



# Investor Update

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## Key Investment Highlights:

ASX: ACW

Market cap: Approximately A\$32mn

- **Xanamem™, a promising research drug for Alzheimer's and 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 preclinical and clinical evidence. Early development funded by Wellcome Trust**
- **IND filing and Phase II study planned for 2016; funded through to completion of Phase II**
- **Expected to be used in combination with other Alzheimer's therapies**
- **Patent protection to 2031**

## Message from the CEO

Welcome to the final issue of the Actinogen Medical Investor Update for 2015. It is my pleasure to report on another period of strong development for Actinogen Medical and continued success with the research of our lead compound, Xanamem™.

We have now finalised the protocol design for our Phase II trial of Xanamem™ in Alzheimer's disease – titled "**Xanadu**" to make it easier to communicate.

**Xanadu** aims to demonstrate the effectiveness of Xanamem™ in treating patients with mild Alzheimer's disease, and is on track to start recruiting patients in the second quarter of 2016. Around 200 patients will be treated in Australia, the UK and the US under a US FDA Investigational New Drug (IND) application. The final patients are expected to be recruited in late 2017, with the results available soon after. It's a double-blind placebo controlled study, so no results will be available until the blind is broken at the end of the study.

This excellent progress with **Xanadu** follows extremely positive Phase I trial results for Xanamem™ announced in September. That trial confirmed Xanamem™ crosses the blood-brain barrier, demonstrating it is effectively delivered to the brain, its primary site of action in Alzheimer's disease. These results provide important further endorsement of the underlying design principles and development goals for Xanamem™.

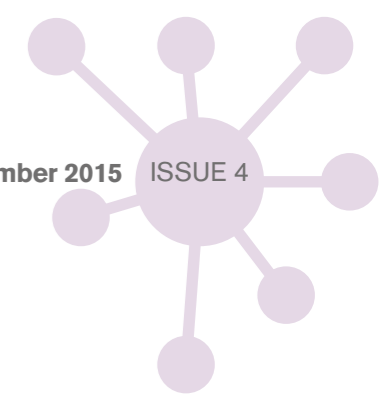
Alongside this excellent research progress, we continue to advance our plans to ensure that Actinogen Medical is "partner-ready". The recent appointment of Dr Laura Issa as our Director of Strategy and Business Development is an important step towards this aim. Laura

is a highly credentialed pharmaceutical commercialisation and business development professional and her depth and breadth of experience adds substantial value to Actinogen Medical.

The significance of developing a treatment for a disease like Alzheimer's cannot be underestimated and this was a key theme at our very successful "*Understanding Alzheimer's*" symposium held in October. The event, which was attended by around 70 investors and market participants covered the entire life cycle of the disease, from drug discovery through to the day-to-day impact Alzheimer's has on carers and loved ones. Speakers included Dr Bryce Vissel of the Garvan Institute, Professor Craig Ritchie of the University of Edinburgh, Dr Katrina Kelin, Director of Neuroscience at Eli Lilly and Imelda Gilmore, a patient advocate from Alzheimer's Australia. As well as outlining different developments in Alzheimer's treatment and the complexity of research in the field, the symposium highlighted the desperate need for new treatments for what is one of the biggest health issues of our time.

With the completion of the preliminary Xanamem™ research, we now aggressively move to the next key phase in Actinogen Medical's development, where we become an active Phase II research company. We are only months away from initiating patient recruitment in **Xanadu**, and I would like to take this opportunity to thank all shareholders for their continued support during this very important and successful year for Actinogen. I look forward to updating you on our progress with **Xanadu** and Actinogen in 2016 and wish everyone a very safe and happy holiday season.

Dr Bill Ketelbey  
 Chief Executive Officer  
 @billketelbey



## Appointment of Dr Laura Issa as Director of Strategy and Business Development



Actinogen Medical is pleased to announce it has recently appointed Dr Laura Issa as Director of Strategy and Business Development, initially on an interim basis. Laura brings to the role significant experience in commercial business development in the pharmaceutical industry, combined with medical research expertise. Laura will drive the refinement of the business

Dr Laura Issa

plan, and the strategic options identified by the Board to grow the company. She will scope the development opportunities for Xanamem™ and ensure Actinogen Medical is always ready for potential partnership prospects. Prior to joining Actinogen Medical, Laura was the Director of Regional Licensing and Business Development at Merck Sharp Dohme Australia.

## Surf the Web with Actinogen Medical

Actinogen Medical is excited to announce that it will soon launch a new and improved corporate website.

The redeveloped site will have improved navigation and will provide a seamless experience for investors and interested parties that want to keep up to date with all Actinogen Medical news.

The new website will provide a secure platform for all Actinogen Medical's publicly available information and host important documents and promotional material regarding the development of our business and product pipeline. Construction of this new website will take place over the course of the next month.

We will announce an official launch date in due course, so stay tuned for more news leading up to the relaunch of [www.actinogen.com.au](http://www.actinogen.com.au)



**Merry Christmas and a Happy New Year from the team at Actinogen Medical.**



## Xanadu Trial Update

Over the last few months we have made significant progress in developing **Xanadu** - our Phase II trial in mild Alzheimer's disease. Plans continue on target to commence the trial in the first half of 2016.

We have finalised the protocol design for **Xanadu** with significant input from our Clinical Advisory Board and the inventors of Xanamem™ at Edinburgh University. The trial will recruit around 200 patients in Australia, the UK and the US under a US FDA Investigational New Drug (IND) application. Results from the trial are expected in late 2017 or early 2018. Some basic design features are laid out in the table below.

This excellent progress follows extremely positive results from the final Phase I trial of Xanamem™ with the trial confirming that the drug crosses the blood-brain barrier and is effectively delivered to the brain, its primary site of action in Alzheimer's disease.

**The results were particularly encouraging as they confirm Xanamem™ reaches the brain in concentrations that are predicted to very effectively inhibit the 11β-HSD1 enzyme in the brain.**

The results were particularly encouraging as they confirm Xanamem™ reaches the brain in concentrations that are predicted to very effectively inhibit the 11β-HSD1 enzyme in the brain. The 11β-HSD1 enzyme produces cortisol, the "stress hormone", and excess cortisol is associated with memory loss, and β-amyloid plaque build-up and nerve death, in the brain – the hallmarks of Alzheimer's disease. Inhibition of the 11β-HSD1 enzyme leads to decreased cortisol levels, which has been shown in animal models of Alzheimer's disease to reverse memory loss and the β-amyloid plaques in the brain.

"We are particularly pleased with these much anticipated results showing that Xanamem™ effectively crosses the blood-brain barrier. The results further endorse the underlying design principles of Xanamem™, demonstrating that we remain on track to develop a promising new effective treatment for Alzheimer's disease. This is a disease where new treatments are desperately needed to help millions of patients worldwide," said Actinogen Medical CEO, Dr Bill Ketelbey.

**The results further endorse the underlying design principles of Xanamem™, demonstrating that we remain on track to develop a promising new effective treatment for Alzheimer's disease.**

Design Feature	Description
Patient Number	200 - US, UK, AUS
Treatment Course	12 weeks
Patient Eligibility	Mild Alzheimer's: MMSE 20 – 26 Stable or failing on standard therapy: acetylcholinesterases or memantine
Xanamem™ Dosage	35mg twice daily
Primary End Point	ADCOMS
Secondary End Points	Multiple, including ADAS-Cog, MMSE, CDR & CSF Aβ and Tau
First Patient Enrolment	Expected Q2, 2016

Design principles for the Xanadu trial

**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 nerve death in the brain. 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**

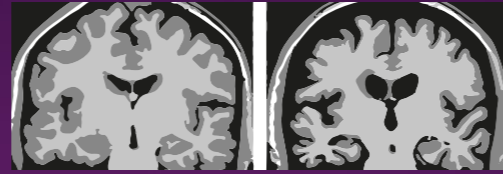
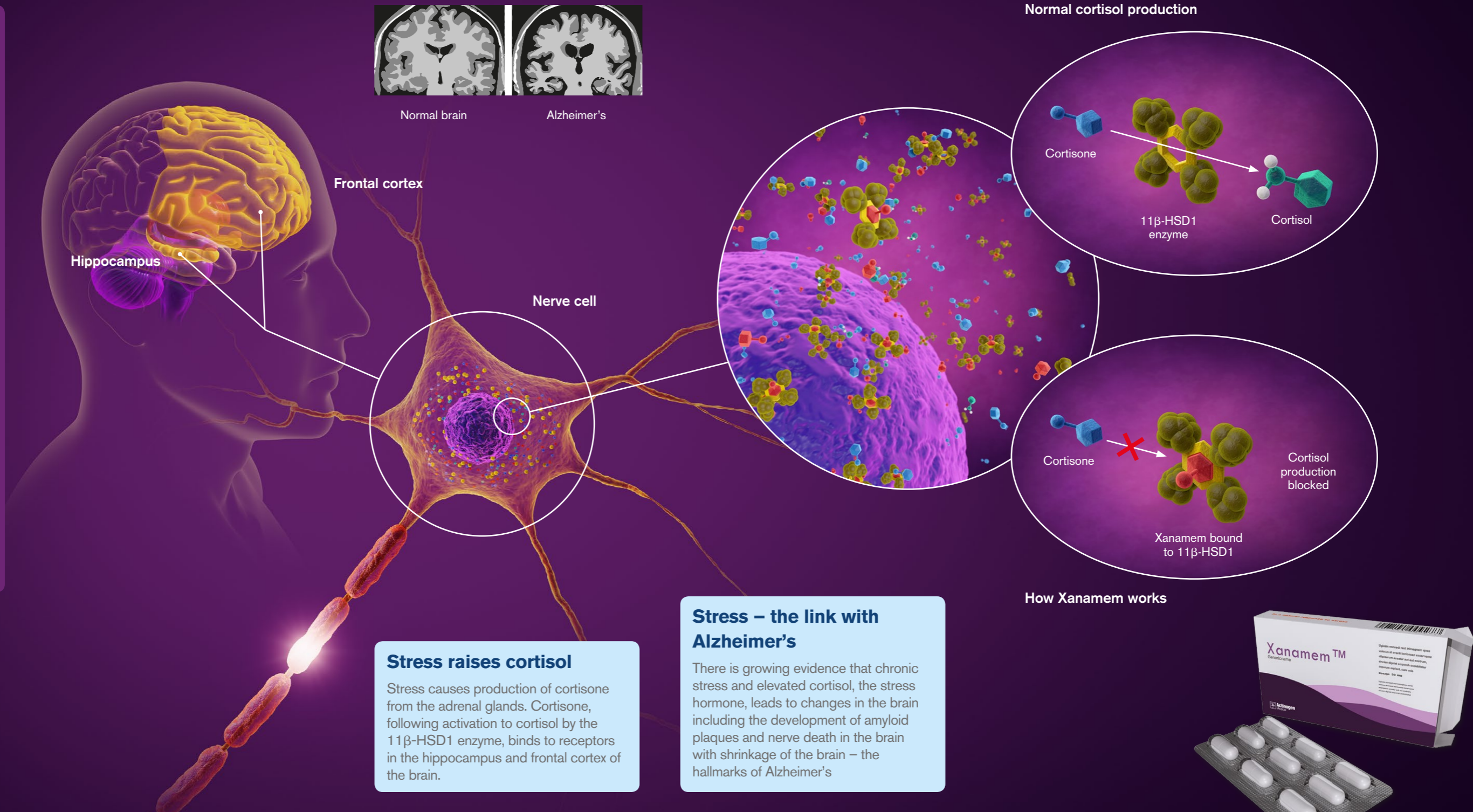
Affects 11% over 65 and 32% older than 75

**A leading  
cause of death**

Contributes to 1 in 3 deaths globally – 1:2 in Australia

**Doubling every  
20 years**

47m people currently living with dementia globally and set to double every 20 years



Normal brain Alzheimer's

**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 nerve death in the brain with shrinkage of the brain – the hallmarks of Alzheimer's



<p><b>FAQs</b></p>	<p><b>What is AD?</b> It usually starts with short-term memory loss. Symptoms then include problems with language, disorientation, mood swings, motivation, self-care and behaviour.</p>	<p><b>What causes AD?</b> 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.</p>	<p><b>Is it different from dementia?</b> Alzheimer's disease is the most common form of dementia, representing about 70% of cases.</p>	<p><b>Why is it increasing?</b> Increasing age is one of the biggest risk factors, and with the developed world life expectancy approaching 85 years, 1 in 3 will develop Alzheimer's.</p>	<p><b>How is it treated?</b> There are only four medications currently available but their benefit is small. No medication clearly delays or stops the progression of the disease.</p>
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## Presentations and Conferences



Actinogen Medical has conducted a series of very productive presentations at various industry and investor conferences across Australia over the past few months, giving the company the opportunity to update investors and the wider biotechnology community about its progress with Xanamem™.

In October, CEO Dr Bill Ketelbey presented at the Ausbiotech Invest Conference – an investment conference organized by Australia’s peak life sciences body which is designed to showcase Australian life science companies to potential partners and investors.

The conference, which was attended by more than 250 senior-level delegates from the life sciences community featured panel discussions, keynote speeches, and presentations from biotech and medtech companies. Dr Ketelbey also attended the Ausbiotech National Conference, held in parallel with Ausbiotech Invest, where he met with a number of potential pharmaceutical partners.

In addition, Dr Ketelbey presented alongside fellow emerging ASX-listed companies at the 2015 Australian Microcap Investment Conference. This conference, which was attended by more than 400 institutional investors, analysts, stockbrokers, financial planners and family office representatives from Australia and across the globe, showcases Australia’s leading microcap companies from a range of industries, including life sciences, technology, resources and manufacturing.

Earlier this month, Dr Ketelbey also attended and presented at the latest ASX CEO Sessions in Brisbane.

<http://www.finnewsnetwork.com.au/MediaCenter/AsxMediaCenter.aspx?Site=FNN566>

## In the news



Actinogen Medical has achieved some good, positive media coverage of late, with journalist Tim Boreham writing a piece on the Company and its development of Xanamem™ in his Criterion column in **The Australian** in October.

Tim’s article noted Xanamem™’s novel mechanism of action in treating Alzheimer’s disease as well as the drug’s potential to treat other diseases such as Parkinson’s disease, schizophrenia and depression, diabetes and post-traumatic stress disorder. The column noted that: “Actinogen is valued at \$30m. Compare that to the Nasdaq-listed Avanir Pharma, picked off by Otsuka Pharma for \$US3.5 billion after phase-two results.”

Meanwhile, Professor Craig Ritchie, Professor of the Psychiatry of Ageing at the University of Edinburgh and Chairman of Actinogen’s Clinical Advisory Board was interviewed by Sue Dunlevy of **News Limited**, on the development of Xanamem™ and the latest developments in Alzheimer’s research.

In the article, Professor Ritchie noted that a combination of therapies was likely required for Alzheimer’s as was the case for cancer. He said that medicines alone won’t combat the disease, cognitive stimulation and lifestyle changes will also be required.

Elsewhere, there have been a number of reports on Alzheimer’s disease and potential treatments:

**BBC News** reported in October that Alzheimer’s disease could be potentially detected decades before onset through a virtual reality test. The function of brain cells in people aged 18 to 30 were tested through a virtual maze and those with a high genetic risk of Alzheimer’s could be identified by their performance, according to German neuroscientists.

Meanwhile, **Forbes Magazine** published a profile of Dr Howard Fillit, director of the Alzheimer’s Drug Discovery Foundation in which he speaks about new developments in Alzheimer’s treatments. Dr Fillit said that in three to five years, “we’re going to have potentially more than one drug approved that has some disease-modifying effect,” noting that nearly 100 human trials of potential Alzheimer’s treatments are now underway.

**The Telegraph** reported on a new study by University College London that showed that the existing Alzheimer’s drug, Aricept, could prevent the need for late stage Alzheimer’s disease sufferers to go into care.

The study said that Aricept could allow these sufferers to continue to function in their homes and continue to eat, dress themselves and go shopping for at least 12 months, but GPs are stopping the medication too early.

## Understanding Alzheimer’s Symposium

Actinogen Medical was thrilled to host a very successful investor symposium “Understanding Alzheimer’s” at Sydney’s Sofitel Wentworth Hotel in October.

Around 70 investors attended the event, which provided an in-depth examination of the whole lifecycle of Alzheimer’s disease, from new drug discovery, clinical investigation and commercialization, to the experience of living with an Alzheimer’s disease sufferer.

Alongside CEO Dr Bill Ketelbey, the symposium featured Professor Craig Ritchie, Professor of Psychiatry of Ageing at the University of Edinburgh and Chairman of Actinogen Medical’s Clinical Advisory Board. Professor Ritchie spoke about some of the latest developments in treating the disease, noting that there was limited evidence for a single pharmacological intervention in the disease and a combination of therapies was likely needed for effective treatment.

Professor Ritchie highlighted the significant medical need – noting that the costs of treating Alzheimer’s disease each year was equivalent to NASA’s total budget since its inception in 1958 of € 515 billion or the entire annual GDP of countries like Sweden, Norway or Belgium.

Dr Bryce Vissel, Laboratory Head – Neurodegenerative Diseases at the Garvan Institute presented on research discoveries, noting the importance of finding a new treatment for dementia given 1,800 new cases are diagnosed in Australia each week or one person diagnosed every six minutes. He said targeting beta-amyloid, or the protein pieces that clump together and form plaques in the brain was probably not the answer for treating the disease and different treatment approaches were needed in order to develop an effective treatment. Stem cells and inflammation were some of the emerging directions for Alzheimer’s treatments, he told the audience.

Eli Lilly’s Medical Director of Neuroscience, Dr Katarina Kelin noted that while the potential to slow the progression of Alzheimer’s disease could be just around the corner, any innovation needs to be integrated into the wider healthcare system, so that any breakthroughs in treatment could reach patients in a timely and effective manner.

**The costs of treating Alzheimer’s disease each year was equivalent to NASA’s total budget since its inception in 1958 of € 515 billion or the entire annual GDP of countries like Sweden, Norway or Belgium.**

Meanwhile, Alzheimer’s Australia patient advocate, Imelda Gilmore, gave a heartbreaking account of the impact that the dreadful disease has on loved ones and families. Her husband was diagnosed with Alzheimer’s and Imelda gave a deeply moving account on how the disease impacted her relationship, the strains of being a primary carer and breadwinner and the effect it had on her children.

To view the event please click here: <https://www.youtube.com/watch?v=vk2Sxwz2boM>



## Actinogen Medical

For further information, please contact:

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### Board:

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

### Senior Management:

<b>Mr Vincent Ruffles</b>	Vice President of Clinical Research
<b>Dr Laura Issa</b>	Director of Strategy and Business Development

## Actinogen Medical – Fast Facts

ASX Code: ACW

Market capitalisation: Approximately \$32mn

### Top Shareholders:

Edinburgh Technology Fund Limited	7.94%
Tisia Nominees Pty Ltd (Henderson Family Account)	5.42%
JK Nominees Pty Ltd (The JK Fund A/C)	5.03%
Mr Martin Rogers	4.12%
Webinvest Pty Ltd (OLSB Unit A/C)	3.86%
Warmbi SARL	3.61%
Mr Jason Peterson & Mrs Lisa Peterson (J&L Peterson S/F A/C)	3.05%
Denlin Nominees Pty Ltd	2.84%
Oaktone Nominees Pty Ltd	2.43%
Ketelbey, John William	2.04%

### Company name change to Actinogen Medical

The Company is pleased to announce that it is now formally known as Actinogen Medical Limited following a vote at the recent Annual General Meeting to change the name from Actinogen Limited.

ACW share performance since the acquisition of Xanamem™

