



Investment Note

Healthcare Sector

4 June 2018

Actinogen Medical Ltd (ASX: ACW)

Positive developments lessen ACW's risk profile...

Summary

- ACW recently raised \$15m via a strongly supportive institutional placement and announced positive outcome for the interim analysis of XanADu.** These developments are without a doubt a positive for ACW and somewhat lessens ACW's risk profile. In our view, along with its November 2017 raising which fully funded its Phase II study, this placement and the additional \$2m SPP puts ACW in a strong balance sheet position. Further, the institutional support from the likes of BVF, Platinum Investment Management and Australian Ethical Investment should not be taken lightly and is a testament to the expertise of ACW's management team and the potential of Xanamem (not just for Alzheimer's disease but also potentially other indications).
- Successful \$15m raising with strong interest from institutional investors.** ACW has successfully raised \$15 million via an institutional placement, subject to shareholder approval (see below). ACW's Placement saw strong interest from institutional investors such as specialist USA biotech investment fund Biotechnology Value Fund, L.P. and certain of its affiliates (BVF) (taking a cornerstone position of \$10.5m), Platinum Investment Management Ltd and Australian Ethical Investment. Once complete, BVF will be the largest shareholder in Actinogen with 19.9% of the ordinary shares on issue prior to the SPP.
- Details of the Placement.** The shares will be issued in two tranches, with Tranche 1 to issue 187.1 million shares to BVF under the current 25% allowance on 28 May 2018, totalling \$9.4m. These shares will be issued at \$0.05 a share, representing an 13.4% premium to the 5-day value weighted average price (VWAP). The issue of the additional 112.9 million shares will raise \$5.6m and is subject to shareholder approval.
- Share Purchase Plan (SPP) remains open till 11 July 2018.** A SPP soon to be open to existing shareholders on the register as at 22 May 2018 to raise a further \$2m, bringing the total capital raised to a maximum of \$17m. The SPP will be offered at the same price as the Placement and eligible shareholders will have the opportunity to acquire up to \$15,000 of new fully paid ordinary shares.
- How the funds will be utilised?** ACW's management team intends on using the funds to advance the ACW's development plan which includes, amongst others, a study exploring a higher dose of Xanamem in Alzheimer's disease and studies conducted in alternative clinical indications (that is, expansion of the development plan for Xanamem into these new indications).
- Positive outcome for Interim Analysis of XanADu (ACW's Phase II clinical trial of Xanamem in Alzheimer's disease).** On a further positive note, a planned interim analysis of ACW's Phase II XanADu trial conducted by an independent Data Safety Monitoring Board (DSMB) concluded and recommended to ACW that the Phase II trial continue without modification. DSMB's recommendation implies: (1) the positive benefit-risk safety profile of Xanamem 10mg daily; (2) no treatment-related serious adverse events; (3) continuation of the trial without modification. According to ACW, as of 28 May 2018, 101 patients have been enrolled in the trial. This represents ~57% of the total 174 planned enrolment. Enrolment is expected to complete in Q4 CY18, and top-line results available by Q2 CY19.

Rating

Speculative Buy

Share Price (A\$)

\$0.05

Capital Structure

Shares on Issue (m)	940.3M
Market Cap (A\$m)	44.2M

Board and Management

Dr. Geoff Brooke	Non-executive Chairman
Dr. Bill Ketelbey	CEO
Vincent Ruffles	VP: Clinical Research
Dr. Jason Loveridge	Non-Executive Director
Dr. George Morstyn	Non-Executive Director

Major Share Holders

Biotechnology Value Fund, L.P. (through its nominees)	19.90%
Edinburgh Technology Fund Ltd	5.12%
JK Nominees Pty Ltd	4.25%
Warambi SARL	2.33%
Mr. Martin Rogers	2.13%
Sunset Capital Management Pty Ltd	2.13%

Note: Details on capital structure and major shareholders reflects Tranche 1 only as Tranche 2 is subject to shareholder approval and the SPP closes on 11 July 2018.

Investment Thesis

ACW's valuation and share price will be driven by the following factors:

- Results in early 2019 for Phase II study, XanADu.
- Possible application of Xanamem to other indications such as diabetes.
- If ACW was able to form commercial partnership agreements with pharmaceutical companies.
- Strong management team and Xanamem Clinical Advisory Board.
- Successful capital raising in November 2017 and the current \$15 m placement via strong institutional backing is a testament to ACW's expertise and the potential of its drug candidate.
- The Company has the ability to finish the Phase II study in Alzheimer's disease and expand into other indications.

Key Risks

We see the following key risks, but are not limited to:

- No material results/conclusions but the outcome of the interim analysis of Phase II study is a significant positive in our view.
- ACW remains loss making and hence a speculative investment.

Company Description

Actinogen Medical is an ASX-listed biotechnology company (**ASX: ACW**) focused on research and development of treatments for Alzheimer's disease and the cognitive decline associated with neurodegenerative diseases and metabolic diseases, like Type 2 diabetes. ACW's drug candidate Xanamem is designed to block the production of cortisol in the brain. By reducing cortisol in the brain, ACW believes Xanamem will be able to slow and possibly prevent the cognitive decline associated with Alzheimer's disease. ACW is currently undertaking a Phase II study XanADu, which is a Phase II efficacy and safety trial of Xanamem in patients with mild Alzheimer's disease. Recruitment and treatment of patients started in 2017, with results expected in early 2019. ACW's management team and scientific advisory board includes world-renowned Alzheimer's disease and dementia researchers, as well as industry specialists in drug design and clinical trial management.

Key investment drivers

We believe the following investment drivers are worth further consideration by investors:

#1 Results in early 2019 for Phase II study, XanADu...with positive interim analysis...

In 2016, ACW announced its Phase II study, XanADu, which aims to examine the efficacy and safety of Xanamem in patients with mild AD. In terms of study design, according to ClinicalTrials.gov, XanADu is a double-blind, randomised, placebo-controlled study of 174 patients conducted at 20 sites across Australia, UK and USA. ACW began recruiting patients in 2017 and expects top-line results in early 2019. In our view, the planned interim analysis of ACW's Phase II XanADu trial conducted by an independent Data Safety Monitoring Board (DSMB) concluded and recommended to ACW that the Phase II trial continue without modification – is a significant positive for ACW. DSMB's recommendation implies: (1) the positive benefit-risk safety profile of Xanamem 10mg daily; (2) no treatment-related serious adverse events; (3) continuation of the trial without modification. According to ACW, as of 23 May 2018, 100 patients have been enrolled in the trial. This represents ~57% of the total 174 planned enrolment. Enrolment is expected to complete in Q4 CY18, and top-line results available by Q2 CY19.

#2 \$15m raising via placement (and potentially \$2m via SPP) de-risks ACW. These recent developments are without a doubt, positive for ACW and somewhat lessens ACW's risk profile. In our view, along with its November 2017 raising, this placement and SPP puts ACW in a strong balance sheet position.

#3 Possible application of Xanamem to other indications such as diabetes.

Separately, ACW believes that Xanamem could assist in the treatment of Type 2 diabetes. Type 2 Diabetes is a chronic disease that affects over 422 million people globally. Current treatments in use control blood glucose levels but have no effect on preventing dementia. Interestingly, patients with diabetes, especially, Type 2 diabetes have higher levels of cortisol and twice the risk of developing dementia. Drugs currently used in practice have not been appropriate in reducing cortisol levels. By inhibiting cortisol production, it is believed that cognition may improve for patients. ACW has collaborated with the University of Edinburgh for a Phase II trial of Xanamem in Diabetes Cognitive Impairment, are ongoing.

#4 Strong management team and Xanamem Clinical Advisory Board.

ACW's management team and scientific advisory board includes world-renowned Alzheimer's disease and dementia researchers, and industry specialists in drug design and clinical trial management. Key members of the Xanamem Clinical Advisory Board include **(1) Professor Craig Ritchie (Chair)**, a leading authority on dementia and has been a senior investigator on more than 30 drug trials; **(2) Professor Colin Masters (AO)**, a leading researcher in AD and other neurodegenerative diseases with a career spanning over 35 years; and **(3) Professor Jeffrey Cummings**, a leader in clinical trials and developing new therapies for brain diseases. Professor Cummings contribution to Alzheimer's disease research has been recognized through the Henderson Award of the American Geriatrics Society (2006), the Research Award of the John Douglas French Alzheimer's Research Foundation (2008), and the Ronald and Nancy Reagan Research Award of the national Alzheimer's Association (2008). In 2010, he was honoured by the American Association of Geriatric Psychiatry with their Distinguished Scientist Award.

Refresher on Actinogen Medical (ACW)...

Actinogen Medical is an ASX-listed biotech company (**ASX: ACW**) focused on research and development of treatments for Alzheimer's disease and the cognitive decline associated with neurodegenerative diseases and metabolic diseases, like Type 2 diabetes. ACW's drug candidate Xanamem is designed to block the production of cortisol in the brain. By reducing cortisol in the brain, ACW believes Xanamem will be able to

slow and possibly prevent the cognitive decline associated with Alzheimer's disease. ACW is currently undertaking a Phase II study XanADu, which is a Phase II efficacy and safety trial of Xanamem in patients with mild Alzheimer's disease. Recruitment and treatment of patients started in 2017, with results expected in early 2019. ACW's management team and scientific advisory board includes world-renowned Alzheimer's disease and dementia researchers, as well as industry specialists in drug design and clinical trial management.

ACW pre-clinical trials and Phase I. According to ACW's management, in preclinical studies, using mouse model of Alzheimer's disease, *"Xanamem was found to be effective in improving cognitive function and in clearing amyloid plaques from the brain. The improved cognitive function was observed after only 4 weeks of treatment and was maintained for at least 41 weeks"*. Hence, ACW has conducted all necessary studies confirming Xanamem has an acceptable safety profile to proceed into the current Phase II clinical study. Importantly, the studies confirmed that Xanamem can cross the blood-brain-barrier at appropriate concentrations to inhibit production of cortisol in the hippocampus and frontal cortex of the brain (the primary site of action).

How Xanamem works? According to the Company, studies have shown that patients with AD have high levels of cortisol (the stress hormone) in the hippocampus and the frontal cortex, and this is associated with recent memory loss and dementia. In terms of mechanism of action, Xanamem blocks the activity of 11 β -HSD1, the enzyme that converts inactive cortisone into its active form, cortisol in the brain. By inhibiting or blocking this enzyme activity, the amount of cortisol in the brain is reduced and hence theoretically, should prevent AD.

Phase II – early 2019 is a key date. In 2016, ACW announced its Phase II study, XanADu, which aims examine the efficacy and safety Xanamem in patients with mild AD. In terms of study design, according to ClinicalTrials.gov, XanADu is a double-blind, randomised, placebo-controlled study of 174 patients conducted at 20 sites across Australia, UK and USA. ACW began recruiting patients in 2017 and expects top-line results in early 2019.

Other indications – Diabetes. Separately, ACW believes that Xanamem could assist in the treatment of Type 2 diabetes. Type 2 Diabetes is a chronic disease that affects over 422 million people globally. Current treatments in use control blood glucose levels but have no effect on preventing dementia. Interestingly, patients with diabetes, especially, Type 2 diabetes have higher levels of cortisol and twice the risk of developing dementia. Drugs currently used in practice have not been appropriate in reducing cortisol levels. By inhibiting cortisol production, it is believed that cognition may improve for patients. ACW has collaborated with the University of Edinburgh for a Phase II trial of Xanamem in Diabetes Cognitive Impairment, are ongoing.

Experienced Board of Directors, Management Team and Scientific Advisory Board...

ACW's management team and scientific advisory board includes world-renowned Alzheimer's disease and dementia researchers, and industry specialists in drug design and clinical trial management. Key members of the Xanamem Clinical Advisory Board include:

- **Professor Craig Ritchie (Chair).** Professor Ritchie is a leading authority on dementia and has been a senior investigator on more than 30 drug trials. Professor Ritchie is the Chair of the Scottish Dementia Research Consortium, Professor of the Psychiatry of Ageing and Director of the Centre for Dementia Prevention at the University of Edinburgh, Associate Director of the Wellcome Trust Clinical Research Facility and Co Coordinator at IMI-EPAD.

- **Professor Colin Masters (AO).** Professor Masters' is a leading researcher in AD and other neurodegenerative diseases with a career spanning over 35 years. Professor Masters is the Laureate Professor of Dementia Research and Head, Neurodegeneration Division at The Florey Institute, The University of Melbourne and a consultant at the Royal Melbourne Hospital.
- **Professor Jeffrey Cummings.** Professor Cummings is a leader in clinical trials and developing new therapies for brain diseases. Professor Cummings contribution to Alzheimer's disease research has been recognized through the Henderson Award of the American Geriatrics Society (2006), the Research Award of the John Douglas French Alzheimer's Research Foundation (2008), and the Ronald and Nancy Reagan Research Award of the national Alzheimer's Association (2008). In 2010, he was honoured by the American Association of Geriatric Psychiatry with their Distinguished Scientist Award. Professor Cummings is the Camille and Larry Ruvo Chair of the Neurological Institute of Cleveland Clinic and Professor of Medicine (Neurology), Cleveland Clinic Lerner College of Medicine, Case Western Reserve University.

Key members of ACW's scientific development panel include:

- **Professor Alan Boyd.** Professor Boyd has a medical research career spanning 30-year pharmaceutical, initially with Glaxo Group Research Ltd. He has held roles in global pharmaceutical companies, including Director of Clinical and Medical Affairs, Head of Medical Research, and Director of Research and Development. Professor Boyd has qualifications in Biochemistry and Medicine from the University of Birmingham and is also President of the Faculty of Pharmaceutical Medicine, Royal College of Physicians, UK.
- **Professor Brian Walker.** Professor Walker medical research career spans over 20 years. Professor Walker is still based at University of Edinburgh and more recently has taken up his new post of Pro Vice Chancellor – Research Strategy and Resources and Chair of Medicine at Newcastle University, UK.
- **Professor Scott Webster.** Prof Webster has over 17 years' experience in drug discovery industry. He has a successful track record in medicines discovery, leading programmes through preclinical discovery, clinical development and licensing. Professor Webster was pivotal in the discovery and development of Xanamem and other compounds currently in development for acute pancreatitis and multiple organ failure.

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