

# Investor Update

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## 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 mid-2015; funded through to completion of these studies**
- **IND filing and Phase II study planned for 2016**
- **Expected to be synergistic with other AD therapies – marketed and in research**
- **Patent protection to 2031**
- **Tight capital structure with top 20 shareholders owning more than 70%**

## Message from the CEO

Welcome to the latest edition of the Actinogen Medical Investor Update. It gives me considerable pleasure to provide this update on the continued excellent progress of the development of our novel lead drug Xanamem™ for the treatment of patients with Alzheimer's disease and its prodromal stage, Mild Cognitive Impairment.

We've had a number of significant achievements since the last Investor Update. These include the recruitment of the first participants in our second Phase 1 study and the subsequent dosing escalation in the second cohort. Additionally, and very significantly, we established our Xanamem™ Clinical Advisory Board with the appointment of three world leading experts in early and prodromal Alzheimer's disease to sit on the Advisory Board.

The appointment of Professors Craig Ritchie, Colin Masters and Jeff Cummings to the Advisory Board represents a real coup for Actinogen Medical. They bring significant global experience in Alzheimer's disease research and their collective intellect and expertise will position Xanamem™ clinical research at the forefront of the diagnosis and treatment of early and prodromal Alzheimer's disease. I had the pleasure of hosting the inaugural meeting of the Advisory Board when in Europe in March and we have already received the Advisory Board's sign-off on the outline of the Phase 2 study of Xanamem™ in Alzheimer's disease. I am hugely impressed not only with the Advisory Boards significant expertise, but their commitment and passion for our goal of developing Xanamem™ as a promising new treatment for Alzheimer's disease

Xanamem™'s novel mechanism of action is something that really excites me given my experience in developing other Alzheimer's drugs. By blocking the production of cortisol, Xanamem™ is different to existing therapies on the market, and those in research. Pleasingly, we continue to have had very good feedback from key opinion leaders on the development of Xanamem™ which gives me great confidence as we progress through the clinical research, towards commercialization.

I recently attended the 12th International Conference on Alzheimer's disease and Parkinson's disease (ADPD 2015) in Nice France, where I was able to concurrently host the first Xanamem™ Clinical Advisory Board meeting. It was striking how many major sessions and papers were chaired and presented at this Conference by members of our Advisory Board, reflecting on their global standing in Alzheimer's research.

We also held a series of meetings with research and pharmaceutical manufacturing companies while in Europe and the UK and conducted a successful investor roadshow Hong Kong, adding to those held throughout Australia during February and March.

In this issue of the Investor Update, we provide details on the investor roadshows and the Advisory Board appointments, and an update on the progress made with the second Phase I trial for Xanamem™

It's been a productive couple of months since the last update and I would like to thank all shareholders for their ongoing support. I look forward to sharing the details of the Company's ongoing progress in the months ahead.

Dr Bill Ketelbey  
Chief Executive Officer  
Actinogen Medical

 @billketelbey

## Xanamem™ Clinical Advisory Board Appointed



**Professor Craig Ritchie**

- Professor of Psychiatry of Aging, University of Edinburgh, UK
- Senior Investigator in over 30 Alzheimer's clinical trials
- Published extensively on dementia



**Professor Colin Masters**

- Professor, University of Melbourne, Australia
- Executive Director of Mental Health Research Institute
- Senior Deputy Director of the Florey Institute of Neuroscience and Mental Health

### Xanamem™ Clinical Advisory Board



**Professor Jeffrey Cummings**

- Professor of Medicine (Neurology), Cleveland Clinic, Ohio and Nevada, USA
- Chair of the Neurological Institute of Cleveland Clinic
- Edited 39 books and published over 650 papers

In March, Actinogen appointed a powerhouse Advisory Board of world-class Alzheimer's experts to help drive the development of its novel lead research candidate, Xanamem™.

The Advisory Board is made up of globally recognized leaders in Alzheimer's disease and adds to the Company's breadth and depth of expertise in this area. The Board will be chaired by **Professor Craig Ritchie**, Professor of Psychiatry of Ageing at the University of Edinburgh and a leading authority on clinical trials and dementia.

Professor Ritchie is joined by **Professor Colin Masters**, the Executive Director of the Mental Health Research Institute, Laureate Professor at the University of Melbourne and Senior Deputy Director of the Florey Institute of Neuroscience and Mental Health, and **Professor Jeff Cummings**, the Chair of the

Neurological Institute of Cleveland Clinic and Professor of Medicine (Neurology), Cleveland Clinic Lerner College of Medicine of Case Western Reserve University.

The Advisory Board is already actively working on the Phase II trial design with the aim of designing the optimum study to best demonstrate the efficacy and safety of Xanamem™ in patients with early and prodromal (previously termed Mild Cognitive Impairment) Alzheimer's disease.

Professor Ritchie said that he welcomed the opportunity to work with Actinogen given his faith in Xanamem™'s mechanism of action in targeting cortisol and because Actinogen Medical had the right capabilities to run these types of trials.

"[Targeting cortisol] is a sensible approach and there's a compelling argument that Xanamem™ is a major therapeutic option for the future," he said.

Professor Ritchie added that there was confidence in Xanamem™ in improving symptoms of people with Alzheimer's disease and the first trials had shown symptomatic benefits.

Professor Masters also welcomed Actinogen's new approach, noting that these new trends in Alzheimer's treatment "needed to be explored".

"[Xanamem™]'s target, cortisol, has not been properly tested before so that is why it is of interest," he said.

New approaches were especially relevant given the limitations of existing Alzheimer's therapies and as there had been little progress in Alzheimer's drug development over the past 12-15 years.

"We don't really have good drugs – they may work for a few months in a small group of people but they don't make a difference in the long-term treatment of the disease," Professor Ritchie said.

Focusing on therapies such as Xanamem™, which targets early and prodromal Alzheimer's disease, was also especially relevant given the trend towards earlier diagnosis of the disease.

Professor Ritchie pointed to the trend to moving further upstream in the disease diagnosis and identifying when the disease starts.

"The focus in the research community is identifying people with Alzheimer's disease before they get Alzheimer's dementia as the two are not synonymous," he said.

"The challenge is identifying people at the earlier stages when they have subtle memory and psychological problems and before they get full blown dementia."

The hope is Xanamem™ will provide the opportunity to develop a therapy to manage the disease even at an early stage.

Professor Masters said it was important to be able to target specific causative mechanisms for Alzheimer's and "understanding how the brain degenerates and then look for therapies aimed at addressing that."

Professor Ritchie also noted the recent development of a number of global collaborative initiatives to identify people before they had Alzheimer's symptoms and developing the infrastructure to do the right type of trial on these patients.

### 13th April Newsflash!

**Xanamem™** receives patent extension to 2031.

See announcement on website for details.

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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 11 $\beta$ -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.

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## STATISTICS ON ALZHEIMERS

### Increasing with age

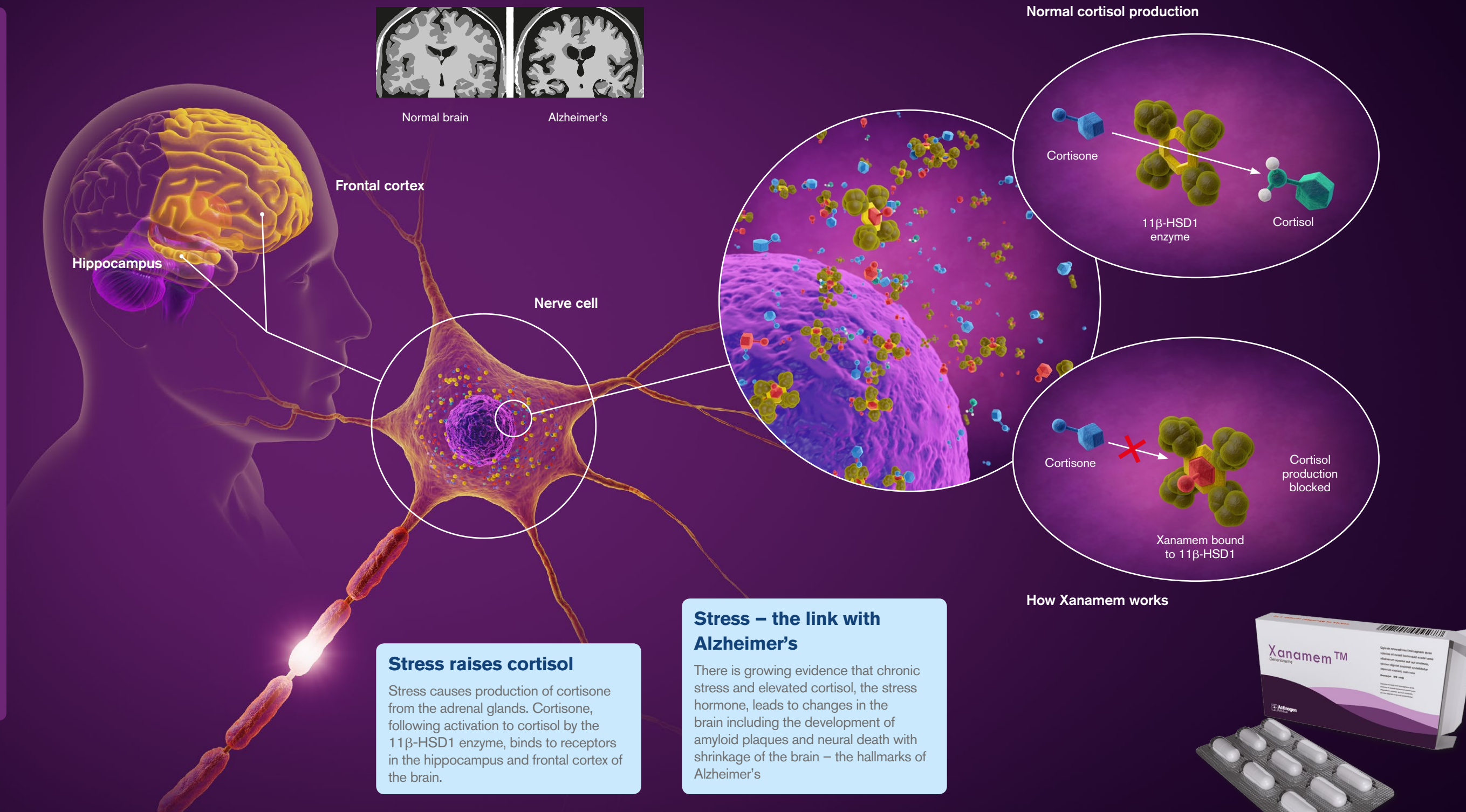
1 in 4 will get AD by age 85, and 1 in 2 by age 95. Average longevity in the developed world is already around 85 years

### 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 \$1 trillion by 2050







Dr Janakan Krishnarajah,  
CEO/Medical Director of Linear

Xanamem™ trial update

Following the recent successful recruitment and dosing of the first cohort of 8 participants with 10mg of Xanamem™ in Actinogen Medical's second phase I study, the company is pleased to announce that the second cohort of patients was dosed with 20mg in late March.

This follows the results of the first cohort dosing being reviewed by the independent Dose Escalation Committee. The Committee was satisfied with the safety, tolerability and pharmacokinetic results and allowed for dose escalation to 20mg for the second cohort.

In the double-blinded, placebo controlled study, 24 healthy volunteers are being dosed with 10mg, 20mg and 35mg of Xanamem™, in a multiple ascending dose (MAD) with eight volunteers in each cohort. The primary endpoint of the study is to confirm how the body absorbs and metabolises Xanamem™ and the optimal dose for the drug.

Two follow-on Phase I studies are expected shortly. The first will be a fast fed study of Xanamem™ in a cohort of twelve patients. The second will involve a cohort of four patients to confirm the central nervous system pharmacokinetics of Xanamem™.

These data will form the basis for designing the next study – a Phase II

efficacy and safety study in patients with Alzheimer's disease and its prodromal stage, mild cognitive impairment.

The trial is being conducted at Linear Clinical Research, a world-class clinical trial facility that is part of the QEII Hospital in Perth, Western Australia. Results from the trial are expected in mid-2015.

Linear Clinical Research Principal Investigator, Dr Janakan Krishnarajah said: "Having the second cohorts dosed in the trial is great progress in developing Xanamem™ as a novel new approach to treating Alzheimer's disease. It is so important to investigate new approaches to the disease given the huge and growing burden of Alzheimer's on our society and the changing competitive landscape for treatment."

Actinogen Medical Chief Executive Officer, Dr Bill Ketelbey added: "We are extremely pleased to be progressing so well with our second Phase I trial and the dosing of our second cohort is an important step in our aim to demonstrate that Xanamem™ is a valuable treatment option for Alzheimer's disease. We are increasingly encouraged about the potential of Xanamem™ given its novel mechanism of action – one that offers great hope in Alzheimer's disease, and in a number of other neurological and metabolic diseases."

Still Alice highlights devastation of early onset Alzheimer's disease

The recently screened, multi-award winning film Still Alice highlighted the plight of patients with early onset Alzheimer's disease and the debilitating impact that the condition has on both patients and their loved ones.

The film was a stark portrayal of Dr Alice Howland, a linguistics professor at Columbia University diagnosed with early-onset Alzheimer's disease and the effect the condition had on her quality of life, her career and her family. Julianne Moore won the Academy Award for Best Actress, along with a host of other awards for her performance in the lead role. The film is based on the bestselling 2007 book by Lisa Genova of the same name.

The film is a stark reminder that Alzheimer's is not necessarily an old person's disease, but one that can strike at any age. It also highlights the desperate need for new and effective therapies for Alzheimer's – we are hopeful that Xanamem™ will answer that need.

We'd encourage you to see the film or read the book. They give a striking account of the disease from the patient's perspective and provide real insight into the effect of this disease on the patient and those around them.



Presentations: Investment and Research

CEO, Dr Bill Ketelbey will be presenting at a number of Investment and Clinical Research meetings over the next 6 weeks, including:

- AC4R – held in conjunction with Alzheimer's Disease International 2015 – Perth
- ASX Investor Series – Sydney
- Brain Medicine – the New Frontier – Melbourne
- ASX Spotlight Series – Singapore, Hong Kong

# BRAIN MEDICINE

THE NEW FRONTIER

Factors such as stress and an ageing population mean that brain diseases such as Alzheimer's are becoming the leading health issues of the 21st century.

Forbes magazine recently predicted neuroscience will be the next hot bed of innovation with a boom in brain drug development. Australian companies are at the forefront of developing the new wave of treatments for these devastating diseases.

**Join Us** for a luncheon and panel discussion to hear what three innovative Australian biotechs are doing to tackle this new wave of growth:

Innate Immuno**therapeutics**    **Actinogen Medical**    **Bionomics**

■ 12:30PM - 2:00PM ■ THURSDAY 30 APRIL 2015 ■

■ RACV CITY CLUB, 501 BOURKE STREET, MELBOURNE ■

RSVP by 20th April to Steven Anderson at sanderson@buchanwe.com.au

**Buchan** event, proudly sponsored by **ASX** and **social science**

On the Road

Actinogen Medical conducted a series of very productive meetings with pharmaceutical companies and investors in Australia, Europe and Hong Kong during February and March.

CEO, Dr. Bill Ketelbey and Chairman, Martin Rogers have held a series of investor related roadshows and meetings in Perth, Brisbane, Sydney and Melbourne since the last Investor Update. More recently they held similar investor meetings in Hong Kong. These meetings provided an opportunity to showcase Actinogen Medical, and our promising lead research compound Xanamem, to the investment community.

Actinogen's Vice President of Clinical Research, Vincent Ruffles met with key pharmaceutical companies in both London and Newcastle to present an update on the clinical development of

Xanamem™ and to discuss potential commercial partnerships for the drug.

Bill and Vincent visited the University of Edinburgh to meet with, amongst others, Professor Brian Walker and the team that invented Xanamem™. They also met with Professor Craig Ritchie, the Chair of the Xanamem™ Clinical Advisory Board to discuss the progress of Actinogen's second Phase I trial and future development of the drug.

Additionally, Bill and Vincent attended the 12th International Conference on Alzheimer's Disease and Parkinson's Diseases (ADPD 2015) in Nice, France, where they concurrently hosted the inaugural meeting of the Xanamem™ Clinical Advisory Board, on the 20th of March.

Source: HD Wallpapers.

## Actinogen Medical

For further information, please contact:

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### Board:

<b>Mr Martin Rogers</b>	Non-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
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## Actinogen Medical – Fast Facts

ASX Code: ACW

**Market capitalisation: Approximately \$40m**

### Top Shareholders:

Edinburgh Technology Fund Limited	9.78%
JK Nominees Pty Ltd	7.05%
Tisia Nominees Pty Ltd	6.83%
Mr Martin Rogers	5.08%
Warmbi SARL	4.41%
Denlin Nominees Pty Ltd	4.06%
Webinvest Pty Ltd	4.03%
Mr Jason Peterson & Mrs Lisa Peterson	3.56%
Oaktone Nominees Pty Ltd	2.99%
Dr John William Ketelbey	2.48%

ACW share performance since the acquisition of Xanamem™

