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Actinogen Medical Limited
(ASX: ACW)

July 5, 2016
Target Price: A$0.27
Recent Price: A$0.07

Market Data

Fiscal Year	June
Industry	BioTech
Market Cap	A$42.5M
Price/Earnings (ttm)	N/A
Price/Book (mrq)	2.9x
Price/Sales (ttm)	349x
Top 20 % Ownership	52.2%
Shares Outstanding	606.7M
Equity Float	385.4M
Avg. Volume (3 mo.)	1.5M

As of July 4, 2016

Income Statement Snapshot

	TTM
Revenue	$0.12M
Net Loss	($5.4M)

Balance Sheet Snapshot

	MRQ
Cash*	$7.9M
Debt	$0.0M

**Includes $5.2 million in available-for-sale financial investments*

Company Website
actinogen.com/

Company Overview

Actinogen Medical ("Actinogen", "ASX:ACW", or the "Company") is focused on an innovative treatment for reducing cognitive impairment in chronic neurodegenerative and metabolic diseases, such as Alzheimer's and diabetes. ACW's drug candidate Xanamem™, works by inhibiting cortisol (the "stress" hormone) production at sites in the brain important for cognition. Actinogen has completed a series of Phase I clinical trials to establish the safety and feasibility of Xanamem for further clinical development. The Company is currently entering a global Phase II clinical trial, with the final patients expected to be recruited in 2Q 2018. The multi-billion dollar Alzheimer's disease (AD) market is in desperate need of new medical treatments. The results from the Phase II study, if positive, will likely generate substantial investment or acquisition interest from major pharmaceutical industry players. The Company's headquarters are based in Sydney, Australia.

Valuation

Based on an rNPV (risk-adjusted net present value) of Xanamem for use in mild AD and diabetes cognitive impairment (DCI), we derive a target price of A$0.27, almost four times the current valuation.

Investment Highlights

- Recent technological advances should increase the success rate of Alzheimer's clinical trials
- Current AD treatments have limited efficacy; in spite of this, AD drugs currently generate billions per year in revenue
- Xanamem is currently entering a Phase II trial for Mild AD in the US, AU, and UK
- Xanamem's two Phase I trials in 88 patients showed safety and tolerability, while demonstrating pharmacologically active concentrations in cerebrospinal fluid (CSF)
- There is a significant association between excess cortisol and AD/dementia
- Xanamem's novel mechanism of action inhibits the stress hormone cortisol through selective inhibition of the 11β–HSD1 enzyme in the brain
- Discovery and early development of Xanamem funded by the Wellcome Trust (provides over £700 million a year in health care funding); ~$25 million invested
- ThomsonReuters named Xanamem one of the top 5 drugs in Phase I development globally
- There are six other 11β–HSD1 inhibitors in clinical development (not all in CNS disease), validating the target
- Xanamem has high CNS penetration (Pfizer CNS Multi-parameter Optimization (MPO) calculator score = 5.2); this score demonstrates that Xanamem efficiently crosses the blood-brain barrier in a high enough dose to effectively block the 11β–HSD1 enzyme in the brain
- Cognitive enhancement was seen in a mouse model of UE2316, a Xanamem analogue
- Patent protection is granted through 2031
- The total estimated worldwide cost of dementia in 2015 was $818 billion; this total is projected to increase to $1 trillion in 2018 and $2 trillion in 2030 (source: Alzheimer's Disease International's World Alzheimer Report 2015)
- Xanamem is preparing to enter a Phase II clinical trial for diabetes cognitive impairment (DCI); previous research makes a compelling argument for using 11β-HSD1 inhibitors to treat DCI

Investment Highlights

Recent technological advances should increase the success rate of Alzheimer's clinical trials. Over the past decade, Alzheimer's clinical trials have performed extremely poorly. A 2014 research study from Jeffrey Cummings, Travis Morstorf, and Kate Zhong, stated that from 2002 to 2012, Alzheimer's drugs had an overall failure rate of 99.6%. The only drug that was approved during this time period was *N*-methyl-D-aspartate (NMDA)-receptor antagonist, memantine in 2003. In spite of what is, at best, a modest improvement in the symptoms of patients with moderate to severe Alzheimer's disease, memantine generated $1.8 billion in revenue in 2014, thus proving the significant demand for any new Alzheimer's drugs that improve the symptoms/underlying disease state of patients. Post 2012, there have been no new approvals of Alzheimer's drugs.

In spite of the large number of recent failures in AD drugs, significant amounts of funding have gone toward AD research. In June 2015, a new company called Denali Therapeutics raised $217 million in venture capital, the largest amount ever raised for a biotech startup. Denali is focused on treating neurodegenerative diseases, with a primary focus on AD and Parkinson's disease. In March 2015, the world's first venture capital fund dedicated to discovering new treatments for dementia raised $100 million, and was backed in part by funding from the British government and several of the world's largest drug companies, including GlaxoSmithKline, Johnson & Johnson, Eli Lilly, Pfizer and Biogen Idec. Prominent researchers are also becoming more excited about the potential of new AD treatments. Dr. Howard Fillit of the Alzheimer's Drug Discovery Foundation stated that in three to five years "we're going to have potentially more than one drug approved that has some disease-modifying effect."

These large investments in AD and neurological research indicate that many prominent companies and researchers believe that we are beginning to acquire the scientific tools needed to improve the overall success rates of AD clinical trials. Much of the excitement rests around the early detection of Alzheimer's, which would allow patients to begin treatment before symptoms become too severe. Scientific consensus now believes that changes in the brain from AD occur decades before memory loss and other cognitive symptoms become visible. Due to this, early detection can allow treatment to begin at an earlier stage of Alzheimer's and lead to better management of symptoms and the disease as a whole.

Currently, Alzheimer's is detected through a combination of memory questionnaires and PET/MRI brain scans. Multiple other tests are in development, including, but not limited to, biomarker- based blood tests, saliva tests, and virtual reality tests. These tests could allow for a simple diagnosis of some patients decades before onset of the disease, thus allowing treatment to begin before serious symptoms occur. If accurate and economical, this test could potentially have a significant impact on treating patients with early AD. Early detection is thought to have the potential to increase the efficacy of AD drugs, as these drugs could have more of a cognitive effect early in the disease.

A recent Phase Ib clinical trial from Biogen Idec on aducanumab showcased the potential of treating early stage Alzheimer's patients, along with the possible valuation gains from showing disease modifying effects. According to Alfred Sandrock, the chief medical officer and senior vice president of Biogen Idec, "This is the first time an investigational drug for Alzheimer's disease has demonstrated a statistically significant reduction on amyloid plaque as well as a statistically significant slowing of clinical impairment in patients with prodromal or mild disease." The success of this trial added $40 billion to Biogen's market cap, demonstrating the significant valuation gains for any company showing a positive effect in treating early AD. The fact that this was a Phase Ib trial also shows that early stage trials can lead to these valuation gains.

Current AD treatments have limited efficacy; in spite of this, AD drugs currently generate billions per year in revenue. There are currently five drugs approved to treat AD. Three of these drugs are cholinesterase inhibitors, one drug is a NMDA-receptor antagonist, and one is a combination cholinesterase inhibitor/NMDA-receptor antagonist. The following table shows the list of FDA-approved Alzheimer's drugs:

Drug name	Brand name	Approved For	FDA Approved
1. donepezil	Aricept	All stages	1996
2. galantamine	Razadyne	Mild to moderate	2001
3. memantine	Namenda	Moderate to severe	2003
4. rivastigmine	Exelon	All stages	2000
5. donepezil and memantine	Namzaric	Moderate to severe	2014

Source: alz.org

At its peak, Aricept was generating $4.4 billion in annual sales in the U.S., representing about 50% of the market. This is in spite of the limited efficacy of Aricept. Market leaders Namenda, Aricept, and Exelon generated $4.3 billion in total sales in 2013 (Source: GlobalData PharmaPoint report, Aricept was generic in 2013), and GlobalData expects the AD treatment market to reach over $13 billion in 2023, driven by approvals of new drugs for AD. Cholinesterase inhibitors only improve symptoms over the near-term, without slowing the underlying disease state. The current sales of AD drugs show the significant demand for Alzheimer's treatments, as all currently approved drugs have limited efficacy at best and still generate $4.3+ billion in revenue per year. A drug with positive efficacy, safety, economics, and ease of administration could be one of the world's top selling drugs in a short period of time, particularly if patients are treated at an earlier stage than they are currently, as this would increase the potential patient population beyond current figures.

Xanamem is currently entering a Phase II trial for Mild AD in the US, AU, and UK. Xanamem is currently entering a double-blind, placebo-controlled randomized Phase II study (called the XanADu trial). The final patients for the Phase II XanADu trial are expected to be recruited in 2Q18; recruitment is scheduled to begin in 2H16. Top line results are expected in 4Q18. The trial will include 200 patients across 20 worldwide trial sites. ACW recently raised $10 million, thus funding the Phase II study fully through completion. The optimum dosage for Xanamem, as indicated by results for Xanamem,'s Phase I trial, is 35mg twice daily.

The trial will ultimately recruit 200 patients aged 50+ with mild dementia due to probable AD who will be screened for the following criteria: MMSE (mini-mental state examination)20-26 (inclusive), and CDR (Clinical Dementia Rating) 0.5 or 1.0, and receiving a stable dose of AChEl and/or memantine (at least 3 months) or treatment naïve. The patients will be treated with 35 mg of Xanamem twice daily for 12 weeks.

The primary endpoint will measure performance through changes in ADCOMposite Scores (ADCOMs, composite data derived from Alzheimer's Disease Assessment Scales-Cognitive subscale version 14 [ADAS-Cog v14], Clinical Dementia Rating Scale-Sum of Boxes [CDR-SOB], and Mini-Mental Status Examination [MMSE]) and ADAS-Cog v14.

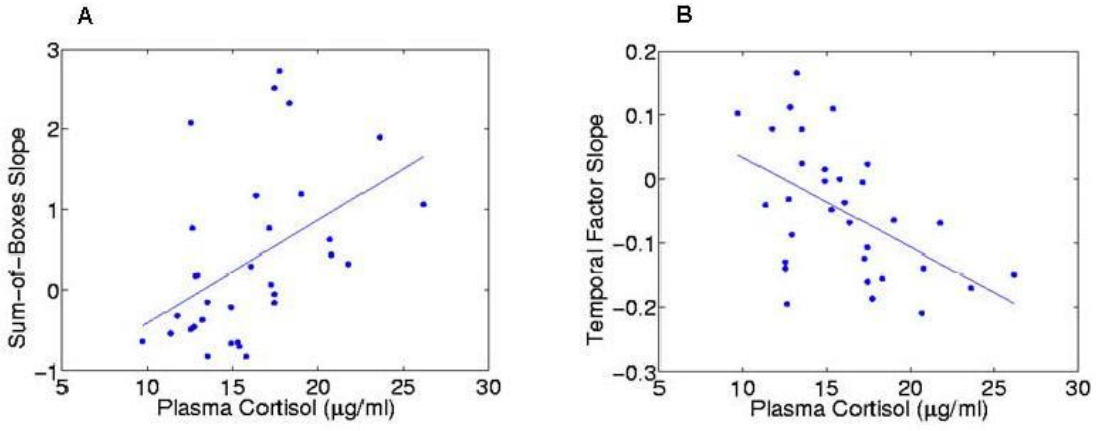
Secondary endpoints will include changes to the Rey Auditory Verbal Learning Test (RAVLT), CDR-SOB, MMSE, Neuropsychiatric Inventory (NPI), Neuropsychological Test Batteries (NTB) – Executive Domain.

There will also be exploratory endpoints, including CSF sampling for beta amyloid and tau clearance, and ApoE genotyping.

In our view, positive Phase II results would likely lead to a significant increase in ACW's stock valuation and a likely partnership with a major pharmaceutical company. ACW is confident that it has a complete data set, and that Xanamem will be partner ready if the drug reaches the partnering stage.

Xanamem's two Phase I trials in 88 patients showed safety and tolerability, while demonstrating pharmacologically-active concentrations in cerebrospinal fluid (CSF). In 2H15, ACW successfully completed its second Phase I trial and its second animal toxicology study. The Phase I trial had three sub-studies – a Multiple Ascending Dose study in 24 subjects, a fed/fasted study in 12 subjects, and a CNS pharmacokinetic study in 4 subjects. Safety and tolerability was shown at the highest doses (35mg twice daily). Further, the demonstration of pharmacologically-active concentrations in the CSF indicates that Xanamem has a higher probability for potential efficacy than previous 11β–HSD1 inhibitors.

There are significant links between excess cortisol and AD/dementia. Excess cortisol is associated with memory loss, amyloid plaques and neurodegeneration – the hallmarks of AD. Extensive research and evidence has been completed linking increased cortisol with cognitive impairment. Higher hypothalamic-pituitary-adrenal (HPA) activity, as reflected by increased cortisol levels, is associated with more rapid disease progression in subjects with Alzheimer type dementia (DAT). According to Csernansky et al 2006, higher HPA activity, as reflected by increased plasma cortisol levels, is associated with more rapid disease progression in individuals with mild or very mild DAT. There were correlations between plasma cortisol levels, memory impairment, and smaller hippocampal volume. Increased activity of the HPA axis (reflected by increased plasma cortisol) may thus be associated with a faster degeneration of the Alzheimer's disease process. The following charts from Csernansky et al shows the positive relationship between increased cortisol and cognitive impairment (as measured by sum-of-boxes and temporal factor):

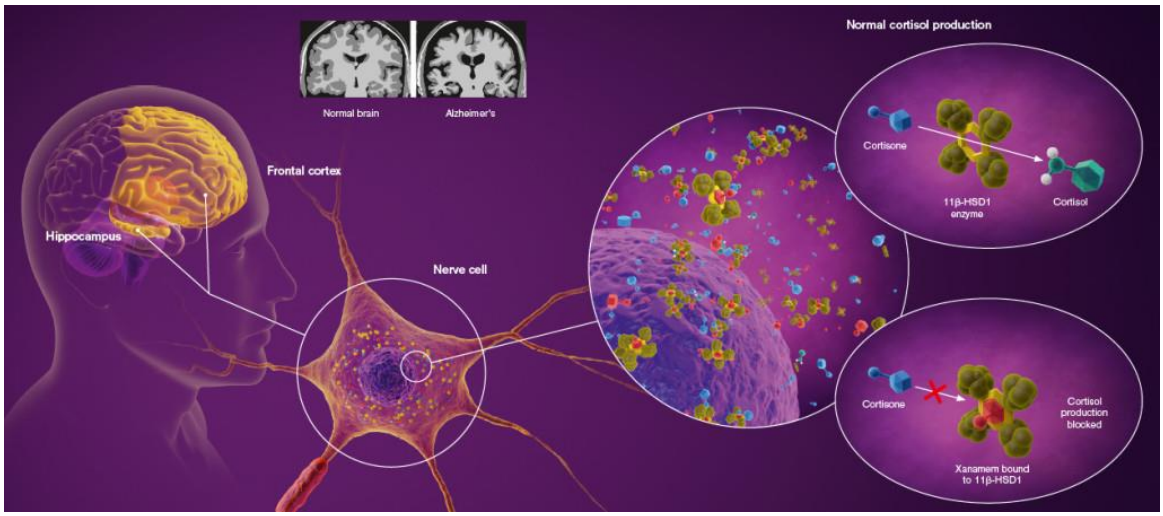


Hippocampal volume, as measured by MRI, is an objective measure of Alzheimer's. The effects of cortisol are primarily seen in the hippocampus and frontal cortex, which are the areas of the brain most affected by

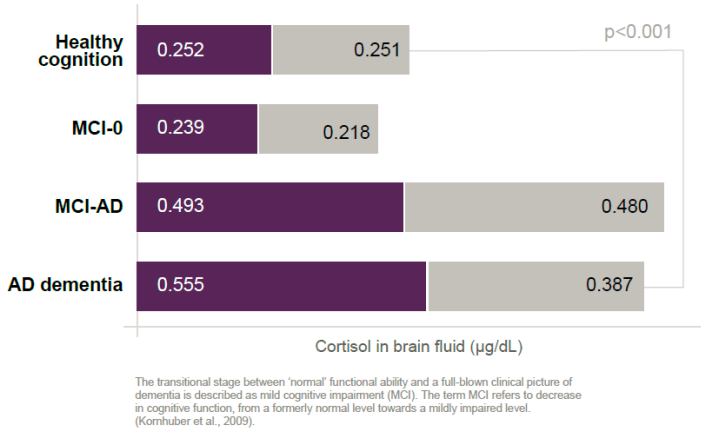
Alzheimer's, particularly early Alzheimer's. Older humans with elevated cortisol levels show reduced hippocampal volume and lower scores on hippocampal-dependent memory tests.

11β–HSD1 inhibitors also have symptomatic effects that are independent of any actual change in the underlying Alzheimer's disease. 11β–HSD1 inhibitors in phase II trials have reduced plasma glucose, blood pressure, and body weight and improved the patient's lipid profile. The above factors also influence the progression of dementia. Xanamem, given its targeted focus on inhibiting 11β–HSD1 in the hippocampus and frontal cortex, could have a significant impact in slowing the progress of AD.

Xanamem's novel mechanism of action inhibits the stress hormone cortisol through selective inhibition of 11β–HSD1 enzyme in the brain.



As can be seen in the above mechanism of action picture, Xanamem inhibits 11β–HSD1 through binding to the HSD1 enzyme (right side in the picture), thus blocking cortisol production. Xanamem is designed to cross the blood-brain barrier in effective concentrations, which we believe is a key differentiator versus any other 11β–HSD1 inhibitor failing CNS clinical trials, and could suggest improved efficacy over these other 11β–HSD1 inhibitors. Xanamem focuses on inhibiting 11β–HSD1 in the hippocampus and frontal cortex, as shown in the leftmost picture above. As stated earlier in the report, the hippocampus and frontal cortex are the areas of the brain most affected by Alzheimer's, in particular early Alzheimer's. This evidence was shown in a study performed by Popp et al 2015, which stated that "after controlling for possible confounders including CSF measures of amyloid beta1-42 and total tau, higher baseline CSF cortisol levels were associated with faster clinical worsening and cognitive decline in mild cognitive impairment (MCI)-AD. The findings suggest that HPA-axis dysregulation occurs at the MCI stage of AD and may accelerate disease progression and cognitive decline."



This provides good support for the efficacy potential of a cortisol inhibitor like Xanamem, in mild Alzheimer's patients, which is the patient population that Actinogen's Phase II trial is focused on.

Discovery and early development of Xanamem funded by the Wellcome Trust (provides over £700 million a year in health care funding); ~$25 million invested. The discovery and early development of Xanamem was funded by the Wellcome Trust. The UK-based Wellcome Trust invested over $25 million into Xanamem over seven years, including funding the initial Phase I single ascending dose study of Xanamem. The Wellcome Trust is a world-renowned, politically and financially independent charitable organization. The Wellcome Trust is well known for funding exciting scientific discoveries, including funding the Wellcome Trust Sanger Institute, which mapped 30% of the human genome.

ThomsonReuters named Xanamem one of the top 5 drugs in Phase I development globally. The ThomsonReuters recommendation and the large amount of funding provided by the Wellcome Trust provide further proof of Xanamem's significant potential.

There are six other 11β–HSD1 inhibitors in clinical development, which validates the target. Multiple 11β–HSD1 inhibitors are in clinical development by major pharmaceutical companies, which validates the target. As the below chart from ACW shows, there is currently one other 11β–HSD1 inhibitor recruiting for a Phase I clinical trial in AD (ASP3662 and ^{11}C-AS2471907). ABT-384 failed its Phase II trial in mild to moderate AD.

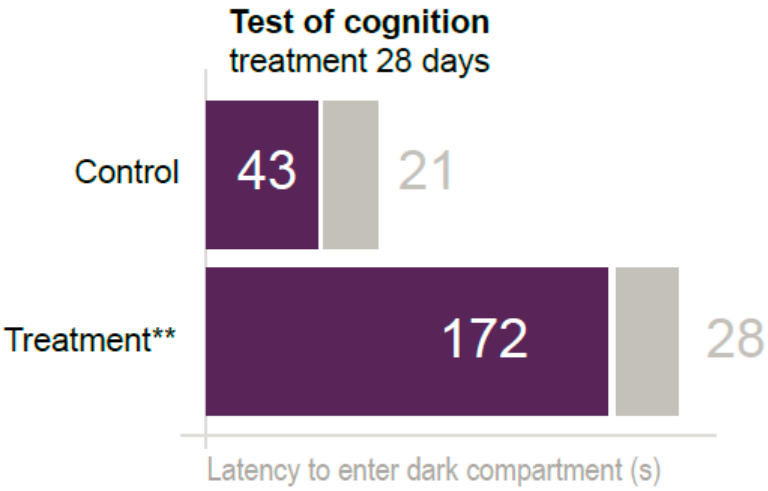
Compound	Sponsor	Study	Indication	Primary Endpoint	Source
ASP3662	Astellas	Ph II (recruiting) NCT02372578	Painful diabetic peripheral neuropathy	Analgesic efficacy	https://clincialtrials.gov
ASP3662 and ^{11}C-AS2471907	Astellas	Ph I (recruiting) NCT02194491	Alzheimer's disease	PET occupancy	https://clincialtrials.gov
BI-135585/ VTP-34072	Boehringer Ingelheim Vitae Pharmaceuticals	Ph II (completed) NCT02150824	T2DM metabolic syndrome	Did not meet primary efficacy end-point: fasting plasma glucose	https://clincialtrials.gov
AZD-4017 (open innovation)	University of Birmingham	Ph II (recruiting) NCT02017444	Idiopathic intracranial hypertension	Change in intracranial pressure at 12 weeks	https://clincialtrials.gov
AZD-4017 (open innovation)	University of Birmingham	Ph II (recruiting)	bone turnover in post-menopausal osteopenia	Change in biochemical markers of bone turn-over	http://www.hra.nhs.uk
ABT-384	Abbott	Ph II (completed) NCT01137526	Mild-moderate AD	Did not show non-inferiority to donepezil ADAS-Cog	https://clincialtrials.gov

Source: ACW ppt

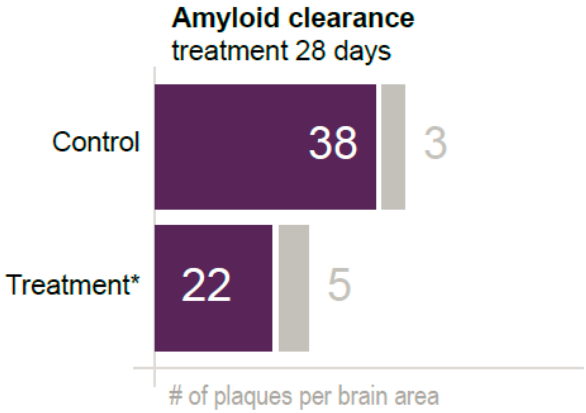
Xanamem has high CNS penetration (Pfizer CNS Multi-parameter Optimization (MPO) calculator score = 5.2); this score demonstrates that Xanamem efficiently crosses the blood-brain barrier in a high enough dose to effectively block the 11β–HSD1 enzyme in the brain. Xanamem's high CNS MPO score (5.2) is significantly higher than the other 11β–HSD1 inhibitor to be tested in AD (Abbott's ABT-384, which had a high CNS MPO score of 3.4). The CNS MPO score is a multi-parameter approach that determines which physiochemical properties will achieve optimal CNS penetration. ABT-384 failed its Phase II clinical trial in mild-moderate AD. The highest dose used in the ABT study would deliver a maximum of only 11% 11β–HSD1 production. Comparably, Xanamem has shown that it achieves higher plasma levels at a lower dose, delivers higher concentrations of the drug to the CSF, and is more potent and has higher free fraction. Given these factors, it is expected that Xanamem would have much higher 11β–HSD1 inhibition in the brain.

These concentrations were shown in Xanamem's Phase I multiple ascending dose study, and a manuscript titled *"Xanamem™ a novel 11β–HSD1 inhibitor with potential to provide durable symptomatic and disease modifying benefits in Alzheimer's disease"* will confirm that Xanamem crosses the blood-brain barrier and is delivered to the brain in effective concentrations. These results could generate further excitement in ACW, and could portend a higher probability of success in the Company's Phase II clinical trial.

Cognitive enhancement was seen in a mouse model of UE2316. In preclinical mouse models of UE2316, a close analogue of Xanamem, significant evidence of strong results were obtained. Mice with normal learning and memory avoided reentering a compartment where they had previously been shocked ($P<0.004$). This is shown in the following chart, with the treatment arm having a much longer timeframe to enter the dark compartment:



Additionally, a reduction of a-beta plagues were seen, with the treatment arm having a much lower number of plaques per brain area:



This indicates that there may be an AD disease modifying component to Xanamem, along with the expected potential symptomatic benefit. If it is shown that Xanamem alters AD, we believe it would likely increase the overall value of the drug.

Patent protection is granted through 2031. Having patent protection through 2031 ensures that ACW will be able to sell Xanamem (if approved) for a significant period of time without additional competition from generic drugs.

The total estimated worldwide cost of dementia in 2015 was $818 billion; this total is projected to increase to $1 trillion in 2018 and $2 trillion in 2030 (source: Alzheimer's Disease International's World Alzheimer Report 2015). The dementia burden is increasing significantly. 46.8 million people worldwide are living with dementia (2015); this total is projected to increase 74.7 million in 2030 and 131.5 million in 2050. These figures are projected to increase the worldwide cost of dementia from $818 billion in 2015 to $2 trillion in 2030. Additionally, Alzheimer's affects 11% of people over the age of 65 and 32% of people over the age of 75. As populations worldwide continue to age, Alzheimer's and

dementia will become a more significant problem. These figures and the lack of effective treatments for dementia make treating dementia potentially the #1 worldwide medical problem going forward.

This market size, combined with a lack of effective treatments, is driving the significant valuations currently seen in Alzheimer's, which include a $40 billion valuation gain from Biogen Idec following positive Phase Ib results, a $1.4 billion valuation for Axovant Sciences, which is entering a Phase II/III clinical trial (its drug was originally obtained from GlaxoSmithKline for only $5 million), a number of other multibillion dollar transactions in the Alzheimer's space (examples including Avanir Pharma being acquired by Otsuka Pharma for $3.5 billion following Phase II results, and Allergan acquiring a number of drugs used to treat neurological disorders from Heptares for $3.3 billion), and the $217 million funding for Denali Therapeutics, which was the largest amount ever raised for a biotech startup.

Xanamem is preparing to enter a Phase II clinical trial for diabetes cognitive impairment (DCI); previous research makes a compelling argument for using 11β-HSD1 inhibitors to treat DCI. Carbenoxolone (a 11β-HSD1 inhibitor) has been shown to improve cognition in type 2 diabetes patients. According to Sandeep et al 2004, 11β-HSD1 may afford a mechanistically tractable new therapeutic target to prevent or ameliorate age-associated cognitive dysfunction in healthy elderly subjects and in patients with type 2 diabetes. Due to this, the conclusion was that the re-exploitation of an old drug, carbenoxolone (with amiloride), may merit further evaluation until more selective inhibitors for brain 11β-HSD1 are developed. This conclusion was drawn from two randomized, double-blind, placebo-controlled crossover studies, which showed improvements in verbal fluency in 10 healthy elderly men after 4 weeks ($p<0.01$), and in verbal memory in 12 elderly patients with type 2 diabetes after 6 weeks ($p<0.01$). Given the established potential for 11β-HSD1 inhibitors to treat DCI, we believe that Xanamem's clinical trial results in this area could be compelling.

ACW has completed the Phase II trial design for DCI and plans to begin the trial in late 2016, with top line results expected to be reported in 4Q18. Given promising prior research on carbenoxolone, Xanamem may provide a compelling treatment for DCI.

Xanamem is also being developed for Parkinson's disease dementia(PDD). There are also strong links between cortisol and neurological diseases, including PD dementia. Due to this, ACW is currently planning a Phase II trial for the use of Xanamem in PDD. Trial dates are still to be decided.

Valuation

Company Name	Ticker	Share Price (USD)	Market Cap (USD)	Cash (MRQ, USD)	Total Debt (MRQ, USD)
Cerecor Inc	CERC	2.25	$19.5M	$16.6M	$4.8M
Neurotrope Inc	NTRP	0.45	$22.2M	$10.1M	$0.0M
Addex Therapeutics Ltd	ADXN.S	2.41	$26.5M	N/A	N/A
Prana Biotechnology Ltd	PBT.AX	0.08	$41.4M	N/A	N/A
Cantabio Pharmaceuticals Inc	CTBO.PK	2.32	$62.2M	$.1M	$0.M
Saniona AB	SANION.ST	2.97	$62.M	$5.6M	$0.M
Anavex Life Sciences Corp	AVXL.O	5.89	$210.3M	$12.M	$0.1M
vTv Therapeutics Inc	VTVT.O	6.03	$197.9M	$75.5M	$0.0M
Voyager Therapeutics Inc	VYGR.O	11.16	$298.5M	$204.M	$0.0M
Axovant Sciences Ltd	AXON.K	13.40	$1,328.6M	$276.3M	$0.0M
Intra-Cellular Therapies Inc	ITCI.O	39.68	$1,715.4M	$456.1M	$0.0M
	Median		*$62.2M*	*$16.6M*	*$0.0M*
	average		*$337.2M*	*$107.3M*	*$.5M*
Actinogen Medical Ltd	**ACW.AX**	**0.06**	**$33.6M**	**$7.6M**	**$0.0M**

Source: ThomsonReuters, as of July 4, 2016

Based on an rNPV of Xanamem for use in mild AD and DCI, we derive a target price of A$0.27. Some notes regarding our valuation of Xanamem are as follows:

- As the peer chart above shows, there is a wide chasm in the valuations between companies developing drugs for AD and other neurological disorders that have shown what is perceived as positive efficacy and those companies that have yet to show efficacy in human trials. Due to this, we expect that positive results from Xanamem's Phase II AD trial would cause a significant increase in the value of the stock. We also believe that positive results from Xanamem's Phase II DCI trial would cause a large increase in valuation, although it would not be as significant as the gain from a positive trial in AD.
- The potential patient population for Xanamem should be significant. This is due to the fact that Xanamem could probably be combined with other currently available therapies, along with the fact that the target of inhibiting cortisol should apply to the vast majority of AD patients, while other therapies may be targeting smaller subsets of AD.
- Top line results are expected in 4Q18. In the interim, we believe that publications supporting the cortisol/AD hypothesis and the impact that Xanamem can have on inhibiting cortisol in the brain could provide positive catalysts for improvements in share price. Two presentations, *"Xanamem™ a novel 11β–HSD1 inhibitor with potential to provide durable symptomatic and disease modifying benefits in Alzheimer's disease"* and *"Plasma cortisol, amyloid-β and cognitive decline in preclinical Alzheimer's disease"* will be presented at the Alzheimer's Association International Conference (AAIC) which takes place from July 22nd-July 28th. Additional presentations are expected to be presented over the next 6 months.
- Our probability of Xanamem successfully getting through phase III trials for AD and DCI is 5% and 15%, respectively. The 5% success rate for AD is above the less than 0.4% success rate seen since 2002; this is due to advances in testing, patient screening, and the focus on early stage Alzheimer's patients.

- If Xanamem shows any disease modifying effects, we would expect any licensing deals earned to go up in value.
- 11β-HSD1 is a known target for both AD and DCI. If Xanamem is delivering larger concentrations to the brain as compared to previous 11β-HSD1 inhibitors, Xanamem may show superior efficacy as compared to other 11β-HSD1 inhibitors. Further, the focus on earlier stage mild AD patients could increase the probability of positive efficacy.
- As a small molecule drug, Xanamem is not expensive to make. This will make it more economic and make it more likely than Xanamem is reimbursed by insurance companies.
- Xanamem is easy to take (orally), which increases its marketability.
- If positive Phase II results occur, we expect the Company to partner its drug or sell it outright. We would expect the deal to be lucrative and believe that multiple partners would be vying to license/purchase the drug.

Risks

There is no guarantee that the Company's clinical trials for mild AD or DCI will show statistically significant efficacy. There is no guarantee that the Company will achieve its primary endpoints in its upcoming clinical trials. However, the Company has shown promising early data in Phase I trials and preclinical data, including showing improved blood brain barrier penetration and possible evidence of AD disease reversal in mouse models.

ACW's future capital needs are uncertain. While near-term capital needs are fairly certain, longer-term capital needs are uncertain, and will be driven by such factors as clinical trial results, clinical trial design, potential partnering with other pharma or biotech companies, and initiating clinical trials in new diseases. Depending on how multiple factors occur, the Company's capital raise needs could change significantly.

There is no guarantee that Xanamem will continue to show strong safety data. There is no guarantee that Xanamem will continue to show strong safety data. Results to date have indicated that the Company's drugs are safe, including at the highest tested doses (35 mg twice per day).

It is likely that the future commercial potential of Xanamem will depend heavily on future partnership agreements. We are currently modeling for ACW to partner their drugs following Phase II trials. Future potential cash flows from ACW's drugs will depend heavily on the company or companies that ACW partners with. This decision will likely impact Phase III trial designs, milestones/royalties received, and where and how effectively their drugs are marketed if approved for commercial use.

MCI-AD	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
MCI-AD Patients - U.S.	4,700,000	4,747,000	4,889,410	5,036,092	5,187,175	5,342,790	5,503,074	5,668,166	5,838,211	6,013,358	6,193,758	6,379,571	6,570,958	6,768,087	6,971,130	7,180,263
MCI-AD Patients - RoW	7,480,000	7,554,800	7,630,348	7,706,651	7,783,718	7,861,555	7,940,171	8,019,572	8,099,768	8,180,766	8,262,573	8,345,199	8,428,651	8,512,938	8,598,067	8,684,048
Price of Xanamem per patient	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000
Penetration Rate - U.S.	0%	0%	0%	0%	0%	0%	0%	0%	0%	2%	4%	6%	7%	8%	8%	8%
Penetration Rate - RoW										1%	1%	2%	2%	2%	2%	2%
Total Sales	0	0	0	0	0	0	0	0	0	967,025,884	1,982,256,403	3,047,713,510	3,644,810,816	4,270,234,255	4,377,910,232	4,488,612,178
Royalty Rate										10%	10%	10%	10%	10%	10%	10%
Royalty Revenue	0%	0%	0%	0%	0%	0%	0	0	0	96,702,588	198,225,640	304,771,351	364,481,082	427,023,425	437,791,023	448,861,218
License Fee (assuming successful phase 2 trial)				350,000,000												
Milestone Payment (assuming successful phase 3 trial)								600,000,000								
Milestone Payment (assuming successful NDA)									200,000,000							

Discount Rate		15%
NPV (License Payment)		US$304.3M
Prob of Success (License Payment)	25%	**US$76.1M**
NPV (Milestone Payment & Royalties)		US$597.8M
Prob of Success (Milestone Payment & Royalties)	5%	**US$29.9M**
Combined NPV		**US$106.0M**

DCI	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
DCI Patients - U.S.	1,018,500	1,049,055	1,080,527	1,112,942	1,146,331	1,180,721	1,216,142	1,252,627	1,290,205	1,328,911	1,368,779	1,409,842	1,452,137	1,495,702	1,540,573	1,586,790
DCI Patients - RoW	2,750,000	2,832,500	2,917,475	3,004,999	3,095,149	3,188,004	3,283,644	3,382,153	3,483,618	3,588,126	3,695,770	3,806,643	3,920,842	4,038,468	4,159,622	4,284,410
Price of Xanamem per patient	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000	6,000
Penetration Rate - U.S.	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	5%	8%	9%	9%
Penetration Rate - RoW												0%	1%	1%	1%	1%
Total Sales	0	0	0	0	0	0	0	0	0	0	0	0	612,079,149	1,008,706,437	1,168,838,584	1,203,903,742
Royalty Rate												8%	8%	8%	8%	8%
Royalty Revenue	0%	0%	0%	0%	0%	0%	0	0	0	0	0	0	48,966,332	80,696,515	93,507,087	96,312,299
License Fee (assuming successful phase 2 trial)							50,000,000									
Milestone Payment (assuming successful phase 3 trial)											100,000,000					
Milestone Payment (assuming successful NDA)												35,000,000				

Discount Rate		15%
NPV (License Payment)		US$43.5M
Prob of Success (License Payment)	35%	**US$15.2M**
NPV (Milestone Payment & Royalties)		US$69.2M
Prob of Success (Milestone Payment & Royalties)	15%	**US$10.4M**
Combined NPV		**US$25.6M**

Combined NPV	A$176.3M
Net Debt	-A$9.2M
Cash from options/warrants	A$1.1M
Fully Diluted Shares Outstanding (includes additional shares to represent potential future equity raises)	696.4M
Price Per Share	**A$0.27**

Additional Information

Auditor: Ernst & Young
Legal: GTP Legal

Company Information
Company Website

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