Actinogen Medical

August 2015 ISSUE 3

Investor Update

In this Issue

Key Investment Highlights:

ASX: ACW
Market cap: Approximately A$40m

- Xanamem™, a promising research drug for AD and its prodromal stage, Mild Cognitive Impairment
- Significant unmet need in a huge and growing global market
- Novel mechanism of action, targeting the stress hormone cortisol – a key differentiator
- Hypothesis backed by good pre-clinical and clinical evidence. Early development funded by Wellcome Trust
- Final Phase I and preclinical results due second-half 2015
- IND filing and Phase II study planned for 2016; funded through to completion of Phase II
- Expected to be used in combination with other AD therapies
- Patent protection to 2031

Message from the CEO

Welcome to the third issue of the Actinogen Medical Investor Update for 2015. I am delighted to report on what has been another period of strong growth for the Company and excellent progress with our ongoing development of Xanamem™

We have completed the clinical stage of the second Phase 1 study, and we've in fact already received most of the results. Xanamem™ consistently proves, as expected, to be acceptably safe and well tolerated across the full dosage range tested. In addition, the study results have confirmed our understanding of how the body absorbs and metabolises Xanamem™. Within the next few weeks we will have the final results that will help confirm the most appropriate dose to take forward to the Phase II trial, and demonstrate that Xanamem™ is efficiently delivered to the brain, its primary site of action in Alzheimer's disease.

Our successful capital raising in late April demonstrated the significant interest in investing in Actinogen Medical and reflects the massive unmet medical need in Alzheimer's dementia and the good progress being made over recent months, supported out of Wall St, in developing potential new therapies for this disease. We have every expectation of an increasing interest in investing in Actinogen as we ramp up to the start of the Phase II study next year and particularly as we progress through the study recruitment.

Our plans to initiate the Phase II study in patients with mild Alzheimer's and mild cognitive impairment continue apace. We have a near-final protocol synopsis for the study, developed with substantial assistance from our Advisory Board and the inventors of Xanamem™ at Edinburgh University. Pleasingly the capital raising, along with the expected Federal Government R&D rebate, provide us with adequate funds to complete the Phase II research. We currently expect this to be around the end of 2017. We expect positive efficacy results to generate substantial investment interest from major pharmaceutical companies and investors alike. Inevitably, there will be a growing speculation on the results and investor interest in Actinogen Medical will peak as we approach the conclusion of the trail and the data read-out. Investors will be further attracted to the broad platform of additional research ideas to come out of the recent Advisory Board meeting.

Our team continues to find it immensely gratifying to be able to work on developing another potentially effective treatment for this dreaded disease, Alzheimer's

These additional indications, while presenting substantial clinical benefit, also de-risk the investment in Actinogen by generating at least 6 "shots-on-goal" for Xanamem™. Biomedical research is by nature a risky venture, which is obviously matched by equally impressive returns. Our broad portfolio of indications provide a reassuring insurance for our ongoing Alzheimer's research with Xanamem™.

Our team continues to find it immensely gratifying to be able to work on developing another potentially effective treatment for this dreaded disease, Alzheimer's. I would like to thank all our loyal shareholders for their continued support through what has been a difficult time in investment markets and I look forward to regularly updating you on our progress as we lead into the launch of our Phase II study in Alzheimer's disease.

Dr Bill Ketelbey
Chief Executive Officer
@billketelbey

Baker Young initiates coverage on Actinogen with "buy" rating

Adelaide-based stockbroker Baker Young has initiated research coverage on Actinogen with a "buy" rating and target price of $0.36.

The broker said Actinogen shares represent "compelling value" at current levels on a risk-reward basis.

"We believe reward is warranted by the size of the multi-billion dollar Alzheimer's market and desperate need for new medications and the likelihood that definitive results will be available from the Phase II study within the next two-three years, generating substantial investment or acquisition interest from major industry players."

Baker Young also pointed to recent significant re-ratings of US stocks in the Alzheimer's space as a positive.

"Given the reinvigorated interest towards Alzheimer's, we believe this is the best time for small cap biotechs focused on Alzheimer's therapies to attract institutional interest and significant premium in valuation(s)," it said.

The broker also noted that Actinogen's upcoming Phase II trial of its lead drug, Xanamem™ positioned Actinogen "amongst significantly larger peers."

"We believe positive results from this Phase II trial will likely result in a significant partnering transaction … given the current unmet market need, comparable similar transactions and Big Pharma's desire to bring new effective treatments for dementia to market."

As well as the potential for a significant licensing agreement post the Phase II results and renewed investor interest in Alzheimer's drugs, Baker Young notes several reasons to invest in Actinogen, namely the large and unsatisfied global market for Alzheimer's drugs, Xanamem™'s novel mechanism of action, the Company's highly experienced management team and that Actinogen is fully funded through to the completion of its Phase II study.

It also notes Thompson Reuters rating Xanamem™ as a top-five global drug in Phase I development; the drug's long patent to 2031; the multiple indications for Xanamem™ and the expectation that it will be used in combination with other Alzheimer's therapies as reasons to buy the stock.

The full report can be accessed at: www.actinogen.com.au/initiation-of-coverage.pdf

Alzheimer's drugs generating excitement among Wall St investors

There's been a renaissance of investor interest in Alzheimer's drugs, with positive data and solid deals sparking renewed enthusiasm for the sector.

Biogen's release of positive data from its Phase I trial of its investigational Alzheimer's disease treatment, aducanumab in March saw the company's market cap grow by US$40 billion over three months and revived hopes that a treatment targeting amyloid-beta, a hallmark of Alzheimer's, could be realized. The Phase I results showed that aducanumab reduced amyloid plaques and also caused a significant slowing of cognitive decline in Alzheimer's patients.

Meanwhile, Bermuda-based biotech Axovant Sciences, pulled off the biggest biotech initial public offering in history in June, with the stock debuting US$3 billion - double its slated offer price. The debut followed Axovant's buy of GlaxoSmithKline's discarded 5-HT6 inhibitor for Alzheimer's disease, RVT-101. The company now plans to launch a Phase III trial for the drug by the end of the year.

Axovant has solid support from leading biotechnology analyst at Evervore ISI, Mark Schoenebaum. Schoenebaum says Axovant has a 65% chance of success in the upcoming Phase III study and gives the company a solid shot at earning peak blockbuster sales of $US3.5 billion.

Meanwhile, in January, Japanese pharmaceutical group Otsuka Pharma, bought Avanir Pharmaceuticals for US$3.5 billion. The buy followed Avanir's positive Phase II data on AVP-923 for symptomatic treatment of behavioural symptoms in Alzheimer's patients and Avanir's share price more than quadrupling over 2014.

This renewed enthusiasm and interest in Alzheimer's drugs is good news for Actinogen and Xanamem™ as it underpins the recognition of the importance of developing an effective treatment for the disease and the huge market potential. Importantly, none of the compounds mentioned above are likely to be competitors to Xanamem™, instead they are likely to be used in combination with the drug.

Xanamem™ trial update

Excellent progress has been made with the final Phase I study, with provisional results confirming that Xanamem™ is acceptably safe and well-tolerated. In addition, the plasma level of Xanamem™ needed in order to achieve the right concentration in the brain to produce a therapeutic effect was achieved.

These results will be used to determine the Xanamem™ dose for the Phase II study which is expected to enrol its first patient in the first half of 2016. The Phase II study is designed to show the efficacy of Xanamem™ in patients with mild Alzheimer's disease or Mild Cognitive Impairment (MCI). It is planned to be conducted in Australia, the UK and the USA.

The Phase 1 Multiple Ascending Dose (MAD) study involved 24 healthy volunteers. It was a gold-standard, placebo-controlled clinical trial conducted at Linear Clinical Research, a world-class clinical trial facility that is part of the QEII Hospital in Perth, Western Australia.

Excellent progress has been made with the final Phase I study, with provisional results confirming that Xanamem™ is acceptably safe and well-tolerated.

Linear Clinical Research Principal Investigator, Dr Janakan Krishnarajah said: "We have now successfully completed the important dose escalation part of the study. The investigational drug was found to be well tolerated by all participants at all dose levels and importantly there were no serious adverse events noted. The absence of any safety concerns in this important multiple dose study supports the further development of the drug with a Phase 2 study in patients."

An additional 12 healthy volunteers have completed a Phase I Fed-Fasted study at Linear Clinical Research. The results from this study will be used to instruct patients whether to take the drug with or without food.

The Phase II study is designed to show the efficacy of Xanamem™ in patients with mild Alzheimer's disease or Mild Cognitive Impairment (MCI).

The third and final part of this Phase I study has successfully completed the clinical stage, as announced earlier. Only laboratory analysis now remains to complete the full trial. The objective of this study is to show that Xanamem™ crosses the blood-brain barrier. This is necessary to prove that the drug reaches the brain which is where Alzheimer's disease has its greatest impact.

The final preclinical study of Xanamem™ is being performed at Monash University in Melbourne, Victoria. This study will provide the toxicity and toxicokinetic data required to enable the Phase II study patients to take Xanamem™ for 12 weeks. The study is at the halfway mark and progressing very well. The results from this study are expected in October 2015.

At the June Xanamem™ Clinical Advisory Board meeting in Edinburgh, UK the draft Phase II Protocol Synopsis was agreed. There will be one overarching primary objective with preferably separate analyses of endpoints for the Mild AD and MCI patient cohorts. The meeting also agreed on secondary objectives, subject selection criteria, efficacy, exploratory and safety evaluations. The Protocol Synopsis is undergoing a final review with the Xanamem™ Clinical Advisory Board, the University of Edinburgh and Cogstate.

There has been a paradigm shift in clinical science around Alzheimer's dementia and these protocol design refinements from the Clinical Advisory Board aim to leverage the next level cutting edge science.

The next steps for the Phase II study include CRO selection for full outsourcing of the operational management and execution of the study. In addition, a contract has been signed with a specialist regulatory consultancy, ERA Consulting, to update the IB, IMPD and manage the US pre-IND meeting and US FDA submission. In addition, they will conduct a GAP Analysis to ensure the data meets all regulatory and partner expectations supporting a package of preclinical and clinical studies.

A contract has also been signed with High Force, the UK manufacturer of Xanamem™, to make more of the drug for the Phase II study.

Although the immediate focus for Xanamem™ is its potential treatment of Mild AD and MCI, there are plans to explore other indications in the near future. The Edinburgh meeting built upon previous discussions on the potential for Xanamem™, by virtue of its cortisol inhibiting properties, to have a positive effect on patients across a broad range of therapeutic areas.

The Protocol Synopsis is undergoing a final review with the Xanamem™ Clinical Advisory Board, the University of Edinburgh and Cogstate.

Vincent Ruffles said: "These additional indications present a great opportunity to increase the value of Actinogen Medical and its current clinical trial programme as well as to introduce new collaborations with respected international partners, such as the British Heart Foundation."

The indications include: Post-Traumatic Stress Disorder, Post-Myocardial Infarction, Diabetic Foot Ulceration, Diabetes Cognition and Parkinson's Disease Dementia.

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Xanamem™ – A new approach to treating Alzheimer's

Xanamem™ targets the stress hormone cortisol

Actinogen Medical has focussed on a new approach to treating Alzheimer's disease. Xanamem, our lead candidate under development, very effectively blocks the enzyme 11β-HSD1, which activates cortisone to form cortisol, the stress hormone.High levels of cortisone, and its active form cortisol, have been shown in human and animal models to produce clinical signs and symptoms very similar to Alzheimer's disease.

These include impaired memory, amyloid plaques and neural death. The effects are seen particularly in the hippocampus and frontal cortex, the areas of the brain most affected by Alzheimer's, especially early Alzheimer's.

Blocking production of cortisol has been shown to reverse the negative effects of high cortisol levels in the brain.

STATISTICS ON ALZHEIMERS

Increasing with age

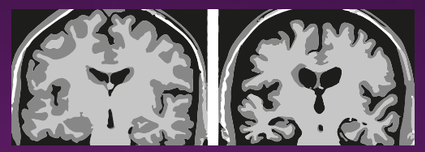
1 in 4 will get AD by age 85, and 1in 2 by age 95. Average longevity in the developed world is already around 85 years

450,000 new cases this year

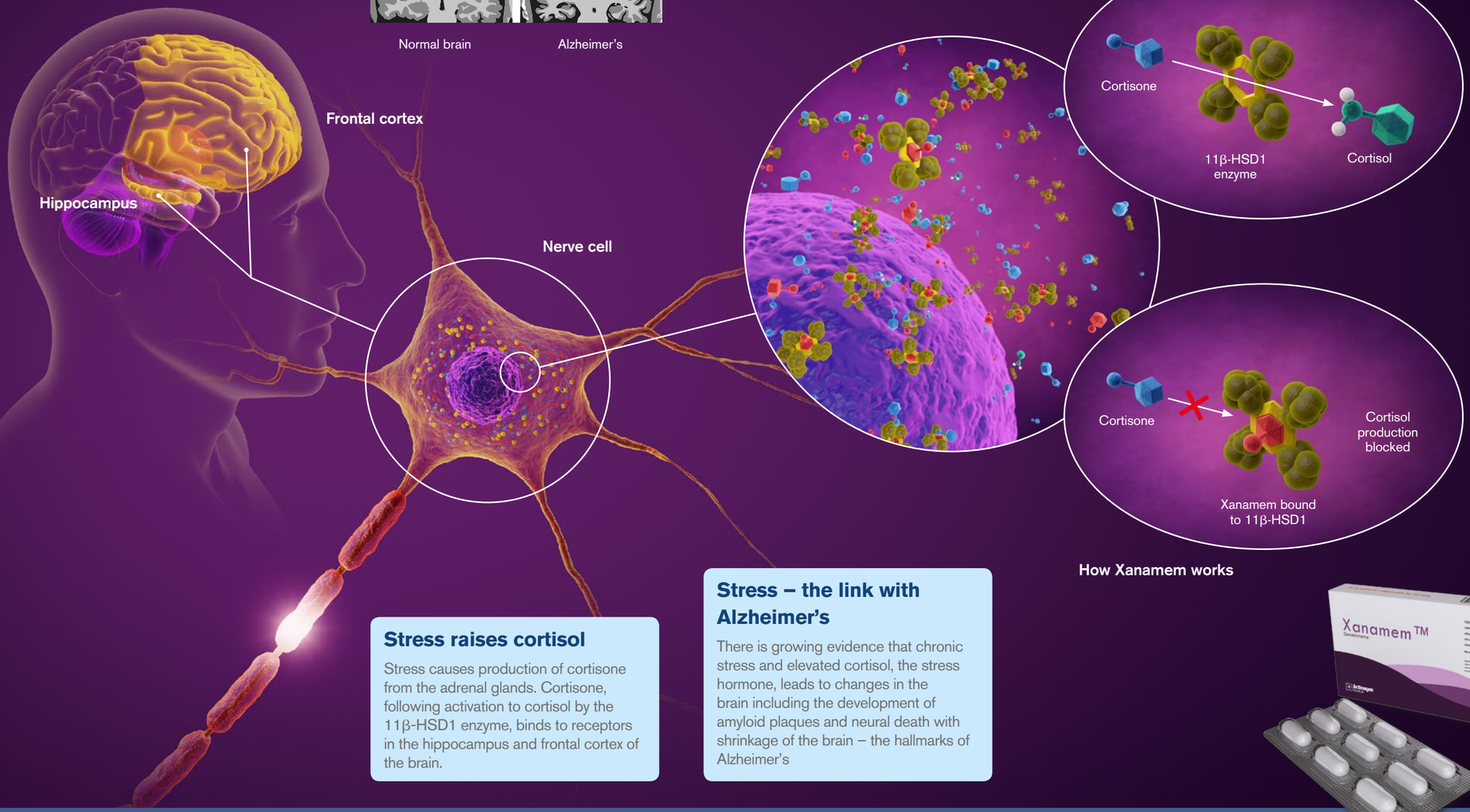
By 2030, there will be 615,000 new cases reported annually, and by 2050 that number will skyrocket to 959,000

US$1 trillion disease by 2050

Cost of treating AD in US $300 billion, rising to $1trillion by 2050



Normal brain Alzheimer's



How Xanamem works

Stress raises cortisol

Stress causes production of cortisone from the adrenal glands. Cortisone, following activation to cortisol by the 11β-HSD1 enzyme, binds to receptors in the hippocampus and frontal cortex of the brain.

Stress – the link with Alzheimer's

There is growing evidence that chronic stress and elevated cortisol, the stress hormone, leads to changes in the brain including the development of amyloid plaques and neural death with shrinkage of the brain – the hallmarks of Alzheimer's

FAQ's

What is AD?

It usually starts with short-term memory loss. Symptoms then include problems with language, disorientation, mood swings, motivation, self-care and behaviour.

What causes AD?

A mix of genetic and environmental factors appear to be involved. There is now growing evidence that chronic stress with elevated cortisol plays a part.

Is it different from dementia?

Alzheimer's disease is the most common form of dementia, representing about 70% of cases.

Why is it increasing?

Increasing age is one of the biggest risk factors, and with the developed world life expectancy approaching 85 years, 1 in 4 will develop Alzheimer's.

How is it treated?

There are only four medications currently available but their benefit is small. No medication clearly delays or stops the progression of the disease.

Connecting with investors

Over the past few months, Actinogen Medical has conducted a series of very productive investor meetings and presentations across Australia and Asia, giving us the opportunity to update the investment community on our promising lead research drug, Xanamem™.

CEO Dr Bill Ketelbey presented at the ASX Investor Series events in Sydney in April and in Perth in June, with both events attracting more than 100 investors and the accompanying interviews via ASX's corporate partner, FNN, gaining widespread media coverage across Fairfax media sites.

Dr Ketelbey also presented alongside Innate Immunotherapeutics and Bionomics – two other ASX-listed companies in the CNS space – at Buchan Consulting's Brain Medicine Event. The presentation was followed by a panel discussion on current issues and developments in brain drugs and the importance of Australian developments in the space.

Actinogen Medical attended the ASX Spotlight Series in Hong Kong and Singapore in May where they met with a range of local institutions and hedge funds, with most Hong Kong investors very interested in Actinogen's development of Xanamem™ and the company's progress.

Dr Ketelbey presented at the Canary Networks Biotech & Healthcare Investor Roadshow earlier this month alongside Benitec Biopharma Chief Business Officer Carl Stubbings and iSonea Board Chairman, Leon L'Huillier

Earlier this month, Actinogen Medical attended the Bioshares Conference in Queenstown, New Zealand and presented the latest information on Actinogen and Xanamem™ to a large audience of biotechnology professionals and investors.

Actinogen's new premises

In June, Actinogen moved to a new office location at:

Level 9, Suite 1
68 Pitt Street
Sydney NSW 2000

In the news

There has been positive media coverage on Actinogen recently, with the company featuring in both *The Australian* and *The Australian Financial Review*.

In April, *The Australian* [link behind paywall] reported that Actinogen was "a step closer to progressing its Phase II study" for Xanamem™ following the dosing of the second cohort in the Phase I trial and noted that the outline of the Phase II trial had already been decided by the company's Advisory Board.

In May, *The Australian Financial Review* [link behind paywall] reported on the Company's successful $10 million capital raising. The article also noted that finding a cure for Alzheimer's "has never been more urgent" noting recent Australian Bureau of Statistics figures that place the disease as the second leading cause of death in Australia.

Elsewhere, there have been a number of news reports on scientific advances in Alzheimer's:

In July, the *San Angelo Standard-Times* reported on the US Alzheimer's Association report that women are more at risk for Alzheimer's disease, while *Eureka Alert!* published an article on a Washington School of Medicine study that noted that changes in biomarkers of Alzheimer's disease during midlife may help identify who will get the disease later in life. *The Guardian* also reported on research that found two licensed drugs stopped brain degeneration in mice.

In June, *The Telegraph* reported on a blood test that could pick up the signs of Alzheimer's disease 10 years before symptoms develop.

Advisory Board conference call

In April, Actinogen held a conference call with its world-class Clinical Advisory board to discuss the development of Actinogen's lead drug candidate, Xanamem™. The call was hosted by Actinogen's CEO, Dr Bill Ketelbey and included all members of the Advisory Board: Professor Craig Ritchie, Professor Colin Masters and Professor Jeff Cummings.

The Board members first spoke about what attracted them to Actinogen, with Professor Ritchie saying that Xanamem™ and the targeting of cortisol was a key reason and the "willingness and the wish really to make a big difference to patients who have Alzheimer's dementia".

"There's a huge amount of work obviously going on in the disease modifying space but I think where we start with Xanamem™ and try and improve symptoms of people with mild early dementia is particularly noteworthy," he said. "I'm very much attracted to the [prospect of] working as a frontline clinician as well as an academic."

Jeff Cummings said a key reason behind him joining was the "need to expand the repertoire of mechanisms" that the scientific community are looking at in Alzheimer's and also "the thinking about therapeutic interventions in Alzheimer's disease."

"The idea of looking at non-amyloid related interventions is a very welcome avenue of therapeutic exploration and I think [Xanamem™] was one of the most interesting compounds I'd seen," he said.

Professor Masters noted that there wasn't an effective therapy for cognitive impairment.

"There's a lot of optimism in the field at the moment that some form of treatment will eventuate and I want to do everything possible to speed up this process. So I think that Xanamem™ has the potential to provide this cognitive benefit that we're seeking," he said.

As for the effectiveness of blocking the HSD1 enzyme and the production of cortisol, Professor Ritchie noted that both animal and human studies had shown that even in people with normal ageing or early symptoms, HSD1 inhibition had improved cognitive function.

"So I think that gave us a great deal of optimism that a specific targeting of this enzyme would be of benefit to people with Alzheimer's dementia."

Left-right: Prof Craig Ritchie, Prof Brain Walker, Prof Colin Masters, Martin Rogers, Dr Bill Ketelbey, Vincent Ruffles, Dr Scott Webster, Prof Jonathan Seckl. Absent: Prof Jeff Cummings.

AFR article highlights Xanamem™'s other indications

A recent article in the *Australian Financial Review*: "**How to get off the slow path of dementia**" highlights the link between diabetes and dementia and discusses how diabetes can lead to two process that can promote dementia and Alzheimer's.

The link between diabetes and Alzheimer's is an important one and also highlights that Xanamem™'s novel mechanism of action – blocking excess cortisol production – offers many additional possible applications relevant to diseases of the central nervous and endocrine/metabolic systems.

Actinogen is working on a number of other indications of the drug, including diabetes. Potential applications of Xanamem™ include: PTSD (post-traumatic stress disorder); cardiovascular disease – post myocardial infarction; diabetes – cognitive dysfunction and diabetic foot ulceration; cognitive dysfunction in Parkinson's disease and cognitive dysfunction in schizophrenia and depression.

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For further information, please contact:

Dr Bill Ketelbey

Chief Executive Officer
Actinogen Medical Limited

Ph: 02 8964 7401

E: bill.ketelbey@actinogen.com.au

A: Level 9, Suite 1
68 Pitt Street
NSW 2000 AUSTRALIA

@billketelbey

Board:

Mr Martin Rogers	Executive Chairman
Dr Bill Ketelbey	Managing Director and CEO
Dr Jason Loveridge	Non-Executive Director
Dr Anton Uvarov	Non-Executive Director

Senior Management:

Mr Vincent Ruffles	Vice President of Clinical Research

Actinogen Medical – Fast Facts

ASX Code: ACW

Market capitalisation: Approximately $40m

Top Shareholders:

Edinburgh Technology Fund Limited	7.94%
Tisia Nominees Pty Ltd	5.55%
JK Nominees Pty Ltd	5.44%
Mr Martin Rogers	4.12%
Warmbi SARL	3.61%
Webinvest Pty Ltd	3.54%
Denlin Nominees Pty Ltd	3.15%
Mr Jason Peterson & Mrs Lisa Peterson	3.05%
Oaktone Nominees Pty Ltd	2.43%
Dr John William Ketelbey	2.04%

ACW share performance since the acquisition of Xanamem™