ASX ANNOUNCEMENT

Actinogen to initiate XanaFX clinical trial in Fragile X syndrome

- The **XanaFX** study will evaluate Xanamem's effect on core symptoms associated with Fragile X syndrome (FXS): **behavioural problems, anxiety, and sleep**
- FXS represents a **compelling therapeutic and commercial opportunity** to address an important unmet medical need with a **significant market opportunity**
- Xanamem in FXS potentially meets the criteria for **Orphan Drug Designation** and **Rare Paediatric Disease Designation**, which could provide attractive regulatory, development, and commercial opportunities
- Actinogen has **partnered with a world class team at Murdoch Children's Research Institute on XanaFX** - the phase II study is expected to commence in 1H CY21
- Broadening the development pipeline strategically **enhances the value and opportunities for Xanamem**, with the new XanaFX study complementing development plans in other disease indications

Sydney, 2 November 2020. Actinogen Medical ASX: ACW ('ACW' or 'the Company') is pleased to provide further details on its recent announcements on the clinical development of Xanamem in **Fragile X syndrome (FXS),** and the upcoming phase II clinical trial **XanaFX ('Xanamem in Fragile X')** in male adolescent FXS patients**.** XanaFX is a trial of its lead drug candidate, Xanamem, in the treatment of the core symptoms associated with FXS: **behavioural problems, anxiety, and sleep.**

A presentation providing an overview of FXS and the unmet medical need, an outline of the XanaFX clinical trial and the strategic rationale for developing Xanamem in this indication, is attached to this announcement.

New indication: Core symptoms associated with FXS (behavioural problems, anxiety, and sleep)

Selection of FXS follows significant clinical interest in evaluating Xanamem across a range of medical conditions associated with raised cortisol.

FXS is a rare genetic disorder characterised by a range of developmental problems, including learning disabilities, behavioural problems including autism features, cognitive impairment, speech and language deficits, sleep issues, anxiety and severe difficulties with regulating stress and emotions. Severe anxiety is particularly problematic in FXS and is experienced by approximately 90% of patients. Additionally, the behavioural anomalies and anxiety associated with FXS have a significant impact on the daily lives of FXS patients and those who care for them. Following FXS diagnosis, which typically occurs around three years of age, life-long treatment is often required for the patient. Currently, there are no approved treatment options for FXS.

Multiple pre-clinical and clinical studies have demonstrated links between raised cortisol and many of the symptoms associated with FXS. Significantly, raised cortisol is associated with cognitive impairment and behavioural problems including social anxiety, hyperactivity and social withdrawal in this patient population; representing an opportunity for Xanamem to potentially address this major unmet medical need. The pharmacological properties of Xanamem and the current understanding of FXS pathology strongly supports Xanamem as a potential treatment given its specific mechanism of action of inhibiting excess cortisol production in the brain.

The commercial and strategic opportunities for Xanamem in the treatment of FXS are considerable. Although FXS is a rare disorder, affecting approximately 1 in 2500-4000 males and 1 in 7000-8000 females globally,

anxiety and behavioural problems in FXS patients present a substantial unmet medical need and market opportunity. The FXS market is expected to reach ~US$250m per annum by 2026.

Potential for Orphan Drug Designation / Rare Paediatric Disease Designation

In addition to market and partnering opportunities, Xanamem in FXS has the potential to be granted **Orphan Drug Designation** from the US Food and Drug Administration (FDA) and other major regulatory authorities. Orphan Drug Designation provides multiple incentives for companies whose drug candidates demonstrate potential in the treatment of rare diseases. These incentives include attractive developmental, regulatory, and commercial advantages, allowing drug candidates priority review and rapid advancement to market. Additional incentives include lessened development and regulatory costs and timelines, and greater competitive protection through regulatory exclusivity. In the USA, orphan drugs that qualify for **Rare Paediatric Disease Designation**, which could include Xanamem**,** may also receive a **Priority Review Voucher** from the FDA upon marketing authorisation, which is tradeable and hence comes with its own substantial commercial value. In recent years, biopharma companies have sold Priority Review Vouchers to other pharmaceutical companies for an average of US$133m.

Actinogen partners with Murdoch Children's Research Institute (MCRI) for XanaFX

XanaFX is a Phase II proof-of-concept study, planned for commencement in 1H 2021 at the Murdoch Children's Research Institute (MCRI) and the Royal Children's Hospital in Melbourne. The MCRI team of investigators are world leaders in Fragile X research and have considerable expertise in paediatric clinical trials and natural history studies in FXS and other rare neurodevelopmental disorders. The team includes **A/Prof. David Godler**, **Prof. David Amor, Prof. Noel Cranswick, Prof. Katrina Williams**, **A/Prof. Mathew Hunter and Dr Emma Baker.** The impressive bibliographic details of the team are provided in the attached presentation.

As far as the Company is aware, XanaFX will be the first study to target cortisol inhibition as a treatment for behavioural problems, anxiety, and sleep issues in FXS patients, representing a new and innovative approach with a strong scientific rationale. The primary endpoint is to confirm that Xanamem is safe and well tolerated in a population of male adolescent FXS patients. Secondary endpoints aim to determine if Xanamem improves behavioural problems including communication, socialisation, and daily living skills, as well as anxiety and sleep. The XanaFX study is **fully funded.**

Corporate update: FXS complements broader development portfolio

Actinogen continues to expand upon its previously announced clinical development strategy of targeting a portfolio of disease indications associated with chronically raised cortisol. The additional disease indications being targeted by the Company reflect the substantial pipeline of opportunities presented with Xanamem and include cognitive impairment associated with both schizophrenia and diabetes. The new study in FXS complements this broad portfolio and reflects the breadth of development opportunities for Xanamem across a range of medical conditions, presenting with a high unmet medical need and significant market potential.

To learn more about Xanamem in FXS, please visit: https://actinogen.com.au/fragile-x-syndrome/

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About Murdoch Children's Research Institute (MCRI)
MCRI is the largest child health research institute in Australia and one of the top three worldwide for research quality and impact. The institute has made over 100 genetic discoveries, led the development of national and international genomic alliances, and is home to Australia's leading paediatric clinical trials centre, Melbourne Children's Trials Centre (MCTC). MCTC currently oversees more than 70 active clinical trials in all phases of drug development, and in a wide range of indications – and a such is one of the largest clinical trials centres in Australia specialising in paediatric disorders.

About Actinogen Medical
Actinogen Medical (ASX:ACW) is an ASX-listed biotechnology company developing novel therapies for neurological, psychiatric and metabolic diseases associated with chronically elevated cortisol. The company is currently developing its lead compound, Xanamem, as a promising new therapy for Alzheimer's disease, Fragile X syndrome, schizophrenia and diabetes. The cognitive dysfunction, behavioural abnormalities, and neuropsychological burden associated with these conditions is significantly 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 – the stress hormone – through the inhibition of the 11β-HSD1 enzyme in the brain. There is a strong association between persistent stress and the production of excess cortisol that leads to detrimental changes in the brain, affecting memory, cognitive function and behaviour and neuropsychological symptoms. The 11β-HSD1 enzyme is particularly highly concentrated in the hippocampus and frontal cortex, areas of the brain impacted by a number of diseases and disorders, including Alzheimer's disease, Fragile X syndrome, schizophrenia, diabetes and other conditions associated with chronically raised cortisol.

The Company's XanaHES Phase I trial exploring the safety and tolerability of Xanamem 20mg once daily in healthy elderly volunteers, confirmed the drug's safety profile with no treatment-related serious adverse events. Additionally, the trial demonstrated that Xanamem produced a statistically significant improvement in cognition over placebo, which, along with other recently generated data, confirms 11β-HSD1 inhibition by Xanamem as a promising potential treatment for cognitive impairment associated with raised cortisol.

The Company plans to initiate Phase II studies of Xanamem in various disease areas in 2021, including MCI due to Alzheimer's disease, and Fragile X syndrome.

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.

Disclaimer
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