	\$125
Janssen	AC immune	2015	ACI-35	Ph Ib	<u>\$509</u>	Undisclosed
Merck	Bionomics	2014	BNC-375	pre-clinical	<u>\$526</u>	\$20
Eli Lilly	AstraZeneca	2014	AZD3293	Ph I	<u>\$500</u>	\$50
Iperian	BMS	2014	IPN007	pre-clinical	<u>\$725</u>	\$175
Otsuka	Lundbeck	2013	Idalopirdine	Ph II	<u>\$825</u>	\$150
Janssen	Orion	2013	ORM-12741	Ph IIa	<u>Undisclosed</u>	\$31