ASX ANNOUNCEMENT

Actinogen announces positive XanaMIA Part A trial topline results for Xanamem®

Sydney, 27 April 2022. Actinogen Medical ASX: ACW ("ACW" or "the Company") is pleased to announce positive topline results for its XanaMIA Part A trial.

Key trial and result features:

- **The dose-ranging, Phase 1b trial comprised 107 healthy, cognitively normal, older adults aged 50-80 years who received 10 mg or 5 mg doses of Xanamem or matching placebo for 6 weeks**
- **Assessed cognitive abilities using the internationally recognized Cogstate computerized Cognitive Test Battery (CTB) supplemented by the International Digit Symbol Substitution Test-Symbols (IDSSTS)**
- **Met primary safety, pharmacodynamic and efficacy endpoints**
- **Confirms Xanamem's ability to rapidly enhance attention and working memory, confirming prior findings with a 20 mg dose**
- **Results are consistent with a prior Positron Emission Tomography (PET) dose-ranging study that indicated dose levels of 10 mg daily or lower are likely to be effective**
- **Actinogen will host a webcast and teleconference call at 11am AEST today to review the topline results as set out in an investor presentation released in a separate announcement to the ASX this morning. The webcast and teleconference call can be accessed via a link on the home page of the Actinogen website: www.actinogen.com.au.**

Topline results in brief

The trial met its objectives. The efficacy endpoint was defined as clinically significant Effect Size (ES) of Xanamem treatment on cognitive ability versus placebo, measured with well validated tests of attention and working memory from the Cogstate CTB. Daily Xanamem doses of 10 mg and 5 mg demonstrated a good safety profile and full pharmacodynamic activity supportive of continued development.

The XanaMIA results confirm Xanamem's ability to enhance cognition even in a cognitively normal population and are consistent with:

1) the prior PET dose-ranging study which found high levels of Xanamem target occupancy at 5 mg and 10 mg daily doses, and;

2) significantly improved attention and working memory tests also seen in the prior XanaHES trial.

Professor John Harrison, international cognition expert, commented:

"These results are an important replication of previous trial findings also conducted in a cognitively normal population. The positive cognitive effects on attention and working memory seen in the XanaMIA trial are a significant step in the development of a new treatment for Alzheimer's Disease with a novel mechanism of action."

Professor Paul Rolan, Actinogen's Chief Medical Officer, said:

"These results consolidate demonstration of the positive effects of Xanamem on cognition, with excellent safety. They are a major boost to our Alzheimer's Disease program and open the door to Xanamem's evaluation in other chronic neurological and psychiatric diseases where poor cognition is a significant complaint."

Dr Steven Gourlay, Actinogen's CEO and MD, said:

We are excited to see the positive clinical data for these lower Xanamem dose levels. Xanamem has the potential to be a novel daily oral therapy for Alzheimer's Disease and other conditions that could be safely used alone or in combination with other therapies. Our future clinical trials will evaluate if Xanamem can make a significant improvement in the lives of patients and their families living with serious neurological and psychiatric conditions."

Trial and topline results in detail

The XanaMIA Part A dose-ranging trial was conducted in a population of 107 healthy, cognitively normal, older adults aged 50-80 years, with a mean age of 64 years and a gender ratio of one male to two females. Trial participants were randomized to receive either 10 mg or 5 mg doses of Xanamem or matching placebo for a six-week treatment period.

A Cogstate computerized CTB was used to assess cognitive abilities and consisted of six distinct tests supplemented by a computerized version of the IDSSTS, performed twice at baseline and again at each subsequent trial visit. Analysis used a MMRM[1] statistical model to generate ES estimates as Z-scores compared to the placebo group, and raw data was used to generate a more conservative ES statistic called "Cohen's d"[2].

Previously, the placebo-controlled XanaHES trial, using a 20 mg dose of Xanamem, demonstrated similar positive effects on working memory, attention and psychomotor function (comprising an "attention" composite). The efficacy objective in this XanaMIA Part A trial was to estimate ES, especially for attention tests, and confirm clinically significant effects. The formal primary efficacy endpoint criterion was one or more cognitive domains showing a Cohen's d ES of ≥ 0.3 during treatment.

The primary efficacy endpoint was met at the end of treatment with 5 mg, where the identification test of visual attention had a Cohen's d of 0.32 and a statistically significant MMRM ES of $Z = 1.97$ ($p < 0.05$). Active Xanamem treatment resulted in clinically significant MMRM ES of $Z = 0.48$ to 1.29 ($p > 0.19$) during treatment on an "Attention Composite" made up of working memory, visual attention and psychomotor function. No improvements were measurable in other tests including the IDSSTS. These results were consistent with those of the prior XanaHES trial.

ACTH hormone levels increased significantly during treatment with both dose levels to approximately twice baseline. There was a slight dose-response, where the 5 mg dose group saw a 2.03-times increase versus a 2.35-times increase in the 10 mg group (versus placebo 1.07-times). Elevated levels typically remained within

[1] MMRM: Mixed Model Repeated Measures, industry standard for trials of this type

[2] Cohen's d is a statistical ratio of mean, raw difference between groups to the pooled groups' standard deviation or variability

the normal laboratory ranges and were in the same range as studies of up to 70 mg daily, consistent with the target dose range for future trials of ≤ 10 mg.

Actinogen will now review detailed results of the XanaMIA Part A trial with academic and industry experts as it finalizes the design of its next Alzheimer's Disease program trial. Detailed results will be published at a future scientific congress and in a peer reviewed journal. The XanaMIA Part B trial is planned to study Xanamem's effects in patients with the early stages of Alzheimer's disease, using a broadly similar design to that of the Part A trial.

Webcast

Actinogen CEO Dr Steven Gourlay and CMO Professor Paul Rolan will host a webcast and teleconference call at 11am AEST today to review the topline results as set out in an investor and media presentation released in a separate announcement to the ASX this morning.

The webcast and teleconference call can be accessed via a link on the home page of the Actinogen website: www.actinogen.com.au.

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Announcement authorised by the Board of Directors of Actinogen Medical

About Actinogen Medical

Actinogen Medical (ACW) is an ASX-listed, biotechnology company developing a novel therapy for neurological diseases associated with dysregulated brain cortisol. There is a strong association between cortisol and detrimental changes in the brain, affecting cognitive function, harm to brain cells and long-term cognitive health.

Cognitive function means how a person understands, remembers and thinks clearly. Cognitive functions include memory, attention, reasoning, awareness and decision-making.

We are currently developing our lead compound, Xanamem®, as a promising new therapy for Alzheimer's Disease, Fragile X Syndrome, Depression and other neurological diseases where reducing cortisol inside brain cells could have a positive impact. The cognitive dysfunction, behavioural abnormalities, and neuropsychological burden associated with these conditions is debilitating for patients, and there is a substantial unmet medical need for new and improved treatments.

About Xanamem®

Xanamem's novel mechanism of action works by blocking the production of intracellular cortisol through the inhibition of the 11β-HSD1 enzyme in the brain. Xanamem is designed to get into the brain after it is absorbed in the intestines upon swallowing its capsule.

Chronically elevated cortisol is associated with cognitive decline in Alzheimer's Disease, potentially linked to cognitive impairment and anxiety in Fragile X Syndrome, and cognitive impairment in Depression and other diseases.

The Company has studied 11β-HSD1 inhibition by Xanamem in more than 300 volunteers and patients, so far finding a statistically significant improvement in cognition over placebo in healthy, older volunteers. A series of Phase 2 studies in multiple diseases is being conducted to further confirm and characterise Xanamem's therapeutic potential.

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. Xanamem® is a trademark of Actinogen Medical.

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