Actinogen's AAT-AD/PD 2020 Presentation: Summary

Actinogen presented the accumulated key findings on Xanamem, inclusive of the most recent data generated and analysed, at the **Advancement in Alzheimer's and Parkinson's Therapies Focus Meeting (AAT-AD/PD)** on 3 April 2020.

Professor Craig Ritchie, Chair of Actinogen's Xanamem Clinical Advisory Board, presented the findings under the title *"Chronically elevated cortisol and cognitive impairment: The therapeutic potential of Xanamem™, a potent inhibitor of the 11β-HSD1 enzyme."* **Link**

Actinogen is developing Xanamem as a novel treatment for cortisol-related cognitive impairment associated with a range of indications, and with key clinical studies now completed, a substantial database has been generated on Xanamem. The presentation summarised the key preclinical and clinical datasets generated to date, and outlined the findings underpinning the therapeutic rationale and clinical potential of Xanamem. Key highlights include:

- Xanamem has been shown to be an efficacious, brain penetrant, highly selective, and potent inhibitor of the 11β-HSD1 enzyme in the brain, with a validated novel mechanism of action and a strong safety profile.
- Xanamem reversibly binds to the 11β-HSD1 enzyme in the brain, effectively inhibiting the intracellular conversion of the inactive cortisone into the active cortisol.
- The Phase I XanaHES study confirmed a robust cognition efficacy signal at 20mg Xanamem daily in healthy elderly patients. Pharmacodynamics - the study of how the body responds to drugs - has been investigated in depth for Xanamem, and as previously reported, the pharmacodynamic outcomes observed with 10mg daily in XanADu, as well as in the 20mg daily XanaHES study, were overwhelmingly positive. These outcomes further support earlier positive cognition and pharmacodynamic data generated in animal and human studies.
- The Phase I Target Occupancy study has demonstrated that Xanamem at doses from 5mg to 30mg daily significantly occupies the 11β-HSD1 enzyme throughout the brain, confirming that Xanamem works as designed to penetrate the brain in concentrations that adequately inhibit the activity of the 11β-HSD1 enzyme, in the brain.
- Reducing excess cortisol levels in the brain provides a strong and rational target for further clinical development as a symptomatic and disease-modifying treatment for Alzheimer's disease, with Actinogen planning to evaluate Xanamem in patients with Mild Cognitive Impairment, linking the positive XanaHES results with Alzheimer's disease.
- The accumulated pre-clinical, Phase I, and Phase II safety and efficacy data positions Xanamem for development against multiple diseases associated with chronically raised cortisol and cognitive impairment.

Actinogen continues to progress the clinical development of Xanamem, targeting a range of promising indications including new trials in Alzheimer's disease, and cognitive impairment in schizophrenia and diabetes, with other indications under evaluation. This R&D pipeline reflects the breadth of therapeutic potential for Xanamem across a range of debilitating medical conditions, many of which have no adequate existing treatments.

The Xanamem dataset presented at the conference is part of a larger body of data being drawn on to enhance Xanamem's drug development strategy, and to inform and optimise the design of the future clinical trials in a broad portfolio of indications of high unmet medical need and significant commercial opportunity.

Xanamem is an investigational product and is not approved for use outside of a clinical trial by the FDA or by any global regulatory authority.