

New data supports link between stress hormone cortisol and worsening cognition

- Stress in midlife can result in cognitive decline in old age
- Increase in stress hormone cortisol associated with cognitive decline
- Xanamem blocks production of cortisol in the brain and can potentially significantly improve cognition

Sydney, 6 February 2018: Actinogen Medical (ASX: ACW) is pleased to announce the latest research that endorses the growing evidence supporting the association between stress and age-related cognitive (learning and memory) decline. The research (Wheelan et al., 2017), concludes that exposure to a period of stress in midlife results in cognitive decline in old age. These research findings are supported by another recent study published in *Nature* (Stuart et al., 2017) that similarly concluded that stress may worsen cognitive decline with age.

Both studies, performed in animal models of aging and Alzheimer's, demonstrate that an increase in stress hormones is associated with cognitive decline. These studies provide further support for the development of Xanamem, a drug specifically designed to block the production of the stress hormone cortisol in the brain. In the early development of Xanamem, the Company demonstrated that blocking the production of cortisol in the brain in an animal model of Alzheimer's disease significantly improved cognition.

Last year Actinogen Medical initiated XanADu, a trial of Xanamem in patients with Alzheimer's disease. If XanADu can demonstrate a similar outcome in Alzheimer's patients, Xanamem could prove to be a major advance in the treatment of this disease. The trial is progressing well, with close to 40% of the study already enrolled. As announced previously, an interim analysis of the first 50 patients is expected to be reported on by the independent Data Safety Monitoring Board in May 2018, and the trial continues on track to enrol the last patient later this year, with top line results expected in the first half of 2019.

"This study adds to the growing evidence that raised cortisol, even in mid-life, is toxic to the brain especially with aging. It highlights the importance of developing effective treatments that decrease the impact of excess cortisol on the brain as a potential way of slowing the progression of Alzheimer's disease. We have demonstrated that reducing stress hormone in the brain works to restore memory in aging animals. We are all eagerly awaiting the results from XanADu to see if a similar benefit can be demonstrated with Xanamem in humans," said Prof Jonathan Seckl from the University of Edinburgh, one of the inventors of Xanamem and an author of the *Psychoneuroendocrinology* paper.

References:

Stuart, K., King, A., Fernandez-Martos, C., Summers, M. and Vickers, J. (2017). Environmental novelty exacerbates stress hormones and A β pathology in an Alzheimer's model. *Nature*.

Wheelan, N., Kenyon, C., Harris, A., Cairns, C., Al Dujaili, E., Seckl, J. and Yau, J. (2017). Midlife stress alters memory and mood-related behaviours in old age: Role of locally activated glucocorticoids. *Psychoneuroendocrinology*, 89, 13-22.

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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 11β-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.