ASX ANNOUNCEMENT

Cognitive improvement demonstrated with Xanamem™

- Statistically significant results demonstrate cognitive improvement in healthy elderly subjects dosed with 20mg Xanamem daily in the XanaHES dose escalation study
- Statistically significant reduction in serum cortisol following treatment with Xanamem 20mg daily
- Xanamem 20mg daily continues to exhibit a good safety profile with no serious adverse events observed
- Results significantly enhance the Xanamem dataset and help shape Actinogen’s drug development strategy for the treatment of Alzheimer’s disease and other neurological and metabolic diseases associated with cognitive impairment
- Company to host a Conference Call on October 1st, 2019 (today) at 10:30am (AEST)

Sydney 1 October 2019: Actinogen Medical ASX: ACW (‘ACW’ or ‘the Company’) is delighted to announce results from the XanaHES (Xanamem in Healthy Elderly Subjects) trial. The results demonstrate a significant improvement in cognition in trial participants dosed with Xanamem 20mg daily for 12 weeks, compared to placebo. This is the first time Xanamem has shown such a clear, statistically significant cognitive improvement in humans.

These breakthrough results reinforce the hypothesis and science underpinning the discovery and development of Xanamem - that lowering persistently raised cortisol levels in the brain is expected to positively enhance cognition.

Results from the study also showed that Xanamem, at a dose of 20mg daily, significantly (p<0.001) reduced serum cortisol levels in the trial participants over the study period. Furthermore, Xanamem 20mg daily exhibited a good safety profile over the 12 weeks of treatment, with no reports of serious adverse events.

Professor Michael Woodward from the Austin Health in Melbourne and one of the leading investigators in the XanADu trial said: “It is just so pleasing and encouraging to see this positive efficacy data for Xanamem, following the disappointment of the XanADu trial. There have been so many past failures with the development of Alzheimer’s drugs, so these promising results offer renewed hope for a treatment breakthrough for this devastating disease”.

As previously announced, the XanADu trial in mild Alzheimer’s patients showed that Xanamem 10mg daily was safe and altered the cortisol pathway but did not demonstrate an improvement in cognition.

The XanaHES trial was primarily designed as a placebo-controlled study to investigate the safety of 20mg Xanamem in healthy elderly subjects, but also included an exploratory assessment of cognition to evaluate the cognitive efficacy of Xanamem, using the industry standard Cogstate Cognitive Test Battery. The Cogstate Battery evaluated six domains of cognition, with the goal of broadly investigating whether 20mg Xanamem daily could positively influence cognition. Results from this trial show cognitive improvement in three of the six domains investigated after 12 weeks treatment (see table 1 below for more detail):

- One Back Test: evaluating working memory - highly statistically significant (p<0.01 with an effect size of 0.83)
- Identification Test: evaluating visual attention – statistically significant (p=0.05 with an effect size of 0.67)
Detection Test: evaluating psychomotor function – trend to statistical significance (p=0.09 with an effect size of 0.76).

Effect size is a quantitative measure of the magnitude of a result indicating that treatment with 20mg Xanamem daily has a potentially important impact on these cognitive domains. See table 1 below for more details.

These results demonstrate an encouraging clinical efficacy signal in cognitive domains that are core to cognitive evaluation across many diseases.

Actinogen Medical Clinical Advisory Board member, Professor Jeff Cummings from the Cleveland Clinic in the USA commented: “These results from the XanaHES study provide Actinogen with evidence of Xanamem’s ability to enhance cognition and inhibit cortisol production. Considering the broad array of medical conditions presenting with cognitive impairment and an associated raised cortisol, these promising results provide many opportunities for the ongoing development of the drug.”

Enhancement of cognition in the XanaHES trial supports Xanamem’s potential for the treatment of Alzheimer’s disease and other conditions associated with cognitive impairment, including mood disorders like bipolar disorder, and schizophrenia.

Actinogen CEO Dr Bill Ketelbey said: “These are the results we have been looking for. They are hugely important for the development of Xanamem and for the potential for Xanamem to treat Alzheimer’s disease and other conditions associated with cognitive impairment”

“As we gather and analyse more data from XanaHES and the other ongoing studies, we are building a much clearer picture of Xanamem’s pharmacology, potential efficacy, safety, and mechanism of action; all of which will aid substantially in planning the future clinical development and commercialisation strategy for the drug.”

“We look forward to sharing Actinogen’s future development plans for Xanamem once they have been reviewed alongside these very pleasing results.”

Table 1: Results summary

<table>
<thead>
<tr>
<th>COGNITIVE EVALUATION (Test)</th>
<th>P value</th>
<th>Effect Size: Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 2</td>
<td>Week 4</td>
</tr>
<tr>
<td>WORKING MEMORY (One Back Test)</td>
<td>&lt;0.01 *</td>
<td>0.64 #</td>
</tr>
<tr>
<td>VISUAL ATTENTION (Identification Test)</td>
<td>0.05 *</td>
<td>0.19</td>
</tr>
<tr>
<td>PSYCHOMOTOR FUNCTION (Detection Test)</td>
<td>0.09</td>
<td>0.47</td>
</tr>
</tbody>
</table>

Notes: * statistical significance achieved; # effect size >0.5 (medium treatment effect); ^ effect size >0.8 (large treatment effect)
Conference Call at 10.30am today

The Company will host a conference call at 10:30am (AEST) on Tuesday 1st October 2019 (today).

The presentation that will be referred to in the call, is attached to this announcement.

The Company invites participants to ask questions during the call. In addition, interested parties may submit questions prior to the call to info@actinogen.com.au.

Participants are encouraged to pre-register for the call here:


You will receive a PIN and diary note for fast-track entry to the call. Alternatively, participants may dial in at the scheduled time using the dial-in number below

Conference ID: 10002238

AUSTRALIA: 1800 870 643
ALTERNATIVE AUSTRALIAN NUMBER: 1800 809 971
OTHER INTERNATIONAL (METERED): +61 7 3145 4010
SYDNEY: 02 9007 3187
NEW ZEALAND: 0800 4530 55
AUCKLAND: 0992 9168 7
CHRISTCHURCH: 0397 4263 2
WELLINGTON: 0497 4773 8
CHINA: 4001 2006 59
FRANCE: 0800 9814 98
GERMANY: 0800 1827 617
HONG KONG: 8009 66806
JAPAN: 0053 1161 281
SINGAPORE: 8001 0127 85
SOUTH KOREA: 0079 8142 0632 75
UK: 0800 0518 245
USA/CANADA: 1855 8811 339
CHICAGO: 1815 3732 080
LOS ANGELES: 1909 2354 020
NEW YORK: 1914 2023 258

ENDS

Actinogen Medical
Dr. Bill Ketelbey
CEO & Managing Director
P: +61 2 8964 7401
E: bill.ketelbey@actinogen.com.au
@BillKetelbey

Investor and Media Enquiries
Arthur Chan
WE Buchan
M: +61 2 9237 2805
E: arthurc@we-buchan.com
About Actinogen Medical

Actinogen Medical (ASX: ACW) is an ASX-listed biotechnology company focused on innovative approaches to treating cognitive decline that occurs in chronic neurological and metabolic diseases. Actinogen Medical is developing its lead compound Xanamem, as a promising new therapy for Alzheimer’s disease, a condition with multibillion-dollar market potential and material human impact. In the US alone, the cost of managing Alzheimer’s disease is estimated to be US$250bn and is projected 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. In addition, Actinogen is currently planning an expanded clinical development program for Xanamem in cognitive impairment in mood disorders and schizophrenia. In the US alone, the collective economic costs of mood disorders and schizophrenia are estimated to exceed $550bn, with the burden increasing every year. The cognitive dysfunction associated with these conditions is significantly debilitating for affected patients, with a substantial unmet medical need for novel, improved treatments.

About Xanamem™

Xanamem’s novel mechanism of action sets it apart from other Alzheimer’s treatments. Xanamem is brain penetrant and works by blocking the excess production of cortisol - the stress hormone – through the inhibition of the 11β-HSD1 enzyme. There is a strong association between chronic stress and excess cortisol that leads to changes in the brain affecting memory. The 11β-HSD1 enzyme is highly concentrated in the hippocampus and frontal cortex, the areas of the brain associated with cognitive impairment in neurological diseases, including Alzheimer’s disease, mood disorders and schizophrenia.

About XanADu

XanADu is a Phase II double-blind, 12-week, randomised, placebo-controlled study to assess the safety, tolerability and efficacy of 10mg Xanamem once daily in subjects with mild dementia due to Alzheimer’s disease. XanADu has fully enrolled 186 patients from 25 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.

About XanaHES

XanaHES is a Phase I, randomised, single blinded, central reader blinded, placebo-controlled, dose escalation study to assess the safety and tolerability of Xanamem™ 20mg & 30mg once daily in healthy elderly volunteers. The XanaHES trial randomised 42 healthy elderly participants to receive either 20mg Xanamem daily (30 subjects) or placebo daily (12 subjects) for 12 weeks. Changes in cognitive performance from baseline to end-of-treatment will be measured as an exploratory efficacy outcome.

Actinogen Medical encourages all current investors to go paperless by registering their details with the designated registry service provider, Link Market Services.
Investor Conference Call

A novel approach to treating cognitive impairment and Alzheimer’s disease

Dr. Bill Ketelbey: CEO & MD

October 2019
# Development Pipeline and Upcoming Catalysts

Multiple studies currently underway with significant upcoming milestones in the near term

<table>
<thead>
<tr>
<th>Studies</th>
<th>1Q CY2019</th>
<th>2Q CY2019</th>
<th>3Q CY2019</th>
<th>4Q CY2019</th>
<th>Key Catalysts</th>
</tr>
</thead>
<tbody>
<tr>
<td>XanADu</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Completed study report</strong> 3Q CY2019</td>
</tr>
<tr>
<td>Phase I Target Occupancy &amp; Homogenate Binding studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Preliminary data received Further results in 3Q &amp; 4Q CY2019</td>
</tr>
<tr>
<td>XanaHES</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Interim results released. Full results for 20mg expected in 4Q CY2019</strong></td>
</tr>
<tr>
<td>Pre-clinical Toxicology studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Results expected over 2H CY2019 and 1H CY2020</td>
</tr>
<tr>
<td>New Indications</td>
<td></td>
<td></td>
<td>Mood disorders and schizophrenia</td>
<td></td>
<td>Design of clinical development plan</td>
</tr>
<tr>
<td>Strategic Development</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ongoing</td>
</tr>
</tbody>
</table>

*Actinogen is fully funded to complete all current studies*
Comprehensive Xanamem Clinical Development Program

The ongoing comprehensive review of the data and results from XanADU and the additional studies will inform the optimal clinical development path.

- Totality of results assessed by Actinogen and expert Clinical Advisory Board
- Key focus today: Assess safety and tolerability of higher doses (to allow higher doses in future trials), with an efficacy assessment included.
- Additional Toxicology Studies: Pre-clinical safety and toxicology studies to allow for longer treatment periods.
- Phase I Target Occupancy, & Homogenate Binding Studies: Measures effects of different Xanamem doses on inhibiting the 11β-HSD1 enzyme in the brain.
- Multiple endpoints and sub analyses will allow insight into Xanamem’s potential and where it is most effective.

The totality of results will inform further Xanamem development.
Single blind placebo-controlled, dose escalation study to assess safety, tolerability and efficacy of Xanamem in healthy elderly subjects – full results expected in 4Q CY2019

12 weeks
Xanamem treatment course
Trial conducted at 1 site in Australia

42
Healthy elderly subjects
(no cognitive impairment)

20mg daily
Xanamem 30 subjects
Placebo 12 subjects

Cognition assessed
Through computerised efficacy tests
(Cogstate CTB¹)

Key objective to expand the Xanamem safety dataset and evaluate potential for higher dosage in future clinical trials

1.Cogstate Cognitive Test Battery
XanaHES included a cognition endpoint to evaluate the cognitive efficacy of Xanamem using the Cogstate Cognitive Test Battery which evaluated six domains. Cognitive improvement demonstrated in three domains.

### XanaHES 20mg Cogstate Cognitive Test Battery: p values and Cohen’s d effect size

<table>
<thead>
<tr>
<th>Cognitive Evaluation (Test)</th>
<th>p value</th>
<th>Treatment Effect Size: Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>Male</td>
</tr>
<tr>
<td>Working Memory</td>
<td>&lt;0.01*</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>(One Back Test)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual Attention</td>
<td>0.05*</td>
<td>0.04*</td>
</tr>
<tr>
<td>(Identification Test)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychomotor Function</td>
<td>0.09</td>
<td>0.94</td>
</tr>
<tr>
<td>(Detection Test)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paired Associate Learning</td>
<td>0.21</td>
<td>0.34</td>
</tr>
<tr>
<td>(CPAL¹ Test)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memory</td>
<td>0.50</td>
<td>0.55</td>
</tr>
<tr>
<td>(CPAL¹ – Delayed Test)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual Learning</td>
<td>0.92</td>
<td>0.41</td>
</tr>
<tr>
<td>(One Card Learning Test)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes: * statistical significance achieved; # effect size >0.5 (moderate treatment effect); Δ effect size >0.8 (large treatment effect)

1: CPAL – Continuous Paired Associate Learning

**Additional details on slide 5**
Breakthrough results demonstrated statistically significant cognitive efficacy signal in multiple cognition domains – based on Cogstate Cognitive Test Battery

**Cognitive Efficacy Signal Achieved (cont’d)**

A novel approach to treating cognitive impairment and Alzheimer’s disease

**Working memory (One Back Test)**

**Strongly statistically significant result**

**Visual attention (Identification Test)**

**Statistically positive signal**

**Psychomotor function (Detection Test)**

**Good trend to a positive result**

Efficacy results of particular interest, reflecting high quality and consistent data in a small study population

Baseline* Mean of Observed Data

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Xanamem</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>0.01</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>0.09</td>
<td></td>
</tr>
</tbody>
</table>

* A novel approach to treating cognitive impairment and Alzheimer's disease
Cortisol Levels Reduced with Acceptable Safety

Efficacy results complemented by the statistically significant reduction in serum cortisol observed in the trial.

**Significant reduction in cortisol levels (all patients)**

**Score:** Efficacy Measure – Cortisol (nmol/L)

<table>
<thead>
<tr>
<th>Study weeks</th>
<th>Baseline*</th>
<th>Wk 2</th>
<th>Wk 4</th>
<th>Wk 8</th>
<th>Wk 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Group</td>
<td>Xanamem</td>
<td>Placebo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P&lt;0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Xanamem achieved an average decrease of 73.2 vs. placebo (p<0.001)

These breakthrough results support the cortisol hypothesis that lowering persistently raised cortisol levels in the brain is expected to positively enhance cognition.
XanADu: Possible Reasons Behind XanADu results

Likely due to the recurrent challenges seen in Alzheimer’s disease drug development

<table>
<thead>
<tr>
<th>Conceptual model of the disease</th>
<th>Stage of disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Causality unknown; cortisol as a target is a hypothesis</td>
<td>▪ Wrong patient population (&quot;too early&quot; or &quot;too late&quot;)</td>
</tr>
<tr>
<td>▪ Diagnoses largely based on highly subjective tools</td>
<td>▪ High heterogeneity as to the real biological drivers behind each individual’s disease state</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome/endpoint measures</th>
<th>Patient recruitment and retention</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Absence of valid biomarkers</td>
<td>▪ Overall patient population may have been too heterogeneous to generalise results</td>
</tr>
<tr>
<td>▪ Subjectivity of outcome assessments flawed</td>
<td></td>
</tr>
</tbody>
</table>

### Xanamem

- Dose: too low or too high?
- Dosing regimen: may need bi-daily dosing?
- Treatment duration: may need to treat for longer?
Xanamem: Phase I Target Occupancy Study & Homogenate Binding Studies

To assist with confirming and optimising Xanamem dosing

**Aim**

To accurately demonstrate the effects different doses of Xanamem have on inhibiting the $11\beta$-HSD1 enzyme in the human brain.

**Phase I Target Occupancy studies**
- Competitive binding, radio-labelled tracer PET imaging assay
- Subject cohorts tested with Xanamem at 5mg, 10mg, 20mg, and 30mg doses.
- Data available from 10-30mg dosing cohorts

**In vitro Homogenate Binding Studies**
- Enzyme occupancy competition studies, saturation binding studies, and enzyme activity assays in rat and human brain sections (ongoing)
- To correlate enzyme occupancy and enzyme activity at incremental doses of Xanamem

Key studies to help interpret XanADu results and support future clinical development strategy
Phase I target occupancy study demonstrates that 10-30mg Xanamem dosed for seven days significantly occupies neuronal 11β-HSD1 throughout the brain.

**Target Occupancy Study: Preliminary Results**

- A novel approach to treating cognitive impairment and Alzheimer's disease
- Phase I target occupancy supports Xanamem as a potent, orally bioavailable and brain-penetrant 11β-HSD1 inhibitor

50% to 85% occupancy, dependent upon brain region, dosage and study subject

Further study data available in 4Q CY2019

Additional ongoing cohorts at 5mg Xanamem and 10mg with delayed PET imaging

Phase I Target Occupancy supports Xanamem as a potent, orally bioavailable and brain-penetrant 11β-HSD1 inhibitor
Long-Term Safety and Toxicology Studies

**Aim**
Evaluate safety and toxicology in rodent (six months) and dog (nine months) studies in preparation for longer term clinical studies

- Studies **required by all regulators - FDA**
- Will allow future **clinical studies beyond 12 weeks**
- Studies **ongoing**
- **No substantive safety issues** observed to date

**Key study to support future clinical development strategy**
Key ongoing Xanamem studies are providing data and results in the near term, with the totality of the information from all studies to inform Actinogen’s strategic review for future clinical development.

Xanamem has demonstrated to be an **efficacious**, **safe**, **brain penetrant**, **orally available**, **selective 11β–HSD1 inhibitor** with significant pharmacodynamic effects on cortisol.

**Next steps**

1. Finalise and complete all ongoing studies
2. Consolidate drug development strategy based on the totality of results and data
3. Further clinical development

---

A novel approach to treating cognitive impairment and Alzheimer's disease
## Development Pipeline and Upcoming Catalysts

Multiple studies currently underway with significant upcoming milestones in the near term

<table>
<thead>
<tr>
<th>Studies</th>
<th>1Q CY2019</th>
<th>2Q CY2019</th>
<th>3Q CY2019</th>
<th>4Q CY2019</th>
<th>Key Catalysts</th>
</tr>
</thead>
<tbody>
<tr>
<td>XanADu</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Completed study report 3Q CY2019</td>
</tr>
<tr>
<td>Phase I Target Occupancy &amp; Homogenate Binding studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Preliminary data received. Further results in 3Q &amp; 4Q CY2019</td>
</tr>
<tr>
<td>XanaHES Phase I higher dose safety study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Interim results released. Full results for 20mg expected in 4Q CY2019</td>
</tr>
<tr>
<td>Pre-clinical Toxicology studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Results expected over 2H CY2019 and 1H CY2020</td>
</tr>
<tr>
<td>New Indications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Design of clinical development plan</td>
</tr>
<tr>
<td>Strategic Development</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ongoing</td>
</tr>
</tbody>
</table>

*Actinogen is fully funded to complete all current studies*
Q&A Session
Appendix:
Background information
Actinogen is developing innovative treatments for cognitive impairment associated with neurological and metabolic diseases with an initial focus on Alzheimer's disease.

**Summary**

- **Xanamem - lead compound**
  - Differentiated with a novel mechanism of action
  - First-in-class, brain penetrant, orally active, small molecule, inhibitor of 11β-HSD1 enzyme
  - Xanamem mechanism of action validated by independent research on the cortisol hypothesis

- **Targeted strategic market focus**
  - Initially focused on developing a treatment for Alzheimer's disease
  - Addressable market worth >US$7.5bn with unmet needs and potential upside.
  - Target indication underpinned by efficacy results from animal model studies.
  - Mood disorders and schizophrenia identified as additional opportunities

- **Clinical stage asset**
  - Advanced clinical stage program assessing Xanamem in Alzheimer’s disease and cognitive impairment in other neurological conditions. Complementary higher dose and target occupancy phase I studies will inform future development

- **Potential value upside**
  - Totality of existing studies will inform further development and commercial potential of Xanamem

- **De-risked opportunity**
  - Fully funded programs
  - Initial data from additional studies indicate brain penetration, good target occupancy and safety profile

- **Experienced leadership**
  - Board and Management with significant drug development and corporate experience, supported by key opinion leaders and Xanamem discovery team

---

A novel approach to treating cognitive impairment and Alzheimer's disease
A novel drug designed to inhibit cortisol production in the brain, with the potential to treat cognitive impairment

**Well researched**
>15 years of R&D completed

**Well tolerated**
Dosed >200 patients with acceptable clinical safety, toxicity & PK / PD\(^1\) profile

**Well protected**
Composition of matter IP coverage, patents granted in all major markets

**Validated in Alzheimer’s disease**
Symptomatic and disease modifying effects (in vivo) and demonstrated effect of cortisol hypothesis (in humans)

**Potential in other diseases**
Secondary focus on cognitive impairment in mood disorders and schizophrenia

**Differentiated mechanism of action:**
Highly selective 11βHSD1 inhibitor in the brain which reduces excess cortisol production

---

**Xanamem is a novel, first-in-class, potent, orally bioavailable and brain-penetrant 11β-HSD1 inhibitor**

1. PK / PD: pharmacokinetic / pharmacodynamic
A growing body of medical literature supports the association between cortisol and Alzheimer's disease.

Raised cortisol associated with Alzheimer's disease

- MCI: mild cognitive impairment; AD: Alzheimer's Disease

- Recent studies also support the association between cortisol and cognitive impairment associated with neuroendocrine dysfunction


Research suggests that lowering cortisol levels may prevent the development / progression of Alzheimer's disease

Many studies support the association between cortisol and Alzheimer’s disease development and progression

- A recent AIBL study provided compelling evidence that elderly subjects with higher plasma cortisol levels are at much greater risk of developing Alzheimer's disease

This study also demonstrated that 50% of those aged 65+ have raised cortisol levels

1. MCI: mild cognitive impairment; AD: Alzheimer’s Disease
2. Recent studies also support the association between cortisol and cognitive impairment associated with neuroendocrine dysfunction
Actinogen is an ASX-listed biotech company focused on innovative approaches to treating cognitive impairment associated with neurological and metabolic diseases.

**Overview**

- Actinogen is developing Xanamem, a novel therapy for Alzheimer’s disease, mood disorders and schizophrenia, with significant market potential.
- Xanamem - lead drug, designed to inhibit cortisol production in the brain, with the potential to treat cognitive impairment.
- Actinogen has completed a Phase II double-blind, 12 week, randomised, placebo-controlled study of Xanamem in Alzheimer’s disease (XanADu).

**Board of Directors**

- **Dr. Geoff Brooke**
  - *Chairman*
  - MBBS; MBA
  - 30+ years experience in the healthcare investment industry
  - Founder and MD of Medvest Inc and GBS Venture Partners
- **Dr. Bill Ketelbey**
  - *CEO & MD*
  - MBCh; FFPM; MBA; GAICD
  - 30+ years experience in healthcare, biotech and pharmaceutical industries
  - Formerly senior international roles at Pfizer and Director at Westmead Institute of Medical Research
- **Dr. George Morstyn**
  - *Non-executive director*
  - MBBS; PhD; FRACP; MAICD
  - 25+ years experience in biotech investment and drug development
  - Board member of Biomedvic, Cancer Therapeutics and Symbio; Former Senior VP and SMO at Amgen
- **Mr. Malcolm McComas**
  - *Non-executive director*
  - BEc, LLB; FAICD; SF Fin
  - 25+ years experience in the financial services industry
  - Chairman of Pharmaxis and Fitzroy River Corporation; formerly senior leadership roles in investment banking

**Key shareholding metrics**

- 49% BVF Partners
- 32% Top 20 (excl. BVF Partners)
- 19% Remaining shareholders

---

A novel approach to treating cognitive impairment and Alzheimer's disease
Advisory Boards
World’s premier academics involved in the development of Xanamem and as a novel treatment for Alzheimer’s disease

Clinical Advisory Board (Alzheimer’s disease)

Positions Xanamem at the forefront of Alzheimer’s drug development

Scientific Advisory Board

Combining deep understanding of cortisol, 11β-HSD1 and drug discovery

Prof. Craig Ritchie Chair

Prof. Colin Masters AO

Prof. Jeffrey Cummings

Prof. Jonathan Seckl

Prof. Brian Walker

Prof. Scott Webster

THE UNIVERSITY of EDINBURGH

The Royal Melbourne Hospital

Cleveland Clinic

THE UNIVERSITY of EDINBURGH

THE UNIVERSITY of EDINBURGH

THE UNIVERSITY of EDINBURGH
IP protection

Actinogen maintains a broad granted composition of matter patent estate, with key patents granted in all major target markets.

Geographic patent overview

- Actinogen’s patent portfolio covers a broad range of neurological and metabolic diseases including Alzheimer’s disease.
- Xanamem patents granted in key markets that account for over 90% of the global Alzheimer’s market.
- Additional patents and patent extension being actively prosecuted.

>90% of the global Alzheimer’s disease market.
Market dynamics of Alzheimer’s disease

Presents a compelling commercial opportunity for Actinogen to target initially

Substantial target market with significant upside¹

<table>
<thead>
<tr>
<th>Cortisol-high, cognition normal</th>
<th>Subjective memory decline</th>
<th>Cognitive and functional decline fulfilling dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>At-risk</td>
<td>Prodromal</td>
<td>Mild</td>
</tr>
<tr>
<td>~25.0m (50% over 65 yrs)</td>
<td>~4.0m</td>
<td>~1.5m</td>
</tr>
</tbody>
</table>

Source: Drugs.com, Biogen, Roche, Datamonitor, Alzheimer’s Association

1. Target market statistics based on the current US treatment landscape
2. Base case annual peak sales assumes: (1) Launch: US 2024, EU5, JP and ROW 2025; (2) Penetration: 30% of mild AD market in 5 years (i.e. ~470,000 in the US); (3) Pricing: US – US$19/day gross (US$12/day net), ROW: 50% of US price

Underpinned by favourable market dynamics

✓ Targeting large addressable markets (US, EU5, JP)
✓ All currently approved drugs are symptomatic treatments (that do not affect disease progression) providing limited benefit
✓ Treatment prices are robust (despite generic competition) – with users paying for modest clinical efficacy

Upside potential for earlier use Key focus

>US$7.5bn

Target annual peak sales (mild AD)²

<table>
<thead>
<tr>
<th>US branded products (gross price)</th>
</tr>
</thead>
<tbody>
<tr>
<td>US$10/day</td>
</tr>
<tr>
<td>US$8/day</td>
</tr>
<tr>
<td>US$18/day</td>
</tr>
</tbody>
</table>

A novel approach to treating cognitive impairment and Alzheimer’s disease

Source: Drugs.com, Biogen, Roche, Datamonitor, Alzheimer’s Association
## Big Pharma interest

Global Big Pharma demonstrating strong M&A interest in acquiring or partnering with companies and licensing novel mechanism of action assets with Alzheimer's disease as the lead/key indication

<table>
<thead>
<tr>
<th>Bidder / Licensee</th>
<th>Deal value (US$bn)</th>
<th>Upfront (US$bn)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AbbVie</td>
<td>0.2</td>
<td></td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Janssen</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Merck</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Biogen</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Pernera</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>Biogen</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>AbbVie</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Allergan</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Novartis</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>Pfizer</td>
<td>1.9</td>
<td></td>
</tr>
<tr>
<td>Takeda</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>Otsuka</td>
<td>3.5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Target / Licensor</th>
<th>Year</th>
<th>Deal type</th>
<th>Candidate</th>
<th>Phase</th>
<th>Novel MoA (not anti-amyloid)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actelis</td>
<td>2017</td>
<td>Partnership</td>
<td>AZD3293</td>
<td>Pre-clinical</td>
<td>✔</td>
</tr>
<tr>
<td>Aelexis</td>
<td>2014</td>
<td>Partnership</td>
<td>ACI-35</td>
<td>I</td>
<td>✗</td>
</tr>
<tr>
<td>Alector</td>
<td>2015</td>
<td>Partnership</td>
<td>BNC-375</td>
<td>I</td>
<td>✗</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>2014</td>
<td>Partnership</td>
<td>BMS-986168</td>
<td>Pre-clinical</td>
<td>✗</td>
</tr>
<tr>
<td>AC Immune</td>
<td>2017</td>
<td>Partnership</td>
<td>IPN007</td>
<td>II</td>
<td>✔</td>
</tr>
<tr>
<td>Bionomics</td>
<td>2014</td>
<td>Partnership</td>
<td>LU AE58054</td>
<td>Pre-clinical</td>
<td>✗</td>
</tr>
<tr>
<td>CHASE</td>
<td>2013</td>
<td>Partnership</td>
<td>CPC-201</td>
<td>Pre-clinical</td>
<td>✔</td>
</tr>
<tr>
<td>Voyager</td>
<td>2016</td>
<td>Partnership</td>
<td>Gene Therapy platform</td>
<td>Pre-clinical</td>
<td>✗</td>
</tr>
<tr>
<td>Denali</td>
<td>2018</td>
<td>Partnership</td>
<td>Brain-penetrant ATV</td>
<td>Pre-clinical</td>
<td>✔</td>
</tr>
<tr>
<td>Merck</td>
<td>2018</td>
<td>Partnership</td>
<td>ACI-3024</td>
<td>Pre-clinical</td>
<td>✗</td>
</tr>
<tr>
<td>Heptares</td>
<td>2018</td>
<td>License</td>
<td>Three M1/M4 agonists</td>
<td>I</td>
<td>✔</td>
</tr>
<tr>
<td>Avantir</td>
<td>2016</td>
<td>License</td>
<td>AVP-786</td>
<td>III</td>
<td>✔</td>
</tr>
</tbody>
</table>

A novel approach to treating cognitive impairment and Alzheimer's disease
XanADu Phase II clinical trial

Double-blind, randomised, placebo-controlled study to assess the efficacy and safety of Xanamem in subjects with mild Alzheimer's disease

Xanamem treatment course
12 weeks

186 patients with mild Alzheimer’s disease (enrolment complete)

10mg daily
Xanamem for 12 weeks (vs. placebo)

Trial conducted at 25 sites in
AUS, USA and UK

Largest AD global clinical trial run by an Australian biotech

1. Study registered on Clinicaltrials.gov: NCT02727699
2. Fully enrolled 26 November 2018
XanADu: Phase II Clinical Trial Completed

Double-blind, randomised, placebo-controlled study to assess the efficacy and safety of Xanamem in subjects with mild Alzheimer's disease\(^1\), with initial results announced 7th May 2019

XanADu initial results

- Efficacy end points were not achieved
- Potent pharmacodynamic modulation of cortisol-related hormones achieved
- Xanamem is well-tolerated with no safety concerns
- Sub-analyses of results currently underway

Possible reasons behind XanADu results

- Recurrent challenges seen in AD drug development
- Xanamem dose / study duration

Ongoing development

- Phase I target occupancy studies
- XanaHES dose escalation study
- Long-term animal toxicology studies
- New indications for future focus selected: mood disorders (such as bipolar disorder) and schizophrenia

---

1. ADAS-COG14: Alzheimer’s Disease Assessment Scales – Cognitive Subscale Score (version 14); ADCOMs: AD COMposite Scores (composite data derived from ADAS-COG14, CDR-SOB and MMSE); CDR-SOB: Clinical Dementia Rating Scale – Sum of Boxes; RAVLT: Rey Auditory Verbal Learning Test; MMSE: Mini-Mental Status Examination; NTB: Neuropsychological Test Batteries; NPI: Neuropsychiatric Inventory
Disclaimer

This presentation has been prepared by Actinogen Medical Limited. ("Actinogen" or the "Company") based on information available to it as at the date of this presentation. The information in this presentation is provided in summary form and does not contain all information necessary to make an investment decision.

This presentation does not constitute an offer, invitation, solicitation or recommendation with respect to the purchase or sale of any security in Actinogen, nor does it constitute financial product advice or take into account any individual's investment objectives, taxation situation, financial situation or needs. An investor must not act on the basis of any matter contained in this presentation but must make its own assessment of Actinogen and conduct its own investigations. Before making an investment decision, investors should consider the appropriateness of the information having regard to their own objectives, financial situation and needs, and seek legal, taxation and financial advice appropriate to their jurisdiction and circumstances. Actinogen is not licensed to provide financial product advice in respect of its securities or any other financial products. Cooling off rights do not apply to the acquisition of Actinogen securities.

Although reasonable care has been taken to ensure that the facts stated in this presentation are accurate and that the opinions expressed are fair and reasonable, no representation or warranty, express or implied, is made as to the fairness, accuracy, completeness or correctness of the information, opinions and conclusions contained in this presentation. To the maximum extent permitted by law, none of Actinogen its officers, directors, employees and agents, nor any other person, accepts any responsibility and liability for the content of this presentation including, without limitation, any liability arising from fault or negligence, for any loss arising from the use of or reliance on any of the information contained in this presentation or otherwise arising in connection with it.

The information presented in this presentation is subject to change without notice and Actinogen does not have any responsibility or obligation to inform you of any matter arising or coming to their notice, after the date of this presentation, which may affect any matter referred to in this presentation.

The distribution of this presentation may be restricted by law and you should observe any such restrictions.

This presentation contains certain forward looking statements that are based on the Company's management's beliefs, assumptions and expectations and on information currently available to management. Such forward looking statements involve known and unknown risks, uncertainties, and other factors which may cause the actual results or performance of Actinogen to be materially different from the results or performance expressed or implied by such forward looking statements. Such forward looking statements are based on numerous assumptions regarding the Company's present and future business strategies and the political and economic environment in which Actinogen will operate in the future, which are subject to change without notice. Past performance is not necessarily a guide to future performance and no representation or warranty is made as to the likelihood of achievement or reasonableness of any forward looking statements or other forecast. To the full extent permitted by law, Actinogen and its directors, officers, employees, advisers, agents and intermediaries disclaim any obligation or undertaking to release any updates or revisions to information to reflect any change in any of the information contained in this presentation (including, but not limited to, any assumptions or expectations set out in the presentation).