



Landmark Research on Excess Cortisol and Alzheimer's Disease

- **Australian CSIRO and university funded AIBL study links excess cortisol and Alzheimer's disease.**
- **Anti-Alzheimer's compound Xanamem™ in clinical testing blocks high cortisol ("stress" hormone) associated with disease progression.**
- **Landmark research on disease mechanism and Actinogen Medical's Xanamem™ presented at Alzheimer's Association International Conference (AAIC) in Toronto 22nd- 28th July.**

Sydney, Australia - July 28, 2016: Actinogen Medical (ASX: ACW), announced today results of its lead compound Xanamem™, a novel, orally administered 11β-HSD1 inhibitor, which demonstrated in a Phase I study that it significantly inhibited production of cortisol in healthy volunteers and successfully crossed the blood-brain barrier. A separate study, the Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL), sponsored by the CSIRO and a number of Australian universities, showed a correlation between elevated cortisol in the blood of a healthy aged population and the subsequent development of Alzheimer's disease in these individuals. When individuals also evidenced a broad build-up of beta-amyloid plaques in the brain, their chances of developing Alzheimer's disease increased even further. The AIBL study (n=416) concluded that targeting ways to lower excess cortisol should be undertaken in battling Alzheimer's disease in the elderly. Both studies were presented at the AAIC, the world's largest Alzheimer's Dementia meeting, taking place this week in Toronto, Canada.

Professor Jeffrey Cummings, M.D., Director, Cleveland Clinic Lou Ruvo Center for Brain Health, United States commented, "these study results demonstrate both the importance of understanding the pathological processes in Alzheimer's and the compelling need for new approaches to treatment. To my eyes, AIBL has provided the most important validation to date for controlling excess cortisol production in individuals at risk for developing dementia. Development of new therapies to inhibit cortisol can show us the impact of blocking this mechanism on disease progression."

In 2016, Actinogen Medical initiated XanADu, the Company's pivotal global Phase II clinical trial investigating Xanamem™ as a treatment for mild Alzheimer's disease. Xanamem™ has been specifically designed to inhibit the excess production of cortisol, the "stress hormone," in the brain. XanADu is being conducted at trial sites in the US, Australia, and the UK, with the primary efficacy endpoints of improvements in scores on the Alzheimer's Disease Composite (ADCOMs) and Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog) version 14 tests. The clinical trial is expected to enrol patients in 2H16.

"The findings from the AIBL study, linking excess cortisol with the development of Alzheimer's disease, provides further strong validation of our ongoing development of Xanamem™," said Dr. Bill Ketelbey, CEO of Actinogen Medical. "Independent validation is clearly emerging that excess cortisol is a key target for treating the disease and our XanADu trial aims to demonstrate that inhibiting cortisol in the brain with Xanamem™ is an effective treatment option for patients with mild Alzheimer's disease. It's particularly exciting to receive this endorsement of Xanamem™'s novel mechanism of action as Alzheimer's is a disease where new approaches to its management are desperately needed to help millions of people worldwide."

Data Presentations at the AAIC Conference

Xanamem™

"Xanamem™ a novel 11β-HSD1 inhibitor with potential to provide durable symptomatic and disease modifying benefits in Alzheimer's disease" (Abstract No. a12215).

Timing: 1:00pm Eastern time, Wednesday, July 27, 2016

Location: P4:388

Professor Craig Ritchie, MD, Ph.D., Chair of the Psychiatry of Ageing and Director of the Centre for Dementia Prevention, The University of Edinburgh, United Kingdom, and author on the Xanamem™ study commented, "in the study, we saw clear signals of an effect through the substantial inhibition of extra-adrenal regeneration of cortisol. We are also excited to see clear evidence of delivery through the blood-brain barrier, which we believe has hampered programs targeting this mechanism in the past. We believe this is a promising compound, and we are excited to see the progress into Phase II testing."

Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL)

"Plasma cortisol, amyloid-β and cognitive decline in preclinical Alzheimer's disease" (Abstract No. a10218).

Timing: 1:00pm Eastern time, Tuesday, July 26, 2016

Location: P3:308

Professor Colin L. Masters, M.D., Co-Head, Neurodegeneration Division of the Florey Institute of Neuroscience and Mental Health, Melbourne, Australia, and co-author on the AIBL study stated, "while the presence of aberrant beta-amyloid and tau proteins in the brain, combined with neural death and cognitive decline, are recognized as the hallmarks of Alzheimer's disease, there is still substantial speculation as to the underlying triggers for the disease. We have demonstrated that when levels of cortisol, the 'stress hormone,' become chronically elevated in the blood, there is a strong correlation with the subsequent development of Alzheimer's disease. This finding, and the results showing synergy with the build-up of beta-amyloid plaques in the brain, suggests a compelling new area of research for the treatment of Alzheimer's."

For information on both presentations you can visit the following links: <http://bit.ly/AIBLposter> and <http://bit.ly/XanamemPoster>.

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About Xanamem™

Xanamem™ is being developed as a promising new therapy for Alzheimer's disease, a condition with a multi-billion dollar market potential. The cost of Alzheimer's treatment in the US alone was estimated to be US\$250bn in 2013, with this cost estimated to increase to US\$1 trillion by 2050, outstripping the cost of treating all other diseases. Alzheimer's disease is now the second leading cause of death in Australia behind ischaemic heart disease. Xanamem™'s novel mechanism of action sets it apart from existing Alzheimer's treatments. It works by blocking the production of cortisol - the stress hormone - in the hippocampus and frontal cortex, the areas of the brain most affected by Alzheimer's disease. There is growing evidence that chronic stress and elevated cortisol levels lead to changes in the brain affecting memory and to the development of amyloid plaques and neural death – the hallmarks of Alzheimer's disease.

About Actinogen Medical

Actinogen Medical is focused on an innovative approach, through the inhibition of excess cortisol production, for treating cognitive impairment in chronic neurodegenerative and metabolic diseases. The lead candidate drug Xanamem™, blocks the development of cortisol which appears to be associated with cognitive impairment and the development of amyloid plaques and neural death in the brain – the hallmarks of Alzheimer’s disease. In 2016, the Company initiated XanADu, a Phase II efficacy and safety trial in mild Alzheimer’s disease. The company encourages all current investors to go paperless by registering their details with the designated registry service provider, Link Market Services.