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ProMIS Neurosciences Inc (PMN – TSE)

Untangling the β-Amyloid Oligomers

Based on our DCF model and a 15% discount rate, PMN is valued at approximately $7.00 per share. We apply a 7% probability of eventual sales of portfolio products in global markets.

Current Price (6/26/18)	$0.40
Valuation	**$7.00**

INITIATION

ProMIS is developing a portfolio of monoclonal antibodies to address AD, ALS and PD. The company's lead candidate, PMN310, is able to selectively target toxic oligomers which are thought to be the cause of neuron death in AD. Two proprietary, data-intensive algorithms are used to identify targets on misfolded proteins called ProMIS and Collective Coordinates which allow for precise and time saving target identification.

ProMIS anticipates launching its first in-human trial in 2019 following additional validation of lead candidate, PMN310. The indication has a target population of over 10 million patients in the US and over 40 million ex-US with dramatic expected increases over the next decades. There is no existing treatment therapy available, providing a strong case for pricing and penetration if the drug is approved.

With several other mAbs having navigated phased trials, there is a precedent for trial design, size and duration. Previous trial failures and additional research have narrowed down the optimal drug design and proper target. While still in early stage development, PMN310 makes a compelling case for success and should hold a dominant position in the market if trials are successful and regulatory approval is granted.

SUMMARY DATA

52-Week High	**$0.73**
52-Week Low	**$0.18**
One-Year Return (%)	**33**
Beta	**-4.00**
Average Daily Volume (sh)	**221,656**
Shares Outstanding (mil)	**246**
Market Capitalization ($mil)	**$98.3**
Short Interest Ratio (days)	**1.19**
Institutional Ownership (%)	**N/A**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2018 Estimate	**N/A**
P/E using 2019 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(in millions of $CAD)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	$0.0 A	$0.0 A	$0.0 A	$0.0 A	$0.0 A
2018	$0.0 A	$0.0 E	$0.0 E	$0.0 E	$0.0 E
2019					$0.0 E
2020					$0.0 E

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	-$0.01 A	-$0.01A	-$0.01 A	-$0.01 A	-$0.03 A
2018	-$0.01 A	-$0.01 E	-$0.01 E	-$0.01 E	-$0.03 E
2019					-$0.06 E
2020					-$0.06 E

INITIATING COVERAGE

We are initiating coverage of ProMIS Neurosciences Inc. (TSE: PMN) with a $7.00[1] price target based on our forecast for product sales after a 2027 launch of its lead candidate PMN310 in the United States, EU and rest of world. The company is developing a monoclonal antibody (mAb) that targets epitopes specific to toxic oligomers implicated in the development of Alzheimer's Disease (AD). The company's lead candidate is currently in pre-clinical development and is expected to begin Phase I trials in 2019. In recent years there have been numerous failures in the AD space and no drug or biologic has ever been approved as a cure for the disease. Despite the poor success rate, much has been learned in the last decades from unsuccessful trials and adjacent research work. Efforts have narrowed down the target to amyloid-beta (Aβ), which comes in several forms. Consensus has built in recent years focusing on the toxic oligomers as the cause of AD, which are small clumps of monomers that accumulate in the brain and kill neurons. ProMIS' PMN310 is able to exclusively target this form of Aβ and is built on a peptide backbone that avoids common side effects.

ProMIS' targeted monoclonal antibodies are built on two proprietary discovery platforms called ProMIS and Collective Coordinates. These algorithms employ protein thermodynamics to predict disease specific epitopes on the surface of misfolded proteins. These computational discovery platforms can be used to address a variety of neurodegenerative diseases including AD, amyotrophic lateral sclerosis (ALS), Parkinson's Disease (PD) and others. The company's current focus is on PMN310, one of a family of mAbs that targets toxic Aβ oligomers.

On March 31, 2018, ProMIS held approximately $1.7 million in cash on its balance sheet and subsequent to the quarter close raised an additional $7.2 million gross proceeds. Current cash levels are expected to support operations until 2H:19. Equity issuances have provided capital over the last several years to support operational expenses; an approach we anticipate will continue in the future. Our forecasts call for ProMIS to consume approximately $8 million in 2018 as manufacturing activities are stepped up in the latter part of the year. The company also has other candidates in development; however, we believe that these efforts will only receive a minimum of management time and corporate funds.

Based on our forecasts which include Phase I, II and III clinical trials and a review period for regulatory agencies, we anticipate a launch of PMN310 in 2027, although there may be opportunities for expedited development. The field of AD drug development programs has thinned over time leaving only a few left standing. We believe that much has been learned from these failures and that ProMIS is targeting the underlying cause of AD with its PMN310 candidate. While success is not guaranteed, we are optimistic on the biologic's chances and adjust our valuation to reflect historical success probabilities. Given the immense market that can be tapped with a successful candidate in the AD space, we anticipate that ProMIS will partner with a global pharmacetical company during or after Phase II results and will also require a global partner to commercialize the drug. There are few competitors with convincing AD therapies in development which should provide a strong negotiating position for the company. In addition to a portfolio of candidates for neurodegenerative diseases, ProMIS has a unique platform that is able to identify unique epitopes on misfolded proteins that is applicable to a broad spectrum of neurodegenerative and other conditions such as ALS and Parkinson's Disease. We initiate on the shares of ProMIS with a target price of $7.00.

INVESTMENT THESIS

ProMIS has the benefit of access to a long history of research and competitor failures to direct its focus on what works. Combining discoveries from those who have come before with a proprietary algorithm that is able to predict the therapeutic targets in neurodegenerative diseases places ProMIS in an advantageous position to construct a precise molecule that can address the underlying cause. Regrettably, the failure rate has been high for AD drugs, and it appears that in the last few quarters, the rate has only accelerated with Merck's verubecestat, vTv's azeliragon and Lilly's lanabecestat among others announcing Phase III disappointments so far this year. Despite setbacks for trials that were initiated years ago, research and diagnostics have advanced to a point where the proper target has become more clear. Scientists' work has also found ways to avoid negative side effects observed in earlier trials, and we are now in a position to have a higher degree of confidence of both the target and the safety and efficacy of the drug.

[1] Price targets and financial statements are denominated in Canadian Dollars

The FDA has recognized the poor success rate for AD drugs and is making a change to its guidance for endpoints recommended to obtain regulatory approval. In the past, improvement in both cognitive and functional criteria were required; however, the agency now believes that a single endpoint is sufficient. They also have recognized the importance of biomarkers for identifying improvement for early stage AD patients.

Key reasons to own ProMIS' shares:

- **Pursuing Large End Market**
  - **Near 6 Million with AD in US**
  - **Over 30 Million with AD Worldwide**
  - **Larger Addressible Market for Earlier Stage Disease**
  - **Number Afflicted Expected to Triple by 2050**
- **No Approved Therapies and Few in Development**
- **New FDA Guidance Supportive of Approval**
  - **Single Endpoint Sufficient**
  - **Surrogate Endpoints Allowed**
  - **Expedited Approval Possible**
- **Candidates Can Uniquely Bind to Toxic AβO**
- **Able to Develop Candidates for Other Neurodegenerative Diseases**
  - **ALS and Parkinson's Disease**
- **Strong IP Protection Around Target Acquisition and mAb Epitopes**

In support of our thesis, we provide a review of AD, its symptoms, diagnosis and current treatment. There have been many Aβ focused monoclonal antibodies in advanced trials that failed to achieve success. We believe that one of the reasons previous drugs have failed is that the clinical programs have ignored the large body of evidence pointing to toxic low molecular weight Aβ oligomers as the source of neuron death. However, much has been learned since these trials were initiated and the pathway cleared by the current frontrunner, Biogen's aducanumab, is a vanguard for PMN310 to follow. Aducanumab's clinical trials and strong and weak points will be discussed. We will review ProMIS' pipeline, proprietary algorithms and how PMN310 is able to address the underlying cause of AD and why the compound should have an improved efficacy and side effect profile compared to others. A separate section reviews the company's anticiapted clinical trial pathway and intellectual property position. In recognition of the importance of the disease and the high rate of failure, the FDA has evolved its stance on trial design which we review in depth. The report will also mention the major participants that have recently made efforts in developing AD candidates. We conclude our report with a review of market size and walk the reader through the assumptions used in the valuation process to generate our target price.

Disease

Alzheimer's Disease

Alzheimer's Disease is a neurodegenerative condition which affects 5.7 million Americans and over 30 million people worldwide.[2] Due to the faster growth of the older population and the higher prevalence of Alzheimer's in those over 65, these numbers are expected to almost double and triple by 2030 and 2050 respectively. AD is also distinguished in that it is the only major disease where deaths have increased over the last decades. Between 2000 and 2013, a report from the Alzheimer's Association found that deaths resulting from stroke, heart disease, and prostate cancer decreased 23%, 14%, and 11%, respectively, while Alzheimer's deaths increased 71%.

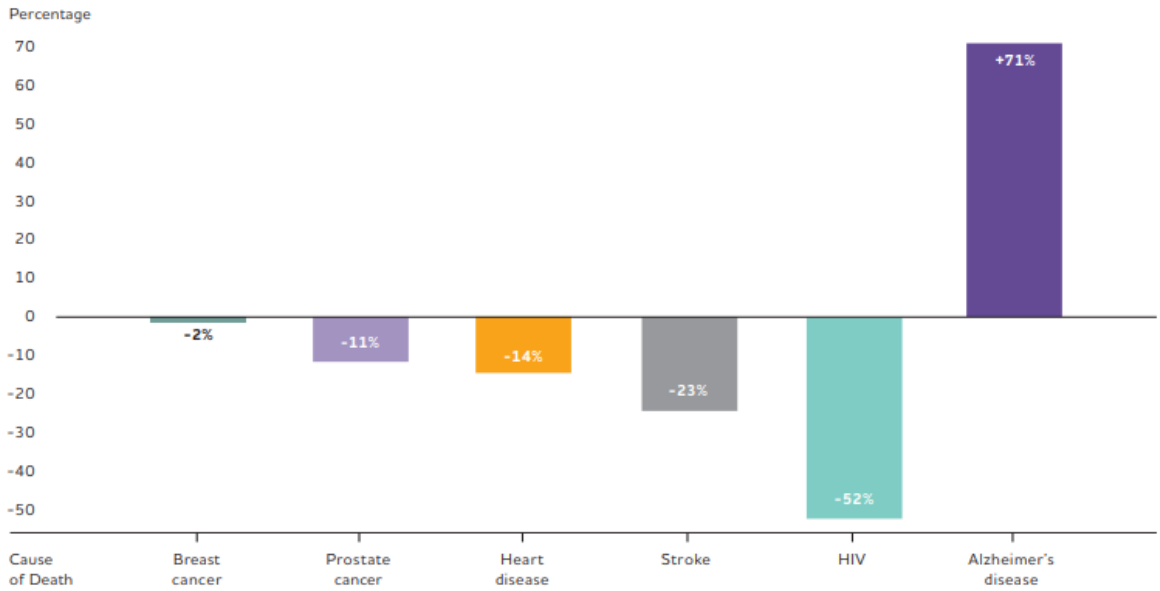
AD is named after Alois Alzheimer who made the first clinical observations of a woman with the disease between the years of 1901 to 1906. He noted that the 50-year old patient experienced memory loss, paranoia and psychological changes. After the patient's death, an autopsy was performed which found shrinkage in and around nerve cells and abnormal deposits that were later identified as Aβ plaques and neurofibrillary tangles.

According to the CDC[3] AD is the 6th leading cause of death in the United States, after stroke and before diabetes. While there are almost 6 million individuals in the US diagnosed with AD, there are many more who are in earlier stages of the disease called mild cognitive impairment (MCI). MCI is seen as a precursor to AD and is measurable by a change in thinking abilities. A person with MCI can carry on normal everyday tasks, but does show some signs of impairment in sensitive testing.

More women than men suffer from AD. According to data cited in the 2016 Alzheimer's Association report, 16% of women and 11% of men 71 and older have the disease. Research is not conclusive on why this difference exists and some attribute it to longer life spans while others have suggested biological or genetic variations. Along racial lines, African-Americans and Hispanics are more likely to suffer from dementia. Research has attributed health, lifestyle and socioeconomic elements as well as higher prevalence of associated health conditions such as cardiovascular disease to the difference.

Deaths from AD are underreported due to other conditions being cited on death certificates. Dementia can cause problems with mobility, nutrition and self care that can lead to pneumonia, which is frequently cited as the main reason. AD is unique among the most common forms of death in the older population in its increasing prevalence. While improvements in health care have led to decreases in the rate of cancer, heart disease and stroke death, AD has increased substantially. This only highlights the need to make progress in this difficult therapeutic area.

Exhibit I – Percent Change in Selected Causes of Death (All Age): 2000 – 2013[4]



[2] WHO Dementia Fact Sheet. December 2017. 60% to 70% of the 50 million people who have dementia have Alzheimer's. http://www.who.int/mediacentre/factsheets/fs362/en/
[3] Center for Disease Control Age Adjusted Death Rates 2016 https://www.cdc.gov/nchs/products/databriefs/db293.htm
[4] National Center for Health Statistics.

The economic burden from Alzheimer's Disease is immense. Some individuals suffer for decades with the disease and require substantial amounts of care either from family members or nursing homes. Statistics from a variety of sources peg the annual cost of care at over $200 billion for unpaid caregivers representing over 18 billion hours of service. Direct cost of care for AD is estimated at $236 billion, with half of this amount absorbed by Medicare.

The estimate of AD prevalence only includes those diagnosed after the onset of symptoms. However, there are many more individuals in the early stages of the disease, and if AD could be detected prior to symptoms developing, the number that would benefit from treatment would be significantly greater.

It is estimated that approximately 15 to 20% of individuals over 65 have MCI, which is approximately 8 to 10 million persons. About a third of this group develop AD within 5 years, a proportion that increases over periods greater than 5 years. While many studies have focused on later stages of the disease, it appears that a preventive approach may be more effective.

AD is usually associated with aging. The first signs of the disease are characterized by a loss in short term memory, followed by a progression to forgetfulness about one's own personal history and relationships. Behavioral changes, confusion about the date and time and becoming lost are other symptoms. In late-stage disease, AD patients cannot speak, total physical care is needed and the body begins to shut down. From the first concrete signs of the disease to death, the progression lasts an average of eight years, however, it can range from two to twenty years, depending on the person and other health conditions.

One of the difficulties with identifying AD is that there are few genetic indicators that allow us to anticipate those predisposed to the disease. Currently, the only way to definitively diagnose AD is with a brain autopsy. In a minority of cases, there are some early indicators of those who may be susceptible. About 1% of the AD population develops the disease as a result of certain genes that overexpress for the amyloid precursor protein (APP), which results in early onset AD. Another group that suffers from AD at a high rate are those 400 thousand Americans with Down Syndrome. This group has an extra copy of chromosome 21, which also codes for the production of APP, leading to Aβ fragments that accumulate into toxic oligomers.

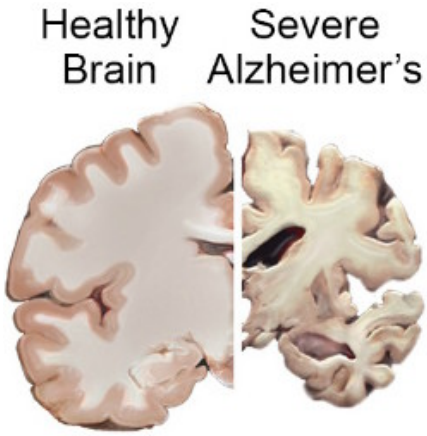
One gene that is closely associated with AD is the apolipoprotein E (APOE) gene on chromosome 19. There are a few forms of APOE, the ε2, ε3 and ε4 alleles. The ε3 allele is the most common and is thought to play a neutral role in the disease, while presence of the ε4 increases the risk of AD and several other diseases including atherosclerosis. Alleles come in pairs, and individuals with both alleles of ε4 are more susceptible to AD than those with one ε4 or no ε4 alleles.[5] It is thought that the ε2 and ε3 forms are more effective at breaking down Aβ than ε4, and the absence of these forms contribute to AD.

The most closely associated risk factor for AD is age. In a minority of cases, early onset Alzheimer's can occur in those under 65, but analysis of data indicates that about 15% of those with AD are in the 65 to 74 age range while 44% are in the 75 to 84 range.[6] Family history is also a predictor, but environmental factors and lifestyle also play a role.

[5] "Although 40-65% of AD patients have at least one copy of the ε4 allele, ApoE4 is not a determinant of the disease - at least a third of patients with AD are ApoE4 negative and some ApoE4 homozygotes never develop the disease. Yet those with two ε4 alleles have up to 20 times the risk of developing AD. There is also evidence that the ApoE2 allele may serve a protective role in AD. Thus, the genotype most at risk for Alzheimer's disease and at an earlier age is ApoE 4,4. Using genotype ApoE 3,3 as a benchmark (with the persons who have this genotype regarded as having a risk level of 1.0), individuals with genotype ApoE4,4 have an odds ratio of 14.9 of developing Alzheimer's disease. Individuals with the ApoE 3,4 genotype face an odds ratio of 3.2, and people with a copy of the 2 allele and the 4 allele (ApoE2,4), have an odds ratio of 2.6. Persons with one copy each of the 2 allele and the 3 allele (ApoE2,3) have an odds ratio of 0.6. Persons with two copies of the 2 allele (ApoE2,2) also have an odds ratio of 0.6." Wikipedia contributors. (2018, May 1). Apolipoprotein E. In *Wikipedia, The Free Encyclopedia*. Retrieved 14:06, May 6, 2018, from https://en.wikipedia.org/w/index.php?title=Apolipoprotein_E&oldid=839158512

[6] 2016 Alzheimer's Disease Facts and Figures. The Alzheimer's Association.

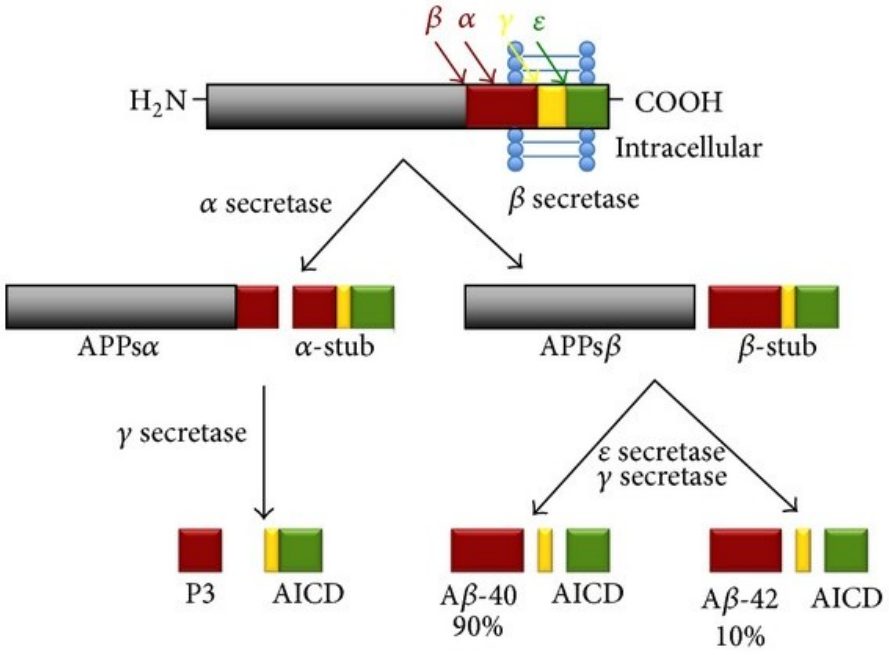
Exhibit II – Normal vs. AD Brain[7]



Formation of Plaques

Autopsies consistenly show the formation of Aβ plaques in the brains of those suffering from AD. The presence of Aβ is a natural occurrence and the body clears it through enzymatic and non-enzymatic pathways. However, in some cases, excessive Aβ is produced and insufficiently cleared, resulting in the buildup of toxic forms of the peptide which damage and destroy neurons. Aβ fragments result from the cleavage of amyloid precursor protein (APP), which is expressed on the surface of cells. Normally, APP is cleaved with the enzyme α-secretase which produces soluble APP and C83. These proteins are disintegrated via normal metabolic processes. In a minority of cases APP is cleaved with β-secretase, which produces soluble APP β, which creates the precondition for γ-secretase to cleave APP again, producing Aβ monomers. These monomers (single strands of Aβ) then combine into oligomers (multiple strands of Aβ) and fibrils (larger masses of Aβ plaque). The exhibit below illustrates how the different α-secretase and β-secretase enzyme cleavage of APP followed by γ- or ε-secretase cleavage can separate the protein strand to produce either harmless peptides or Aβ 40 or 42.

Exhibit III – Cleavage of APP[8]



[7] NIH National Institute on Aging Alzheimer's Disease Fact Sheet. https://www.nia.nih.gov/health/alzheimers-disease-fact-sheet
[8] https://www.researchgate.net/figure/The-processing-of-APP-through-the-beta-site-AbPP-cleaving-enzyme-BACE1-followed-by_fig1_259702028

In the early days of drug development for AD, it was thought that plaques were responsible for causing the disease under the amyloid hypothesis. This theory, which was first proposed in 1991, attributed AD to the accumulation of Aβ in the brain which exists in many forms including monomers, oligomers and fibrils and the first drugs developed focused indiscriminately on this target. However, as research has progressed, there is mounting evidence that plaque is not the problem but rather soluble toxic oligomers[9,10] stand responsible for damaging neurons. ProMIS has shown in its laboratory work that the culprit is a specific low molecular weight array of oligomers, namely dimers, tetramers and dodecamers that are made up of two, four and twelve strands of monomer elements. In contrast to previous positions, some sources have proposed that insoluble fibrillar Aβ is not only non-toxic but may in fact function as a sink for toxic forms of the protein.

Soluble Toxic Aβ Oligomers

There is a large body[11,12,13,14,15,16,17,18,19] of research showing that the presence of amyloid beta oligomers (AβOs) is associated with memory impairment and cognitive deficits. Other research has emerged debunking the relationship between monomers and plaques and AD[20,21,22]. This refinement of the amyloid hypothesis has enabled researchers to focus more precisely on the elements that are responsible for AD. AβOs have been implicated in impaired synaptic plasticity, loss of memory function, synapse elimination and nerve cell death. During the earlier days of AD research, the focus was predominantly on senile plaques due to their prevalence in AD brains. However, researchers began to notice that plaque burden was not associated with the intensity of the disease and that neuronal death occurred in brain regions with no plaques. Later research showed that plaques were also present in healthy brains. This realization combined with research narrowing the focus to oligomers has prompted alert scientists to target their efforts towards AβOs. Early data from the aducanumab trial is supportive of this as the drug binds to AβOs and fibrillary amyloid β, but not Aβ monomers. The study has provided evidence of slowing cognitive deterioration.[23]

Published data supports an inverse correlation between the size of the AβO aggregates and their toxicity. For some time researchers found little correlation between the presence of Aβ aggregates and neuronal damage. This realization shifted the focus of research down the size scale to small soluble oligomers of Aβs. Subsequent work suggested that the degree of toxicity of the AβOs were dependent on the size, aggregation state and diffusion of the complex. Tests provided evidence that neurotoxic activity increased for dimers, trimers and tetramers relative to monomers and fibrils.[24] Research found that the relative rarity of higher order oligomers made it difficult to determine their toxicity; however, due to their low incidence, they may not be a worthwhile target. We include an exhibit below which reconciles the findings of this research illustrating a fluctuating level of toxicity as the size of aggregates increases. Overall, the trend from trimers and tetramers to 24 to 34-mers to fibrils is generally one of lower toxicity, demonstrating less harm as structure size increases.

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[9] Zhao, Li; et al. The Toxicity of Amyloid β Oligomers. Int J Mol Sci. 2012; 13(6): 7303–7327. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3397527/

[10] https://alzres.biomedcentral.com/articles/10.1186/alzrt226

[11] Haass, Christian, Selkoe, Dennis. Soluble protein oligomers in neurodegeneration: lessons from the Alzheimer's amyloid β-peptide. Molecular Cell Biology, February 2007. http://pages.ucsd.edu/~mboyle/COGS163/pdf-files/soluble%20protein%20oligomers%20in%20neurodegeneration-lessons%20from%20the%20alzheimers%20amyloid%20b-peptide-2007.pdf

[12] Verma, Meenakshi; et al. Toxic species in amyloid disorders: Oligomers or mature fibrils. Ann Indian Acad Neurol. 2015 Apr-Jun; 18(2): 138–145. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4445186/

[13] Sengupta, Urmi; et al. The Role of Amyloid-β Oligomers in Toxicity, Propagation, and Immunotherapy. EBioMedicine. 2016 Apr; 6: 42–49.

[14] Jacobsen, JS; et al. Early-onset behavioral and synaptic deficits in a mouse model of Alzheimer's disease. (2006) PNAS 103: 5161-5166

[15] DiChiara, T; et al. Alzheimer's Toxic Amyloid Beta Oligomers: Unwelcome Visitors to the Na/K ATPase alpha3 Docking Station. Yale J Biol Med. 2017 Mar 29;90(1):45-61. eCollection 2017 Mar.

[16] Benilova, Iryna; et al. The toxic Aβ oligomer and Alzheimer's disease: an emperor in need of clothes Nature Neuroscience volume 15, pages 349–357 (2012) doi:10.1038/nn.3028

[17] Sakono, Masafumi; Tamotsu Zako. Amyloid oligomers: formation and toxicity of Aβ oligomers. December 2009; The FEBS Journal. https://febs.onlinelibrary.wiley.com/doi/pdf/10.1111/j.1742-4658.2010.07568.x

[18] Ferreira, Sergio; et al. Soluble Protein Oligomers as Emerging Toxins in Alzheimer's and Other Amyloid Diseases. B Life, 59(4 – 5): 332 – 345, April –May 2007

[19] Kayed, R, Lasagna-Reeves, CA; Molecular Mechanisms of Amyloid Oligomers Toxicity. J Alzheimers Dis. 2013;33 Suppl 1:S67-78. doi: 10.3233/JAD-2012-129001.

[20] Murphy, Paul, LeVine, Harry. Alzheimer's Disease and the β-Amyloid Peptide. J Alzheimers Dis. 2010 Jan; 19(1): 311. doi: 10.3233/JAD-2010-1221. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2813509/

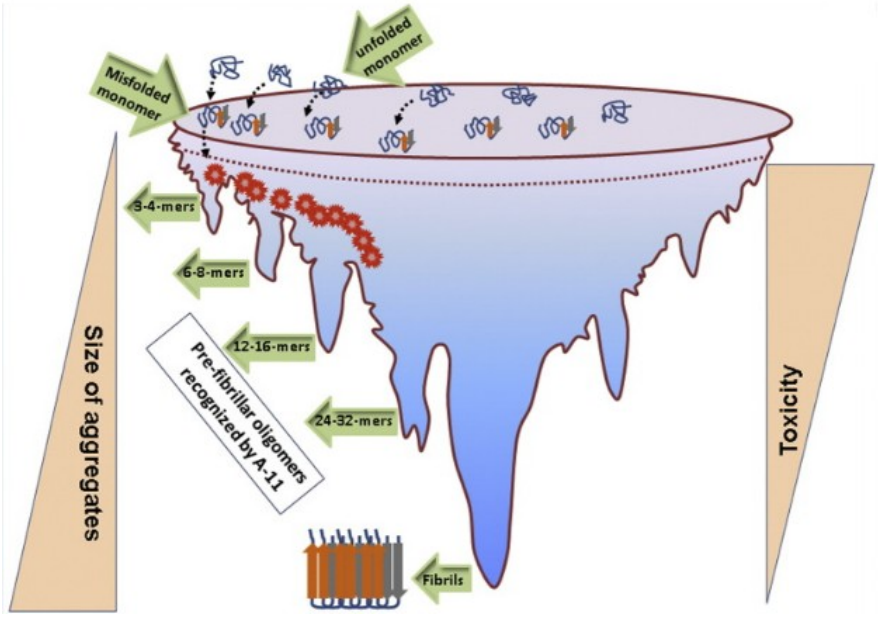
[21] Hyman, BT; et al. The lack of accumulation of senile plaques or amyloid burden in Alzheimer's disease suggests a dynamic balance between amyloid deposition and resolution. J Neuropathol Exp Neurol. 1993 Nov;52(6):594-600. https://www.ncbi.nlm.nih.gov/pubmed/8229078

[22] Giuffrida, ML; et al. The monomer state of beta-amyloid: where the Alzheimer's disease protein meets physiology. Rev Neurosci. 2010;21(2):83-93.

[23] DiChiara, T; et al. Alzheimer's Toxic Amyloid Beta Oligomers: Unwelcome Visitors to the Na/K ATPase alpha3 Docking Station. Yale J Biol Med. 2017 Mar 29;90(1):45-61. eCollection 2017 Mar.

[24] Ono, Kenjiro, et al. Structure–neurotoxicity relationships of amyloid β-protein oligomers. Proc Natl Acad Sci U S A. 2009 Sep 1; 106(35): 14745–14750.

Exhibit IV – Size of βA Aggregates vs. Toxicity[25]



Several mechanisms have been theorized for the cause of AβO toxicity. The causes stem from disruption of the neuronal membrane, calcium homeostasis dysregulation, and interaction with multiple surface receptors.[26] Aβ monomers are released as a product of APP cleavage, which then can form into oligomers. The oligomers attach to cellular prion protein (PrP^C) which mediates cellular dysfunction. The oligomers may also form a pore on the membrane of the neuron allowing the flow of calcium ions to mix with the cytosol, which also causes dysfunction. Binding of the Aβ oligomer also takes place with the NMDA receptor, the insulin receptor and the frizzled[27] receptor which each have negative impacts on cellular viability. Other mechanisms of cell death have also been postulated, such as the inhibition of the neuron's proteasome function by an endocytosed oligomer, which also causes cell death.[28]

Diagnosis

Alzheimer's Disease is currently only diagnosed with certainty by brain autopsy, which includes a microscopic examination of brain tissue identifying the characteristic plaques and neurofibrillary tangles. However, there are a number of other methods used that provide evidence of the disease prior to death. PET scans, Aβ concentration in cerebrospinal fluid (CSF), as well as cognitive and functional tests are used to render a diagnosis. A patient's individual background, along with familial history and behavioral observations are also used to conclude a cause. Memory testing is employed to determine if the disease is at an early, middle or late stage. Some examples of neuropsychological tests are the mini-mental state examination (MMSE), clinical dementia rating sum of boxes (CDR-SB), the mini-cog test and tests for depression, as this is usually contemporary with AD.

Treatment

The current treatment paradigm for AD does not provide a cure or even stop the progression of the disease; however, there are medicines available that will treat its symptoms. Currently there are five approved medications available. Three of them are in the cholinesterase inhibitor class, one is a N-methyl-D-aspartate (NMDA) receptor antagonist and the last is a combination drug of the two classes. Cholinesterase inhibitors treat symptoms related to memory, language, judgment and thought processes and they work by increasing levels of acetylcholine, a chemical that facilitates neurons communication. The NMDA receptor antagonist is called memantine which helps a patient improve memory, attention, reason, language and ability to perform simple tasks. The drug works by

[25] Verma, Meenakshi; et al. Toxic species in amyloid disorders: Oligomers or mature fibrils. Ann Indian Acad Neurol. 2015 Apr-Jun; 18(2): 138–145. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4445186/
[26] Some of the receptors include: Receptor for advanced glycation end products (RAGE) – which are associated with activation of pro-inflammatory pathways, apolipoprotein E (APOE) – which modulate amyloid beta production and cellular uptake, NGF, NMDA, Insulin, Frizzled, PrP^c among others.
[27] Really? A frizzled what? https://en.wikipedia.org/wiki/Frizzled
[28] Sakono, Masafumi; Tamotsu Zako. Amyloid oligomers: formation and toxicity of Aβ oligomers. December 2009; The FEBS Journal. https://febs.onlinelibrary.wiley.com/doi/pdf/10.1111/j.1742-4658.2010.07568.x

regulating glutamate, a chemical involved in information processing, storage and retrieval. The most recent approval in this group was Namazric in 2014, which is a combination therapy using both a cholinesterase inhibitor and memantine. Below we summarize the approved treatments for AD.

Exhibit V – Current AD FDA Approved Treatment

Generic Name	Brand Name	Class	Approved
donepezil	Aricept	Cholinesterase inhibitors	1996
galantamine	Razadyne	Cholinesterase inhibitors	2001
memantine	Namenda	NMDA (N-methyl-D-aspartate) receptor antagonist	2003
rivastigmine	Exelon	Cholinesterase inhibitors	2000
donepezil and memantine	Namzaric	Combination	2014

In Development

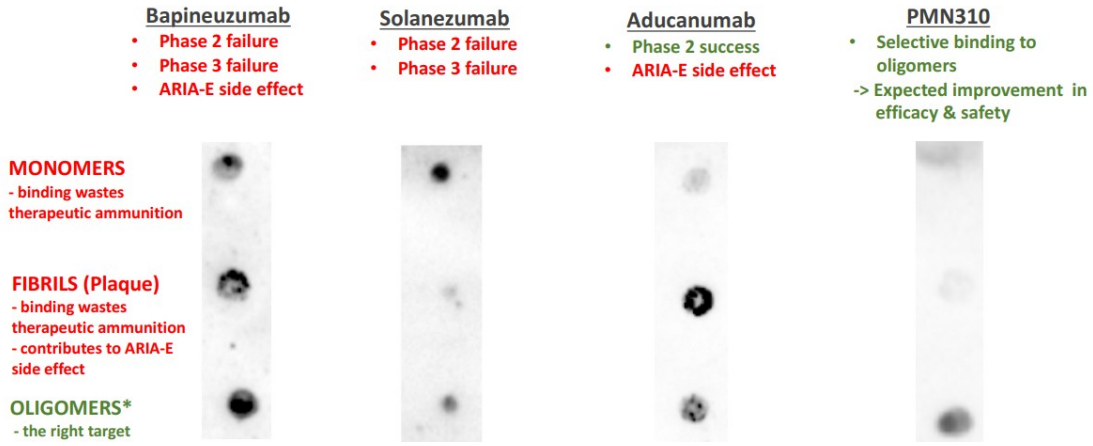
The last several years have been distinguished by the high number of failures announced for development stage Alzheimer's treatments. As of early 2017, there were 105 agents in phased trials for AD[29]. This includes recent defeats which seem to have accelerated in the first half of 2018. In the year to date we have seen disappointments from Eli Lilly's solanezumab and lanabecestat, Merck's verubecestat, vTv's azeliragon and the closure of Pfizer's neuroscience division. Looking back a little further, we show the unsuccessful trials in the pursuit of an AD cure over the 1998 to 2014 period below.

Exhibit VI – High Failure Rate For AD Drugs[30]

While the failures have been disappointing, the results have lead to greater understanding of the structure of an effective drug and the trial design necessary to support statistical significance. One candidate which has displayed efficacy in early stage trials and also targets toxic oligomers is Biogen's aducanumab. While it is not uniquely specific to the low molecular weight oligomers that appear to be the cause of neurotoxicity, it does bind to them. In the following exhibit, we provide a representation of *in vitro* work performed by ProMIS in a "dot blot" test which shows the binding affinity of the listed monoclonal antibody to the forms of Aβ. The darker the dot, the greater the affinity between the drug and the form of Aβ.

[29] Cummings, Jeffrey, et al. Alzheimer's disease drug development pipeline: 2017. Alzheimer's & Dementia: Translational Research & Clinical Interventions 3 (2017) 367-384. https://www.trci.alzdem.com/article/S2352-8737(17)30037-9/fulltext
[30] Graphic: Alan Smith. Source: PhRMA analysis of Adis R&D Insight Database, June 17, 2015.

Exhibit VII – Comparison of Binding Affinities Among Selected mAbs and Aβ Forms[31]



The interpretation of the "dot blot" exhibit provides the rationale why bapineuzumab and solanezumab failed. In the former, the drug bound to all forms of Aβ; since the concentration of monomers and fibrils is 100 to 1000 times that of oligomers, the drug was drawn away by these irrelevant targets. In the latter, the drug only had a very weak affinity to oligomers, but a much higher level of attraction to monomers making it likely that the dose was saturated by monomers.[32] Once again, the wrong target. Aducanumab was doing somewhat better targeting both fibrils and toxic oligomers which provides the rationale behind the biologic's Phase Ib efficacy.

A common side effect for many of the in-development monoclonal antibody candidates include edema, or swelling, of the brain. This condition is known as amyloid-related imaging abnormalities (ARIA) which is associated with inflammation, microhemorrhages and cerebral edema. Two factors contribute to this side effect including the use of the IgG1 isotope as the backbone of the antibody and the binding of the mAb to plaque at higher doses.

Aducanumab

Aducanumab was originally developed by Neurimmune, who later granted Biogen the license for further development in 2007. It is currently in Phase III trials which began in 2015 examining cognitive and functional decline in patients with MCI. Topline results are expected in 2020 representing a targeted 2,700 enrollees in two parallel studies. Aducanumab preferentially binds to aggregated Aβ and targets an epitope that usually doesn't appear on the Aβ monomer, aiding its specificity. Readouts from earlier trials continue to support this hypothesis. The Phase Ib PRIME study showed dose-dependent amyloid removal by up to 70 centiloids,[33] and provided evidence of slowing cognitive decline as per exploratory analysis. There is reason for optimism based on the data provided so far; however, side effects do occur at higher doses of the drug. ARIAs were identified in Phase I work and PRIME data suggested that these abnormalities could be addressed with a specific dose titration schedule. While aducanumab has presented the best evidence of efficacy to date, ProMIS believes that PMN310 can address two of the shortcomings of aducanumab. PMN310 exclusively targets only low molecular weight toxic oligomers and its use of an IgG4 isotype should allow for higher dosing and evasion of ARIA-E.

PMN AD mAbs

The approach for treating AD a decade ago focused on clearing amyloid plaques from the brain under the amyloid hypothesis.[34] The amyloid hypothesis attributes AD to the accumulation of Aβ deposits in the brain and is generally accepted by the scientific community. While targeting Aβ appears to be a straightforward objective, increased understanding of how Aβ is associated with AD has led to an improved approach. One of the reasons for the complexity is that there are multiple types of Aβ, and low molecular weight toxic AβOs are materializing as the culprit in the attack on neurons.

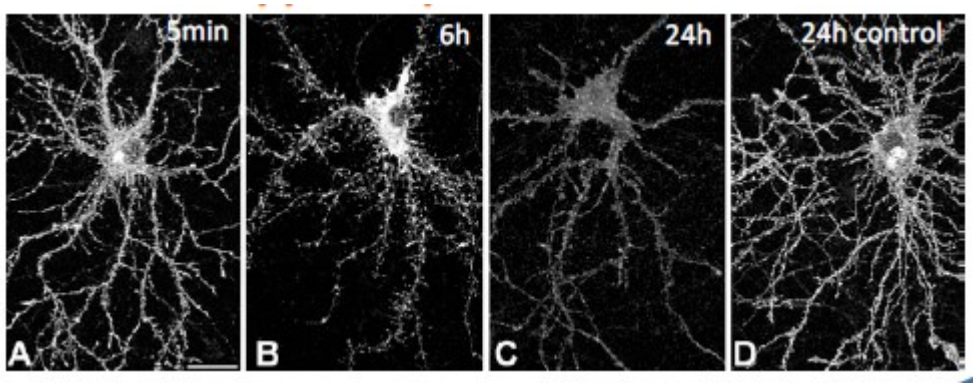
ProMIS has differentiated itself from other biotechnology development companies in its discovery platforms which use complex algorithms to model misfolded proteins. The computer simulated modeling it uses in its proprietary

[31] March 2018 Corporate Presentation
[32] Goure, WF; et al. Targeting the proper amyloid-beta neuronal toxins: a path forward for Alzheimer's disease immunotherapeutics. Alzheimers Res Ther. 2014 Jul 9;6(4):42. doi: 10.1186/alzrt272. eCollection 2014.
[33] A centiloid is a unit of measure on a unified scale for all amyloid-β imaging tracers used in positron emission tomography (PET).
[34] There are two other hypotheses called the presenilin inhibition hypothesis and the double hit hypothesis

ProMIS and Collective Coordinates software is able to identify likely epitopes which express themselves on the surface of these misfolded proteins and also eliminate from consideration other epitopes that appear on non-target molecules. The algorithm is able to detect unique signatures that are particular to misfolded toxic oligomers but do not appear on monomers or fibrils. This specificity allows PMN310 to avoid target distraction and not waste drug on useless classes of Aβ.

A substantial body of evidence has shown that it is the toxic oligomers that are responsible for neuron death. ProMIS conducted *in vitro* work examining the synaptotoxicity of human Aβ oligomers on hippocampal neurons and found that proximity of AβO caused neuron death within 24 hours. Below, in panel C, the death of the neuron is evident 24 hours following exposure to AβO.

Exhibit VIII – Effect of AβO on Hippocampal Neurons[35]



Through its use of its discovery platforms, ProMIS and Collective Coordinates, ProMIS Neurosciences has identified six epitopes that are uniquely expressed on toxic oligomers. After testing the epitopes by introducing them in a murine model to generate antibodies, they are then humanized. A paired monoclonal antibody can be manufactured that will target the epitope and mark it to be neutralized. The epitope that has shown the greatest level of success has been PMN310, which will be used to generate antibodies and subsequently humanized for use in the clinic.

With the specificity of the PMN3xx AD antibody candidates to toxic oligomers and their use of the IgG4 backbone, the company expects to avoid ARIA-E, even at high dose levels. PMN3xx is not distracted by monomers or plaques. This allows for a higher proportion of the mAb to bind to the toxic oligomers and as a result, generate higher efficacy.

Preclinical and Clinical Trials

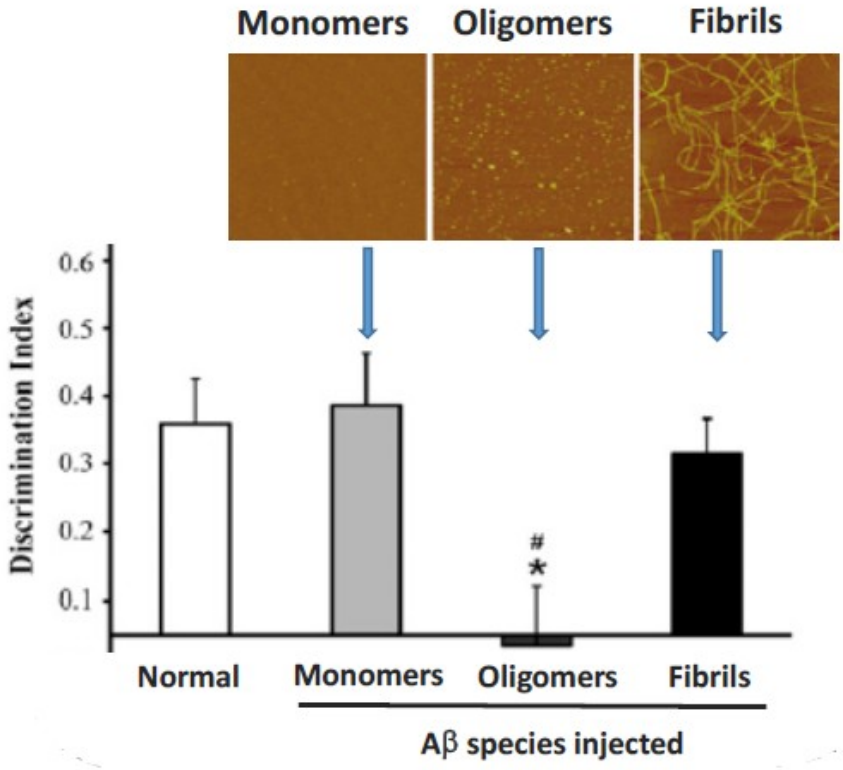
Preclinical *In-vivo*

A substantial amount of preclinical work has been performed to identify the proper target for AD, the unique epitopes that distinguish toxic oligomers and development of the antibodies that will bind to the target.

Work was performed in animal models to measure the impact of different types of Aβ using a discrimination index.[36] This method of measurement exposes a mouse to a object, such as a colored ball or other distinct shape for a period of time. Following the familiarization process, the brains of the test group are injected with Aβ monomers, oligomers and fibrils in parallel with a control group. After a period of time, the animal models are allowed to interact with the object they were previously exposed to and a different novel object. The observers then measure the amount of time spent with each object. Since mice are naturally curious animals, they will spend more time with an object that appears new to them, and less time with a familiar object. In the following exhibit, the results of the study are shown. Time spent with the novel object is significantly greater for the normal, monomer and fibril group. In the oligomer group, the test showed almost no difference in time spent with the two objects, suggesting that the oligomer-exposed mouse did not maintain memory of the initial object.

[35] ProMIS Corporate Presentation, March 2018.
[36] The discrimination index = (time exploring the new object – time exploring familiar object) / total exploration time.

Exhibit IX – Impairment of Recognition Memory[37]

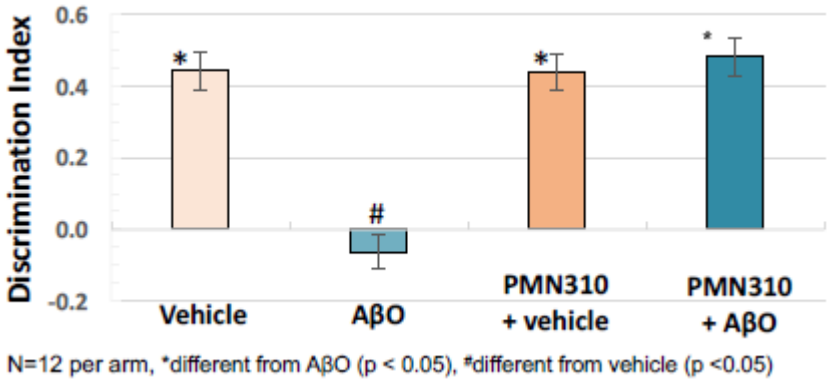


The experiment was performed again, this time examining the effect of PMN310 on the presence of oligomers. *In vitro* work suggested that PMN310 would neutralize the neurotoxic effect of the oligomers and that this could be measured by use of a discrimination index. To test the hypothesis, mice were injected with toxic (prion-like) forms of Aβ and separated into a cohort that is not treated and a cohort that is administered PMN310. A novel object recognition test was administered seven days after injection. Similar to previous *in vivo* work, the test assumes that mice spend more time exploring an object that is new to them than one they have been previously exposed to. In the test arm of this experiment, the animal model treated with PMN310 recognized the familiar object and spent most of its time exploring the new object.

The summary results of the experiment are provided in the following exhibit with measurements along the y-axis representing the discrimination index. The leftmost bar represents the vehicle mouse which was not treated with AβO nor PMN310. This shows the majority of time spent with the new object as one would expect from an animal model with normal memory. The second bar represents the mouse that was injected with AβO, and demonstrates that near equal time was spent exploring each ball, suggesting the mouse did not maintain memory of the first object. The third bar examines PMN310 alone where no impact is expected, yielding a similar result as the vehicle. The fourth bar illustrates the benefit of PMN310 in a mouse with AβO. It is statistically different from the AβO only mouse and similar to the vehicle and vehicle+AβO mouse.

[37] ProMIS Corporate Presentation, March 2018.

Exhibit X – Results of Murine Preclinical Study[38]



N=12 per arm, *different from AβO ($p < 0.05$), #different from vehicle ($p < 0.05$)

IND Preparation

Investigational New Drug (IND) enabling work is being conducted which should be submitted to the FDA in 2019. This is anticipated to be followed shortly after by a humanized PMN310 single ascending dose trial in patients with a clinical diagnosis of mild cognitive impairment. This will be the Phase I trial which is expected to begin enrolling in 2H:19. A read out from the trial should be available in 2020, followed by a Phase II study. If the Phase II is successful, then a Phase III will be launched. Due to the costs of a Phase III trial, and the demand from large pharmaceutical companies for a promising candidate in the AD space, we anticipate that a partner will acquire either the PMN AD mAb portfolio or buy the company outright.

There is no guidance from the company regarding the trial design or duration of the clinical trial work required to submit a successful NDA. However, we believe that Biogen's development process with aducanumab is a good template to follow for ProMIS' trials for PMN310. Much has been learned from this work and the FDA's guidance has been simplified since the aducanumab trial began which is supportive of a faster pathway for new candidates. We also think that there will be immense pressure from stakeholders in all corners to develop a cure, which could streamline the process and advance development.

Phase 1

Biogen conducted two Phase I studies enrolling a total of 250 patients. The first began in June 2011 with 53 enrollees. It was a randomized, blinded, placebo-controlled, single ascending dose study of the safety, tolerability and pharmacokinetics of aducanumab in subjects with mild to moderate AD. Doses started at 0.03 mg/kg and ascended through 7 titrations to 60 mg/kg administered via IV. Primary outcomes examined adverse events and secondary endpoints were centered around pharmacokinetic factors. The study provided sufficient information to justify a Phase Ib study in October 2012.

The second study for aducanumab was a Phase Ib that began in October 2012 and enrolled 197 patients. It was similar to the first Phase I in that it was a randomized, double blinded, placebo-controlled multiple dose study. Patients were prodromal or mild AD. This trial explored adverse events and pharmacokinetic properties. Sufficient data was generated to support a Phase III trial which started almost three years later in August 2015.

Phase 2

Biogen did not perform a Phase II and moved directly to Phase III, due to the strength of their Ib data. We anticipate that a Phase II trial for PMN310 would replace Biogen's Ib, be similar in structure and also include some biomarker endpoints such as Aβ in CSF or other indicator. Phase II trials seek to determine safety, efficacy and an optimal dose. We anticipate a 2020 start to Phase II work for ProMIS. This stage is expected to last two years and enroll in the low hundreds of patients. ProMIS may partner with another pharmaceutical company that will provide funding and expertise to accelerate the process. We note that the FDA has recognized the dire state of AD research and may be open to expedited development of the drug assuming a strong case can be made for safety.

[38] ProMIS Corporate Presentation, March 2018.

Phase 3

Biogen's Phase III aducanumab study consists of two simultaneous and similarly structured trials named ENGAGE and EMERGE that differ only in their trial site locations. ENGAGE and EMERGE are four to five year trials that have an estimated combined enrollment of over 2,700 participants between the ages of 50 and 85. They are multicenter, randomized, double-blind, placebo-controlled and of parallel group design. The primary endpoint is the clinical dementia rating – sum of boxes (CDR-SB)[39] score by week 78. Secondary endpoints are mini-mental state examination (MMSE)[40] score, change from baseline in AD assessment scale and AD cooperative study scales at 78 weeks. The study will continue to follow up with patients for an additional two or three years. The trial is expected to read out in 2020.

Inclusion criteria call for

- A Clinical Dementia Rating (CDR) - Global Score of 0.5.
- Objective evidence of cognitive impairment at screening
- An MMSE score between 24 and 30 (inclusive)
- Must have a positive amyloid Positron Emission Tomography (PET) scan
- Must consent to apolipoprotein E (ApoE) genotyping
- If using drugs to treat AD symptoms, stable doses required for 8 weeks prior to first screening visit
- Must have a reliable informant or caregiver

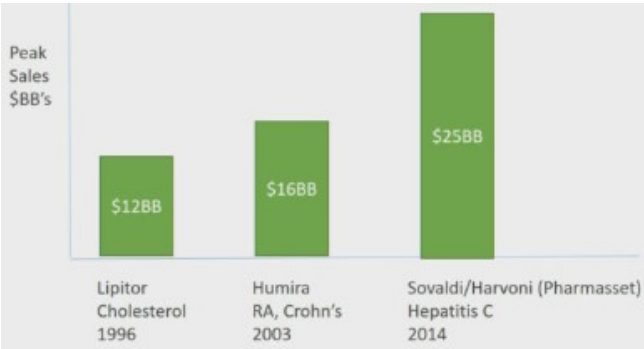
There are also several exclusion criteria that eliminate candidates with other diseases or medical conditions.

The overall time period for the aducanumab in-human clinical trials is about nine years. Phase I was about one year, Phase Ib approximately three years and Phase III about five. We do believe that there are efforts to expedite future clinical trials in this indication given the unmet need for AD, greater understanding of the disease in the last few years and stakeholder commitment to finding a cure.

Company Strategy

ProMIS' strategy is to focus on being best-in-class rather than first-in-class. Looking back, the three largest products in pharma (Lipitor, Humira and Sovaldi/Harvoni) were not the first drugs in their indication, but were rather follow-on products that addressed the weaknesses in predecessors and went on to dominate the class afterwards. The scientists that were responsible for them examined previous compounds to understand how they could be made better, and applied their knowledge to the design of an improved compound. ProMIS has applied this same approach to AD reviewing solanezumab, verubecustat and aducanumab among others. Their process implements this approach through rational drug design and *in silico* models to identify new products that focus on what works and eliminate what does not.

Exhibit XI – Best in Class Examples



[39] The CDR is a 5-point scale used to characterize six domains of cognitive and functional performance applicable to Alzheimer disease and related dementias: Memory, Orientation, Judgment & Problem Solving, Community Affairs, Home & Hobbies, and Personal Care. The necessary information to make each rating is obtained through a semi-structured interview of the patient and a reliable informant or collateral source (e.g., family member) referred to as the CDR Assessment Protocol. http://knightadrc.wustl.edu/cdr/cdr.htm

[40] The Mini–Mental State Examination (MMSE) or Folstein test is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. It is commonly used in medicine and allied health to screen for dementia. It is also used to estimate the severity and progression of cognitive impairment and to follow the course of cognitive changes in an individual over time; thus making it an effective way to document an individual's response to treatment. https://en.wikipedia.org/wiki/Mini%E2%80%93Mental_State_Examination

For AD, the company is pursuing a very specific profile for its candidate:

- No monomer binding
  - Monomers are substantially more prolific than oligomers (1,000:1)
  - Monomer binding draws drug away from desired target
- No plaque binding
  - Plaque binding draws drug away from desired target
  - Plaques may be protective, as they sequester oligomers
  - Plaque binding contributes to ARIA-E
- Highly selective toxic oligomer binding
  - Targets cause of neuronal death
  - Requires high selectivity
  - Must identify the specific epitope
- Personalized medicine with companion diagnostic
  - Identify specific oligomer strains
  - Blood based screening assay
  - Address non-responders

FDA Position on AD Trials

Since the 1990s, the FDA has provided guidance that calls for pivotal trials in AD indications to have dual primary cognitive and funtional endpoints. Dual endpoints have increased the difficulty in generating statistically significant results and may not be appropriate. Arguments for a single endpoint and a focus only on memory judge it sufficient as improvements in cognition are more important for AD patients. Advocates for a single endpoint contend that accepting a drug that helps on only cognitive or functional objectives works if safety is acceptable and there are no other drugs to treat the disease. If a new drug improves memory but has limited impact on functional skills, it should still be considered for FDA approval, because clinically meaningful improvements in either area are critically important.[41] Other advocates claim that using the single endpoint will make investment more attractive as the likelihood of success will increase.

An emerging question regarding AD drug development is whether the treatments that failed in more advanced AD would have worked in patients with earlier stage disease. Over the last two decades, trial inclusion constraints required patients with an AD diagnosis, which may be the wrong population for a preventative treatment. With improvements in diagnostic tests and better identification of biomarkers indicating the onset of AD, it has become easier to identify early stage enrollees who may show the sought after result.

Over 400 trials have been conducted for AD[42] and none of them have been able to generate pivotal results supporting safety and efficacy. The lack of success has prompted a proactive change by the FDA to simplify and clarify trial design in order to generate success and investment in this therapeutic area. The Alzheimer's Association notes that AD is the only disease among the top ten causes of death in the United States "that cannot be prevented, cured or even slowed"[43] highlighting the critical nature of finding a cure.

With drug development for AD in crisis, a response from stakeholders, especially the FDA was needed. In February 2018, the FDA published draft guidance[44] that defined six stages for AD patients, and potentially acceptable endpoints for earlier stage disease. The most notable change was the recognition of biomarkers for determining efficacy. The agency validated the use of a single endpoint to determine cognitive impairment. Sensitive neuropsychological measures were recommended to serve as primary endpoints to support marketing approval. Later stage endpoints were not updated. In conjunction with the pharmaceutical aspect of treatment, the diagnostic approach was also emphasized. Biomarker evidence is critically important in identifying patients with the disease and when treatment is effective. The FDA also recommends sponsors co-developing diagnostic devices for AD to engage with the Division of Neurology Products or the Center for Devices and Radiological Health in the advancement of their device.

[41] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4713036/
[42] http://www.latimes.com/science/sciencenow/la-sci-sn-alzheimers-drug-fail-20180109-story.html
[43] 2016 Alzheimer's Disease Facts and Figures, Alzheimer's Association, 2016,
[44] Early Alzheimer's Disease: Developing Drugs for Treatment Guidance for Industry.
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM596728.pdf

Exhibit XII – FDA's AD Stage Catagorizations

Stage	Pathology	Cognitive Change	Functional Impairments	Dementia Diagnosis	Diagnostic Category	Endpoint	Time to Event
1	Yes	No	No	No	-	Biomarkers	Next Stage
2	Yes	Yes	No	No	-	Neuropsych Perf	Next Stage
3	Yes	Yes	Yes	No	-	Neuropsych Perf	-
4	Yes	Yes	Yes	Yes	Mild	-	-
5	Yes	Yes	Yes	Yes	Moderate	-	-
6	Yes	Yes	Yes	Yes	Severe	-	-

This FDA has evolved its thinking in order to improve its approach to trial design. This shift in approach is a material positive for the structure of new clinical trials for Alzheimer's Disease. ProMIS may be able to obtain expedited consideration from the FDA based on biomarkers and surrogate endpoints and can also use the pathway established by Biogen to effectively navigate towards FDA approval. With knowledge gained from previous failures and the FDA's interest in incentivizing the search for a cure, we see an easier path forward for new AD compounds entering clinical trials. Applying a single endpoint and employing surrogate markers could potentially eliminate two to four years of clinical trial work through more efficient trial design and expedited pathways.

Some examples of measurements that may be used to indicate the presence of AD or show early drug efficacy include neuroimaging of structural anomalies using PET, single-photon emission computed tomography (SPECT), magnetic resonance imaging (MRI) or other imaging technology. Much work has been done to identify and measure biomarkers, such as concentration of AβOs in CSF, the presence of synaptic biomarkers such as SNAP25 or PSD95 in CSF, TNF-α or messenger RNA. While an agreed upon biomarker has not yet been identified, there is an effort being made in order to align with the FDA's guidance and measure risk and treatment efficacy for the disease.

Biomarkers

The FDA has identified biomarkers as an important surrogate endpoint for determining the appropriate population to address and measuring drug efficacy. One of the problems with AD measurement is that by the time functional and cognitive decline is recognized, the damage has been done. This shifts the focus towards early diagnosis. Therefore, researchers and physicians must identify the disease in its earliest stages, or even before it begins in order to halt its advance. This approach will require a indicator which may include genetic data interpretation and biomarker analysis so at-risk patients can be identified early.

Chemistry, Manufacturing and Control (CMC)

Recent capital raises have been undertaken to build up cell-line development, manufacturing process development, and scale-up of manufacturing, which should take place over the next year. Preclinical toxicology will also be required as part of the IND-enabling process prior to the launch of the Phase I trial. Two recent hires were made to guide this process. Toxicology efforts will be headed up by the recent hire of Ernie Bush, who has extensive experience in IND development, evaluation and audits of good laboratory practice (GLP) bioanalytical and toxicology work as well as other biomedical familiarity. Another recent hire was Russ Blacher, who will lead the implementation of the antibody manufacturing process and will focus on quality and compliance, good manufacturing practices (GMP) implementation and the transition of the program to the CRO for Phase I.

ProMIS chose Selexis, SA to undertake cell line development for PMN310 using its proprietary SURE technology Platform. The platform employs a suspension-adapted Chinese hamster ovary (CHO) -K1 epithelial cell line. ProMIS' due diligence found Selexis to have a proven track record for rapid, stable and cost effective production of monoclonal antibodies with processes particularly applicable to PMN310. Selexis is privately held and is headquartered outside of Geneva, Switzerland and in Sunnyvale, California.

Licensing Partners

ProMIS has licensed the exclusive right to use the ProMIS target identification technology from the University of British Columbia (UBC). The company obtained a worldwide license to use Collective Coordinates in November 2015, which is used to predict novel targets in neurodegenerative diseases. These licenses require the payment of a small but undisclosed royalty to the UBC for any products developed using the discovery platforms.

Intellectual Property

ProMIS is highly dependent on its intellectual property protection for its drug portfolio and specialized software that is able to predict therapeutic targets. The company has multiple layers of intellectual property protection for its discovery platforms, predicted epitopes and monoclonal antibodies. The company frames its intellectual property strategy as castle, moat and fence which represents its multi-layered strategy to protect its product, methods and process.

- Castle
    - Antibodies and immunogens
    - Composition of matter
    - Therapeutic and diagnostic applications
- Moat
    - Epitopes identified by the algorithms
    - Sequence and conformation
- Fence (Discovery platforms)
    - Collective Coordinates
    - ProMIS

ProMIS has 45 issued patents and 25 pending applications worldwide. There are issued and pending patents for the Collective Coordinates and ProMIS methods for epitope prediction. There are 5 patents and patents pending for the Aβ epitopes, several other patents in the ALS category and an epitope in the TDP43 group that was filed in May 2017. The three pronged approach provides layers of protection and also provide the foundation for new antibodies in neurodegenerative and other diseases with misfolded proteins.

Significant Event Timeline

ProMIS has a number of recent and upcoming milestones related to development of the PMN3xx series. Looking forward, the company also has several events expected to take place on or around the indicated date.

- PMN 310 named lead development candidate – 1Q:17
- White paper on AD failures and toxic oligomers – 1Q:17
- Private placement for CAD$2.7 MM – 1Q:17
- Anthony Giovinazzo added to board – 1Q:17
- Daniel Geffken appointed as CFO – 1Q:17
- ALS TDP43 patent filed – 2Q:17
- OTCQB Listing (ARFXF) – 4Q:17
- GLP Toxicology – 2018
- Initiate PMN310 Manufacturing – 2Q:18
- Private Placement for CAD$7.2 MM – 2Q:18
- IND Submission – 2H:19
- Phase I trial – 2H:19
- Phase II proof of concept – 2020 to 2021 completion
- Phase III registrational trial – 2022 to 2026
- FDA Submission – 2026
- FDA Approval and First Sales - 2027

RISKS

All investments contain an element of risk which reflects the uncertainty of the business and what it will ultimately achieve. Some investments exhibit higher predictability, with current cash flows and established sales. These enterprises will have a lower level of perceived risk while other companies that are betting on a new technology that has not yet been fully defined have a much higher level of perceived risk.

The specialty pharmaceutical and biotechnology space includes companies at both ends of the spectrum, from mega-cap pharmaceutical powerhouses that have multiple products currently generating revenues, to small operations with a handful of employees conducting pre-clinical studies and many companies in-between. Many of the risks faced by the large pharmaceutical companies and smaller biotechnology-focused firms are similar; however, there are some hazards that are particular to smaller companies that have not yet established themselves or their products.

For smaller early-stage companies with expense structures still below breakeven, investing in growth is an extended effort. The timeframe for taking a new drug through the approval process, pricing negotiation and formulary addition can take multiple years. There also may be several other competitors pursuing similar indications that may dominate market share despite inferior safety or efficacy. The risks of new product launches are substantial.

Even if a company has a strong, experienced team that is launching a new product with a high likelihood of approval, evident formulary addition and a large addressable market, physicians may not use the product due to familiarity with legacy products and a hesitancy to change familiar prescribing practices.

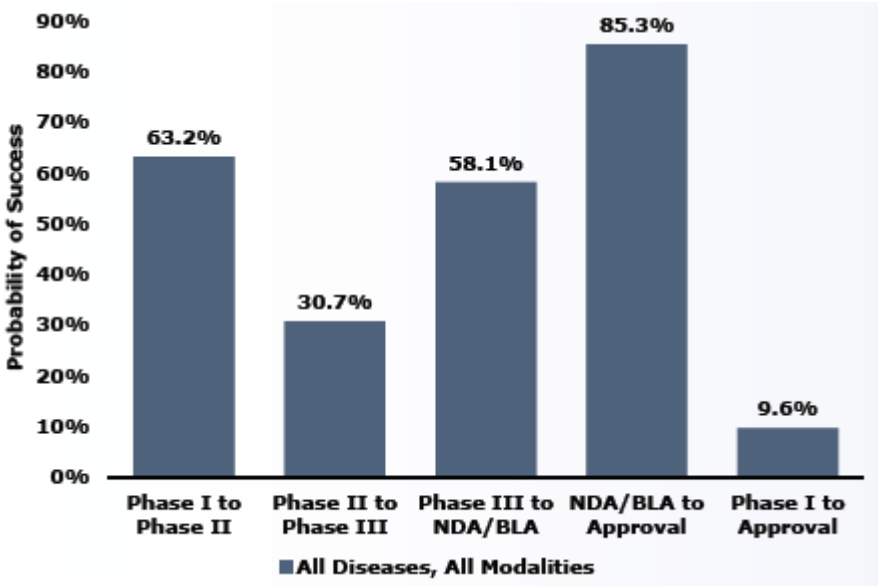
Access to financing is another risk for companies that have not yet achieved positive cash flow. Availability of capital comes and goes in cycles. During periods of improving confidence, new funding may be easy to access; however, during a liquidity crisis or a period of heightened risk perception, even companies with bright prospects may be in trouble if they are dependent on the financial markets to fund their initiatives. If capital is needed to sustain the company and it is not readily available, it may be forced to suspend operations, sell equity at a substantial discount to previous valuations and dilute earlier shareholders. A lack of funding may leave potentially promising growth plans without a viable route to market or force a company to accept onerous terms. The presence of debt during a period of operational losses is another risk early stage companies must face. If debt terms require repayment before profitability is reached, or interest burden is too great, equity is at risk of severe dilution and potentially recapitalization.

All drugs must navigate the regulatory approval process in the US, EU and other countries before commercialization in those regions. This effort is a material uncertainty which may take years and depends upon the needs and desires of the determining authority. Substantial expense is undertaken to bring a molecule or compound through clinical trials and address all of the regulatory agencies' concerns. Companies that have a long history of research success in drug development, with opinion leaders and experts in the field possess important fundamentals that can help mitigate this risk. Previous success with the FDA, EMA or other regulatory agencies is another attractive attribute that reduces risk. Some accelerated pathways to approval are available such as priority review, breakthrough therapy, accelerated approval and fast track, however, changes in sentiment or perceived safety of pharmaceuticals could alter the regulatory environment to demand a more thorough process and these pathways may be extended or additional requirements may be put in place.

ProMIS is developing its monoclonal antibodies and is currently in the preclinical stage conducting IND-enabling work. A Phase I trial is anticipated in 2019 after manufacturing preparations, toxicology work and other needed tasks are performed and an IND is submitted. We also anticipate that a Phase II and III trial will take place, which may be done in conjunction with a partner. We anticipate regulatory submissions to the FDA, EMA, Pharmaceuticals and Medical Devices Agency in Japan and other territories as well. We forecast favorable Phase III data to be published in 2026, immediately followed by regulatory submissions in the US, EU and other regions. We expect the regulatory approval process to take about a year. Regulatory success is not guaranteed and ultimate approval rates for candidates in Phase I trials have historically been around 10%. While we anticipate approval, it may be delayed or not granted.

The next exhibit shows approval rates for drugs in all disease categories. This study also finds that NME biologics have a historical FDA approval rate of 11.5%; however, we note that there have been no approvals in AD since 2014. We adjust the 9.6% approval rate for Phase I to approval downward to reflect PMN310's preclinical status.

Exhibit XIII – Success Rates for FDA Regulatory Approval[45]



ProMIS will rely on third parties for manufacturing, testing and trial management. Risks of poor manufacturing processes, quality control issues and product delays may halt production of a drug if partners are out of compliance with regulatory agency requirements. ProMIS has hired experts to direct and manage these development activities and has implemented a thorough process of inspections and communication to ensure good practices. While the company has made substantial efforts to ensure a productive relationship, the partner may lack the desire or skill to successfully maintain the required good practices and the partner may have other competing products under its control that receive greater attention and focus.

Drug price inflation has gained increased attention over the last several years and has contributed materially to the increase in health care costs over the last decades. As new therapies have been approved, drug prices have set new records and increased at a substantial rate in the United States. The United States is expected to represent the greatest component of value for ProMIS given a large population and favorable pricing. Other risks exist in different regions where pricing can be much lower than that anticipated to cover research and development costs and a profit. Our forecasts assume pricing that is materially below other mAb therapies such as checkpoint inhibitors in cancer which we believe will partially adjust for this risk.

We highlight several risks that result from higher prices and increased spending on pharmaceuticals. New drugs may see delayed introduction in ProMIS' markets and pricing authorities may take a stronger negotiation position for products that are approved. Government action on pricing in the United States has been discussed at length in the media; however, at present there does not appear to be any government mandated change forthcoming. Governments, elected officials and regulators may implement requirements that are less favorable to the pharmaceutical industry. Additionally, governments may impose additional non-price related regulation and disclosure requirements that can increase costs and burden.

While we have discussed a broad variety of risks above, we believe that our forecast parameters, discount rates, success probabilities and valuation metrics address these eventualities and our target price reflects an assumption of these risks faced by all biotechnology companies.

[45]Clinical Development Success Rates 2006-2015. David Thomas, Justin Burns, John Audette, Adam Carroll, Corey Dow-Hygelund, Michael Hay.

PEERS AND COMPETITORS

The AD market has been characterized by dramatic failures over the last few years. This has been blamed on a combination of ineffective trial design and pursuit of the wrong target. The list of disappointments includes Merck's verubecestat, Axovant's interpirdine, Eli Lilly's solanezumab and vTv's azeliragon to name a few. In January, Pfizer announced that it was ending its research programs for Alzheimer's and Parkinson's Disease. The state of the industry is highlighted by the lack of a new drug approval in 15 years for dementia.

A few classes of drugs are being developed. Most candidates fall into one of three categories: disease-modifying immunotherapy, disease-modifying small molecule, and symptom-reducing small molecule groups. The most prolific area for an AD cure is amyloid-related disease-modifying immunotherapy as it represents a way to render toxic forms of Aβ inert. This category is further divided into several subgroups that are focused on different types of Aβ and the source of the protein itself in β-secretase 1 (BACE) inhibitors which prevents cleavage of APP into Aβ monomers. One monoclonal antibody that has shown potential is Biogen's aducanumab, which targets the Aβ plaques and oligomers.

Below are many of the important companies that have contributed to the space, including those with failed candidates.

Exhibit XIV – Peers and Competitors[46]

Ticker	Company	Price	MktCap (MM)	EV (MM)	Drug
JNJ	Janssen subsidiary	$122.32	$327,818	$327,834	JNJ-54861911 (atabacestat)
NVSEF	Novartis	$72.20	$188,206	$200,380	CAD106 & CNP520 target Aβ
RHHBY	Roche	$27.47	$188,813	$187,510	Crenezumab
MRK	Merck	$60.71	$163,328	$181,700	Verubecestat BACE (failed)
ABBV	AbbVie	$92.12	$139,475	$176,760	ABBV-8E12
GSK	GlaxoSmithKline	$40.04	$99,877	$118,170	SB-742457 + Donepezil, Rosiglitazone
LLY	Eli Lilly	$85.11	$86,812	$86,044	Lanabecestat, LY3002813, Solanezumab
AZN	AstraZeneca	$34.88	$44,291	$74,844	Lanabecestat
BIIB	Biogen	$286.21	$60,393	$58,830	BIIB092, BIIB037
TKPHF	Takeda	$40.87	$32,217	$42,570	Pioglitazone
ESALY	Eisai	$71.59	$20,428	$19,820	BAN2401, E2609 - mAb targeting Aβ
HLUYY	Lundbeck	$72.51	$14,647	$14,120	Idalopirdine - 5-HT6 agonist (failed)
MOR	MorphoSys	$30.28	$3,892	$3,230	Gantenerumab - Roche Partner
ACIU	AC Immune	$9.46	$543	$814	9 therapeutic, 3 diagnostic AD candidates
BIOA	BioArctic	22.60 kr	1,665 kr	586.72 kr	mAb targeting Aβ oligomer - BAN2401
AVXL	Anavex Life Sci	$3.33	$149	$123	Ph2 AD: ANAVEX2-73, a Σ-1 Receptor
AXON	Axovant Sciences	$2.32	$250	$114	Intepirdine, symptomatic approach
ALZ	Alzinova AB	17.80 kr	98 kr	83.36 kr	mAb, Vaccine & peptide
VTVT	vTv Therapeutics	$1.59	$54	$15	azeliragon
pvt	Acumen Pharma				mAb/synthetic soluble Aβ oligomers (ADDLs)
pvt	AgeneBio				AGB101
pvt	ArmaGen Tech.				Broad neurodegenerative
pvt	Cognition Thera				CT 1812
pvt	EIP Pharma				Neflamapimod
pvt	Immungenetics				Phase 2 AD asset, thiethylperazine
pvt	Mithridion, Inc				α-secratase, small molecule
pvt	Neurim Pharma				Piromelatine -5-HT-1A and 5-HT-1D receptors
pvt	TauRx Therapeutics				TRx0237 - Tau Aggregation Inhibitor
PMN	ProMIS Neurosciences	CAD 0.40	CAD 98	CAD 97	PMN 310

[46] Price and market capitalization data is as of June 26, 2018

MANAGEMENT PROFILES

Eugene Williams, Executive Chairman
Eugene Williams is a former SVP at Genzyme, with senior roles integrating commercialization, drug development, and deal making. He is also an entrepreneur, as the founder and director of Adheris, which became the largest company in the patient adherence area. He was previously a strategy consultant at Bain and Corporate Decisions Inc. (a Bain Spin off, now part of Oliver Wyman), where he was co-Head of Healthcare and spent extensive time on speeding and improving the drug development process and on commercialization strategies. Mr. Williams was most recently the CEO of Dart Therapeutics, an Orphan Disease drug development company. Mr. Williams holds a B.A. from Harvard University and an M.B.A. from Harvard Business School.

Dr. Elliot Goldstein, President and CEO
Elliot Goldstein brings a unique track record in the clinical, regulatory and commercial development of new pharmaceuticals. Dr. Goldstein began his career with Sandoz Pharmaceuticals (now Novartis), a fourteen-year period on drug development in France, Basel, Switzerland Global Headquarters, including as Head of Clinical R&D in the United States. He subsequently held positions as SVP of Strategic Product Development at SmithKline Beecham (now GSK), CEO of British Biotech (Oxford, UK), Chief Operating Officer and Chief Medical Officer of Maxygen, and President and CMO of a startup biotech devoted to development of biosimilar monoclonal antibodies. Dr. Goldstein holds an M.D. from the University Aix-Marseille II, Marseille, France, and a B.Sc. from McGill University, Montreal.

Dr. Neil Cashman, Chief Scientific Officer and Co-founder
Dr. Cashman is a physician and scientist focused on neurodegenerative diseases. His first academic posting was at Montreal Neurological Institute and Hospital of McGill University. From 1998 to 2005, he was the Diener Professor of Neurodegenerative Diseases at the University of Toronto. In 2005, Professor Cashman moved to the University of British Columbia, where he holds the Canada Research Chair in Neurodegeneration and Protein Misfolding Diseases, and serves as the Director of the UBC ALS Centre. He has procured over $50 million in research grant funding from the CIHR, CRC, NCE, NIH, and various corporations for his work involving protein misfolding and prion technologies. He was awarded the Jonas Salk Prize for biomedical research in 2000, and was elected a Fellow of the Canadian Academy of Health Sciences in 2008. He is recognized worldwide as one of the leading research scientists pioneering the emerging fields of prion biology and protein misfolding diseases, in particular Alzheimer's disease and amyotrophic lateral sclerosis (ALS).

Steven Plotkin, Ph.D, Chief Physics Officer
Prof. Steven Plotkin is a theoretical and computational biophysicist whose research focuses on protein folding and misfolding in neurodegenerative disease, protein evolution and cellular differentiation, and the molecular mechanisms of cancer. He has been a professor at UBC in the Department of Physics and Astronomy since 2001, where he was appointed as the Canada Research Chair in Theoretical Molecular Biophysics. He was an Alfred P. Sloan Research Fellow in 2005-2006, a Killam Faculty Research Fellow in 2010, and is now an associate member of the Genome Sciences and Technology Program, the Bioinformatics Program, and the Institute for Applied Mathematics at the University of British Columbia. Several of his publications have received the Faculty of 1000 designation, placing them in the top 2% of published articles in biology and medicine. Dr. Plotkin is recognized internationally for his fundamental contributions to the energy landscape theory of protein folding, and presents his research findings in protein misfolding and neurodegeneration, and protein geometry and disorder as an invited speaker at several annual conferences and symposia. His research is currently supported by grants from CIHR, NSERC, APRI, ALS-Canada, and Compute Canada.

Daniel Geffken, Chief Financial Officer
Daniel Geffken is a Founding Managing Director of Danforth Advisors, LLC, a consulting firm providing finance, operations and strategic support to life science companies. He brings more than 25 years of experience in the life science industry to his work with ProMIS, ranging from start-ups to publicly traded companies with $1 billion+ market capitalizations. He previously served as COO or CFO of four publicly traded and four privately held life science companies, in addition to his consulting clients. Daniel has been chief financial officer of Homology, Inc, GenePeeks, Inc., Transkaryotic Therapies, Inc., Cidara, Inc., Apellis, Inc. and Stealth BioTherapeutics, Inc. He has raised more than $1 billion in equity and debt securities for life science companies. Mr. Daniel holds a B.S. from The Wharton School, University of Pennsylvania, and M.B.A. from Harvard Business School.

Financial Results

On May 11, 2018, ProMIS published first quarter results providing financial data and management commentary along with the filing of their SEDAR documents for the three month period ending March 31, 2018. Highlights for the quarter included presentation of preclinical data on PMN310 showing it does not bind to plaques, and does show greater binding affinity to neurotoxic oligomers. Research also provided evidence that humanized PMN310 shows similar ability to cross the blood brain barrier as aducanumab in aged mice. Post quarter end, ProMIS completed a private placement for $7.2 million and added Ernest Bush as Head of Pharmacology/Toxicology.

The company reported a net loss of ($1.6) million equivalent to ($0.01) per share compared to 2016 loss of ($1.4) million and also ($0.01) per share. First quarter expenses consisted of research and development expense of $0.8 million and general and administrative expense of $0.8 million. Total expenses rose 14% to $1.6 million.

Research and development increased 8.5% to $0.8 million as the company's AD development programs advanced. Salaries and benefits rose the most, adding $118,000 to costs and employee travel and related increased by $10,000. These line items were offset by lower share based payments and research programs expense. General and administrative expenses expanded 20% on higher investor and public relations and share based compensation partially offset by lower consultant salaries and other professional fees.

Cash and equivalents as of March 31, 2018 stood at $1.7 million; flat with year-end 2017 levels, with exercise in warrants and options roughly equaling cash used. Cash used in operations was ($1.6) million in 1Q:18 compared to ($1.3) million in 1Q:17. Subsequent to the quarter end ProMIS raised $7.2 million in gross proceeds in a private placement.

VALUATION

We are initiating coverage of ProMIS Neurosciences with a price target of $7.00. AD is the sixth most common cause of death in the United States and there are no approved drugs that can stop or slow its advance. Near 36 million persons are thought to suffer with the disease worldwide, and many more fall into its early stages where therapy may be the most effective. Additionally, the number of sufferers is expected to almost triple by 2050. While we are still in early stages with PMN310, the drug appears to address many of the oversights that have scuttled previous attempts at a cure.

The size of the Alzheimer's afflicted population make it one of the largest indications in the pharmaceutical universe. Looking back a few years to 2008, analysts estimated[47] peak annual sales of $5 to $12+ billion for the indication with UBS, Goldman Sachs,[48] Evaluate Pharma and others citing numbers in this range. Our own work estimates that peak sales could be much, much higher. Assuming an addressable and treated population of 10 million with with an annual treatment cost of $20,000 per year equates to $200 billion in AD class revenues.

We anticipate that ProMIS will partner with a large global pharmaceutical company following favorable Phase II data. We expect customary upfront, milestone and royalty payments as part of any arrangement reached. We simplify the relationship with a partner pharmaceutical company by representing all components of value in a 20% royalty rate. The ultimate value of a deal will vary from our estimates depending on safety and efficacy shown in clinical trials, number of buyers seeking the asset, other competitors in the market and conditions in the market at the time of the transaction. Our timeline roughly assumes that a Phase I trial will begin in 2H:19 and will last one year. A two-year Phase II will begin in 2020 followed by the Phase III in 2022 that we expect will provide topline results in early 2026. After a NDA is submitted and approved over the following twelve months, first sales are forecast in 2027. We anticipate that during or after Phase II, ProMIS will begin to work with a major pharma partner who will contribute to funding the Phase III, provide upfront payments, milestones and royalties.

When sales begin in 2027, our forecast calls for a 5% initial penetration rate into the US addressable market that will have grown to ~7 million by then, increasing to 15% over the next three years. Net price is forecast at $40,000 per year per treatment. We believe this is a conservative number as many of the mAb treatments in cancer are between $100 and $200 thousand per course of treatment. To reflect a slower uptake outside of the US, we forecast an initial 2% penetration into ex-US markets of ~37 million rising to 10% over the next four years. Patents and exclusivity are expected to end after 2038, where we forecast a decline in share to 9% for domestic and 6% in ex-US markets. Net price is expected to be about $20,000 per course of treatment, keeping in line with US/ex-US pricing relationships. As mentioned above, we recognize the value of the partnership solely through the estimated royalty rate of 20%. We assume that this is net of all royalties that ProMIS is obligated to pass through to licensees.

Our cash operating expense estimates begin at approximately $8.3 million in 2018 and grow to almost $28 million in the last year of Phase III clinical trials in 2026. This increase over the next eight years reflects the addition of manufacturing costs, and increasingly costly phased trials that are incrementally larger and more extensive. Following launch of PMN310, we anticipate R&D will fall to $5 million per year as the company focuses its efforts on other development candidates. We do not include any value for other programs in this model. G&A expenses are forecasted to increase from $2.3 million in 2018 to almost $4 million by the year of launch. We do not reflect any sales expenses in our DCF model, as these will be assumed by the global partner.

Our discounted cash flow (DCF) model uses a 15% discount rate and a 2% terminal decline rate. Ultimate probability of success is estimated to be 7%.[49] This is a downward adjustment to Phase I success rates of between 10% and 14%[50,51]. This recognizes that manufacturing efforts have started but have not yet been fully implemented and that the IND application has not yet been submitted or cleared. Our model reflects dilution from exercise of options and warrants. Based on the assumptions described and after adjusting for shares, restricted stock and options outstanding, we generate a target price of CAD$7.00.

[47] https://www.fiercebiotech.com/special-report/bapineuzumab-15-top-blockbuster-contenders
[48] ProMIS Corporate Slide Deck: March 2018.
[49] We multiply our DCF model by the ultimate probability of success to calculate target price. Therefore, if the DCF value of the company's cash flows is $100 and there is a 50% probability of success, the value is calculated as $100 x 50% = $50.
[50] Thomas, D.W, Burns, J., Audette, J., Carrol, A., Dow-Hygelund, C., and Hay, M. (2016). Clinical Development Success Rates 2006–2015. San Diego: Biomedtracker.
[51] Wong, Chi Heem, Siah, Kien Wei. Estimation of clinical trial success rates and related parameters. Biostatistics (2018) 00, 00, pp. 1–14; doi:10.1093/biostatistics/kxx069

CONCLUSION

Alzheimer's Disease is frightening condition that takes away an individual's ability to remember, organize logical thought, control emotions and in its last stages even regulate the body's basic functions such as breathing and heartbeat. Not only does it cause terrible harm to the person it afflicts, but it also creates a tremendous burden on immediate family and the health care system. It is the only major disease where the death rate has increased over recent decades and where no disease modifying therapy has been successful. In recent years, many drugs in advanced stages failed to show sufficient evidence of efficacy, which has frightened investment away and led to reallocation of resources elsewhere. However, much research has been conducted that shows these advanced programs have focused on the wrong target. Looking back decades, there is evidence supporting the neurotoxicity of soluble toxic Aβ oligomers. While most programs under the amyloid hypothesis have been targeting monomers and fibrils, one program in particular has also included oligomers. This is Biogen's aducanumab, which we think will be approved after topline is reported in 2020. If approved, this will validate the toxic oligomer target and bring attention to PMN310 and ProMIS as well as attract substantial interest from big pharma who recognize the gaping hole in their therapeutic portfolio.

ProMIS has been able to develop a molecule to address AD that improves upon the failures that have come before. Using its own proprietary discovery platforms it has developed precise solutions for solving neurodegenerative diseases. The company has used this specialized platform to develop PMN310, which is able to specifically target toxic oligomers and exclude other forms of Aβ that are either inert or neuroprotective. This *in silico* approach is expected to have other applications beyond AD in Parkinson's and ALS. Combined with regulatory changes that have simplified and clarified the pathway to approval, we see a possibility that PMN310 may receive expedited treatment if efficacy and safety are supported in Phase II trials.

ProMIS is on track for an IND filing in 1H:19 and a Phase I trial in 2H:19. We see the clinical trial pathway forward as clear given the other programs that have preceded PMN310, additional guidance from the FDA and various diverse stakeholders all aligned in their desire to find a safe and effective treatment for AD. The guidance and effort from the FDA is particularly important as it highlights biomarkers for earlier stage disease as valid endpoints. This should help reduce clinical trial duration and raise the prospect for expedited approval.

Key reasons to own:

- **Pursuing Large End Market**
  - **Near 6 Million with AD in US**
  - **Over 30 Million with AD Worldwide**
  - **Larger Addressible Market for Earlier Stage Disease**
  - **Number Afflicted Expected to Triple by 2050**
- **No Approved Therapies and Few in Development**
- **New FDA Guidance Supportive of Approval**
  - **Single Endpoint Sufficient**
  - **Surrogate Endpoints Allowed**
  - **Expedited Approval Possible**
- **Candidates Can Uniquely Bind to Toxic AβO**
- **Able to Develop Candidates for Other Neurodegenerative Diseases**
  - **ALS and Parkinson's Disease**
- **Strong IP Protection Around Target Acquisition and mAb Epitopes**

We believe ProMIS represents an attractive opportunity to gain exposure to an immense disease area with no other approved therapies. There are almost six million persons with AD in the US and over 30 million outside of the US that suffer from the disease. Additionally, there is a larger population with MCI and pre-Alzheimer's which may benefit even more from toxic oligomer sequestering therapy. The path forward is relatively clear with other assets including aducanumab setting the precedent for trial design. We initiate ProMIS Neurosciences with a valuation of CAD$7.00.

PROJECTED FINANCIALS

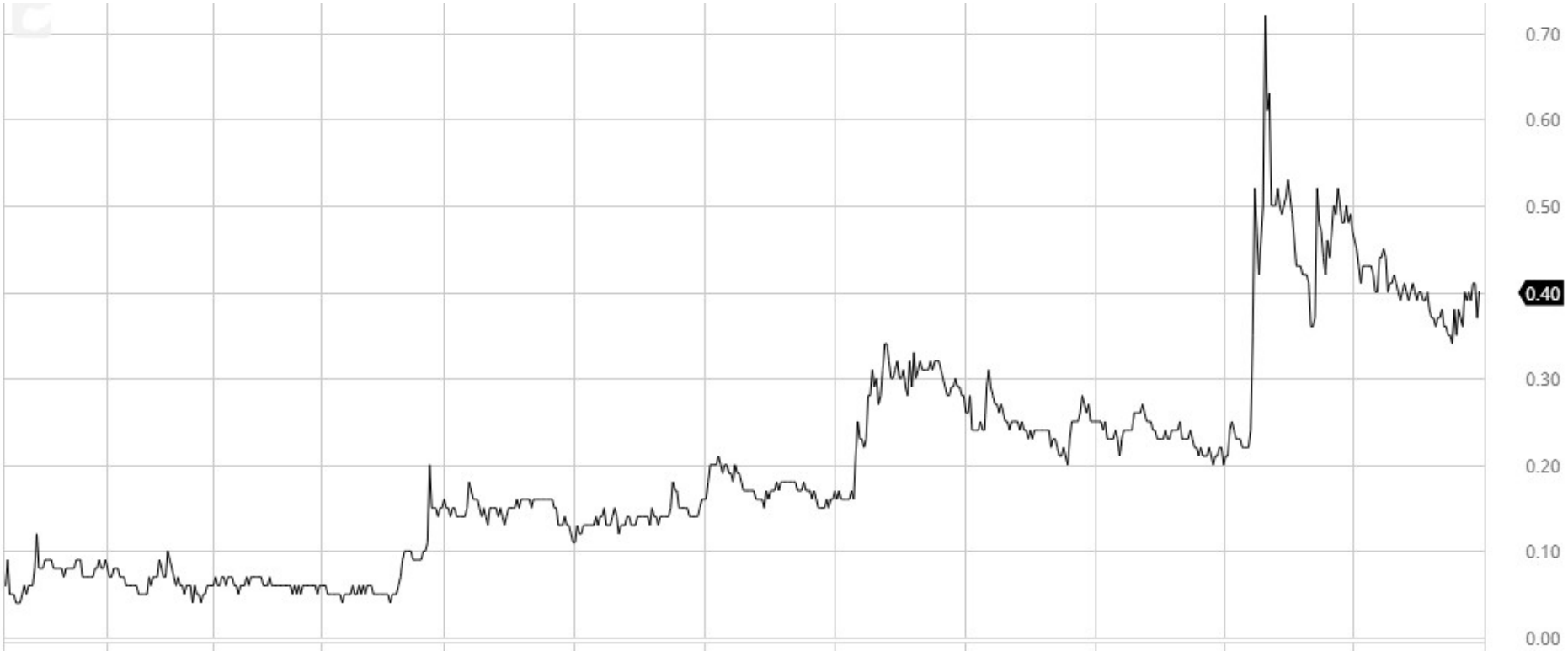
ProMIS Neurosciences Inc - Income Statement

ProMIS Neurosciences Inc.	2017 A	Q1 A	Q2 E	Q3 E	Q4 E	2018 E	2019 E	2020 E
Total Revenues (CAD$)	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**
R&D	$4.0	$0.8	$1.0	$1.0	$3.2	$6.0	$14.4	$16.9
G&A	$2.1	$0.8	$0.5	$0.5	$0.5	$2.3	$2.7	$3.1
Operating Income	($6.0)	($1.6)	($1.5)	($1.5)	($3.7)	($8.3)	($17.1)	($20.0)
Operating Margin								
Amort of Financing & Interest	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Pre-Tax Income	($6.0)	($1.6)	($1.5)	($1.5)	($3.7)	($8.3)	($17.1)	($20.0)
Taxes & Other	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate								
Net Income	($6.0)	($1.6)	($1.5)	($1.5)	($3.7)	($8.3)	($17.1)	($20.0)
Reported EPS	**($0.03)**	**($0.01)**	**($0.01)**	**($0.01)**	**($0.01)**	**($0.03)**	**($0.06)**	**($0.06)**
YOY Growth								
Shares Outstanding	205.8	223.9	245.0	250.0	255.0	243.5	295.0	345.0

Source: Company Filing // Zacks Investment Research, Inc. Estimates

HISTORICAL STOCK PRICE

ProMIS Neurosciences Inc – Three Year Price Chart[52]



[52] Chart provided courtesy of www.barchart.com

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