April 13, 2022

PROMIS NEUROSCIENCES INC.

(TSX: PMN)

BUSINESS DESCRIPTION

ProMIS Neurosciences, based in Toronto, Ontario, and Cambridge, Massachusetts, is a development-stage biotechnology company focused on the discovery and development of therapeutic antibodies selective for toxic oligomers that result from misfolded proteins. Such proteins are associated with the development and progression of neurodegenerative diseases including Alzheimer's disease (AD), amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD), and multiple system atrophy (MSA), among others.

The company's scientific platform features two proprietary target discovery engine algorithms that, collectively, can effectively predict the shape of Disease Specific Epitopes (DSEs) on the molecular surface of misfolded proteins that cause disease. Thus, its computational approach enables the development of selective antibody therapies against these targets. ProMIS' platform is based on the research of co-founder Dr. Neil Cashman, a scientist with over 25 years of experience in neurodegenerative diseases. Dr. Cashman, is a recognized leader in the field of protein misfolding diseases, including AD and ALS, and also serves as the ProMIS' chief scientific officer.

ProMIS' scientific thesis is that misfolded proteins, which expose toxic portions of the protein, are the primary culprit behind disease manifestation, and that efforts to inhibit all forms of the protein, including its abundant normal forms, are ineffective in treating diseases. Under such approaches, much of the administered dose is wasted by binding healthy protein or non-toxic aggregates before it reaches the relevant target in the brain. To date, the amyloid inhibition premise has been a primary focus of candidates for Alzheimer's disease, which has resulted in many failed, late-stage clinical studies. In contrast, ProMIS' platform selectively targets and inhibits only those mis-shaped epitopes exposed on the surface of misfolded proteins, and makes replicas of the misfolded regions, sparing the normal forms of proteins. ProMIS believes that immunizations with those epitopes result in more

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PRICE CHART

KEY STATISTICS

Key Stock Statistics	
Recent price (4/8/22), (CAD)	0.12
52 week high/low (CAD)	0.28-0.11
Shares outstanding (M)	431.7
Market cap (M, CAD)	52
Dividend	NA
Yield	NA

Sector Overview	
Sector	Healthcare
Sector % of S&P 500	13.7%

Financials ($M as of 12/31/21, CAD)	
Cash & Mkt Securities	21.5
Debt	4.9
Working Capital ($M)	21.2
Current Ratio	19.1
Total Debt/Equity (%)	66.0%
Payout ratio	NA
Revenue (M) TTM	NA
Net Income (M) TTM	NA
Net Margin	NA

Risk	
Beta	1.04
Inst. ownership	0%

Valuation	
P/E forward EPS	NA
Price/Sales (TTM)	NA
Price/Book (TTM)	7.0

Top Holders
Next Edge Capital Corp.
Migdal Mutual Funds

Management	
Chairman/CEO	Mr. Eugene Williams
CSO	Dr. Neil Cashman
CDO	Dr. Johanne Kaplan
Company website	https://www.promisneurosciences.com

COMPANY SPONSORED REPORT. SEE LAST PAGE FOR DISCLOSURES.

selective antibodies, which enable a lower effective dose that is expected to result in greater efficacy and a safer product profile. To date, ProMIS has achieved a 100% success rate in generating antibodies against specific identified DSE's.

ProMIS' lead candidate is PMN310, a potential next generation therapy for Alzheimer's disease. It is designed to bind to toxic oligomers, which are misfolded aggregates of smaller units of a healthy protein called monomer. The program is currently undergoing IND enabling activities and is expected to begin a Phase 1b clinical study in AD patients in early 2023. In March 2022, ProMIS announced positive pre-clinical results in a mouse model of AD that showed that PMN310 prevented a cognitive deficit as measured by performance in the water maze task.

Importantly, the Phase 1b study will be an open-label, ascending dose design, and should provide monthly biomarker evidence of effect data that can confirm target engagement as well as safety. We expect the trial to be conducted in a modest five to eight centers, which should enable rapid enrollment.

To prepare for an IND filing to initiate these studies, ProMIS is currently developing its production cell line for antibody manufacturing and is preparing GLP toxicology and pharmacokinetics (PK) studies in nonhuman primates. ProMIS expects to complete the PK studies during the second quarter of 2022. Behind PMN310, ProMIS is advancing a pre-clinical pipeline of candidates for additional neurodegenerative diseases and dementias, including Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS), which also share a common biologic cause – misfolded versions of proteins that perform a normal function, and that should not be inhibited broadly. As with PMN310, the platform selectively targets the toxic misfolded proteins with therapeutics and can detect them with diagnostics. In the case of ALS, antibodies are being designed that target misfolded forms of TDP-43, RACK1, SOD1, and ataxin2, with TDP-43 being the most advanced program.

For ALS, ProMIS is exploring different therapeutic modalities, including "intrabody", or inside the neuron, versions of TDP-43 antibodies that can be vectorized in a gene therapy vector, since physiologically important TDP-43 is active inside the neuron and should be avoided by the intrabodies in order to reduce the possibility of harmful side effects. In addition, ProMIS believes that addressing multiple misfolded protein targets could be beneficial to outcomes in ALS potentially with different modalities, including antibodies, vectorized intrabodies, and ASOs. To date, ProMIS has designated PMN267, focused on TDP-43, as its lead product candidate for treatment of ALS.

COMPETITIVE ADVANTAGE

In our view, ProMIS' approach is validated and differentiated from other treatments and technologies in development due to its accuracy of computational modeling and artificial intelligence that enable the generation of therapeutic antibodies that are highly selective for toxic misfolded proteins and not their normal, physiological forms. The company has run robust simulations that have revealed conformational epitopes that are mostly likely to be exposed on misfolded proteins and provide strong predictability to support its antibody portfolio. Importantly, the company's platform can be applied across multiple degenerative diseases with a common protein misfolding pathogenesis, including Parkinson's Disease (PD), Multiple System Atrophy (MSA), in addition to its more advanced efforts in Alzheimer's and ALS.

ProMIS operates in an extremely attractive market that is among the largest areas of unmet needs across the entire biopharmaceutical industry. To date, neurodegenerative diseases have seen few novel drug approvals, and those approved have provided little more than symptom management or modestly slowed disease progression, rather than significantly impacting the underlying cause of the disease. In particular, Alzheimer's has been associated with multiple high profile failures, which have led to many Big Pharma leaders exiting the field. Before the June 2021 approval of Biogen's Aduhelm, the area had seen only one approval since 2003. However, despite its approval, Aduhelm has seen poor commercial adoption that we attribute to a trial design that failed to capture an unequivocal treatment benefit, which was compounded by its overpricing the drug in the market (it has been subsequently cut in half and seen its Medicare coverage limited) that has drawn considerable scrutiny and cast doubt on the entire field by regulators, insurers and, importantly, biotech investors.

That said, Aduhelm's approval sparked a boost to neurodegenerative disease focused IPO's and other financings for development-stage companies such as ProMIS. With a Phase 3 data readout by Eisai's lecanemab (BAN2401), which has a similar thesis to ProMIS, expected before the end of 2022, we think a positive readout would renew investor interest in the space, as well as enhance increased M&A interest from Big Pharma. We estimate that more than 100 candidates for Alzheimer's disease are currently in the clinic and view PMN310 as potentially representing a best-in-class opportunity.

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PEER COMPARISON

Company	Ticker	Recent Price ($)	52-Week High ($)	52-Week Low ($)	Mkt. Cap ($MIL)	1-yr Price Change (%)	1-yr Rev Growth (%)	1 YR EPS Growth (%)	P/E Ratio	Beta	Yield (%)
PROMIS NEUROSCIENCES INC	**TSX: PMN**	**0.12***	**0.28***	**0.11***	**52***	**-45**	**NM**	**NM**	**NM**	**1.04**	**NA**
ALPHA COGNITION INC	TSXV: ACOG	0.97*	2.49*	0.75*	59*	-19	NM	NM	NM	NM	NA
ACUMEN PHARMACEUTICALS INC	NASDAQ: ABOS	4.01	26.98	3.69	162	-80	NM	NM	NM	NM	NA
ANNOVIS BIO INC	NYSEAM: ANVS	12.15	132	11.73	100	-54	NM	NM	NM	NM	NA

* Statistics in Canadian Dollars (CAD)

We think that the ability to learn from earlier programs and approaches that have disproved prevailing thoughts on Alzheimer's has also positioned ProMIS to enhance its platform. Previous clinical programs have focused on amyloid monomer inhibition or targeting plaques in the brain containing amyloid, both of which have failed to yield an impact on disease manifestation, but have fostered a better understanding of the misfolded protein hypothesis. In addition, the advancement in biomarker detection and brain imaging in the pathology of AD has had a significant impact on ProMIS' design plans to use monthly biomarker analysis to determine more efficiently the effect of PMN310 when it begins clinical study. Further, we think that global regulators and specifically the US FDA have embraced the use of biomarkers to support evidence of effect, which we think could provide opportunities to rapidly conduct and advance the program. As such, we see ProMIS as well positioned to attract increased attention and interest from key stakeholders over the coming quarters.

In our view, ProMIS' antibody capabilities are well positioned to remain at the forefront of research in the neurodegenerative disease space, despite the emergence of several genetic technologies that are attracting interest across the biopharmaceutical industry. For example, we think ProMIS' approach is preferable to RNAi interference, as that technology could effectively address the genetic component of disease, but inhibit healthy amyloid in the process. Moreover, we do not view gene therapy as an ideal alternative for AD, given its permanence and potential to result in an unacceptable safety profile.

Another key differentiator for ProMIS is its access to some of the industry's distinguished leaders, both in its executive suite as well as in its scientific advisory board. As mentioned earlier, the executive team, led by Chief Scientific Officer Dr. Neil Cashman, possesses extensive clinical research experience as pioneers in the field of protein misfolding diseases. Its advisory board, which is chaired by Alzheimer's disease globally recognized thought leader Dr. Rudolph Tanzi, includes multidisciplinary specialists in neurodegenerative diseases, as well as experts in biotech business management, diagnostic product development, and monoclonal antibody design and manufacturing.

Lastly, we view favorably ProMIS' robust and growing IP portfolio, which included 47 patents and 67 applications, as of early 2022.

ANALYST COMMENTARY: EARNINGS

As we see it, ProMIS' progress in advancing its pipeline of candidates for neurodegenerative diseases into human clinical study is more material than its reported financials. During 2021, the company successfully completed several transactions that extended its cash runway and enabled the continuation of execution of its development strategy. Overall, we view its path to clinical value inflection favorably, given that its Phase 1b study will be open label and biomarker checked on a monthly basis, which should provide evidence of effect at a relatively early-stage. In addition, as mentioned earlier, we expect the appetite for M&A and financing for diseases such as Alzheimer's to improve over 2022, as new late-stage data is reported.

As of December 31, 2021, ProMIS had C$21.5 million in available funding for its operations, consisting of cash, cash equivalents and short-term investments, as compared to C$1.1 million at the end of 2020. Management expects this level of funding to support its operations through the end of 2023. In 2021, cash expenditures for PMN310 were C$3.8 million, most of which related to payments to its manufacturing vendor to help prepare ProMIS to be able to file its IND and initiate patient dosing.

We view ProMIS' working capital position of C$21.2 million, and current ratio of 19.1 favorably for being able to execute on its strategy during in 2022. We also note that ProMIS has long-term debt of approximately C$5.0 million on its balance sheet. We expect capital needs to accelerate as ProMIS moves its pipeline candidates further into human clinical studies. However, we foresee continued execution on its developmental strategy, combined with the potential to uplist its stock on Nasdaq, which would introduce the company to a new class of investors and expand its access to capital, and potentially improve investor sentiment towards the field, thus providing a tailwind to its capital access strategy. We estimate that ProMIS' fully diluted share count, including warrants, stock options and registered stock units (RSU), was approximately 560 million as of March 2022. We would expect the company to consolidate its shares ahead of an uplist event during 2022.

Over the longer-term, we see its growing pipeline providing optionality for additional partnering activities. We think its product candidates as well as broad platform discovery capabilities are likely to attract the interest of a Big Pharma industry that is holding its highest level of cash and M&A capabilities in industry history. We expect Big Pharma to be monitoring the field closely before re-entering the market aggressively upon additional validation and maturity of some of these newer therapeutic options. We also think that ProMIS could fortify its balance sheet to keep many of its programs in-house into clinical study, so that it can garner enhanced deal economies, upon program validation.

MANAGEMENT

Mr. Eugene Williams is ProMIS' chief executive officer. Mr. Williams was most recently CEO of Dart Therapeutics, an Orphan Disease drug development company, and was previously a former SVP at Genzyme, with senior roles integrating commercialization, drug development, and deal making. Mr. Williams founded and was a director of Adheris, which became the largest company in the patient adherence area. Notably, during his tenure as co-head of healthcare as a strategy consultant at Bain and Corporate Decisions Inc. (a Bain spin-off, now part of Oliver Wyman), he developed expertise in speeding and improving the drug development process and on commercialization strategies. Mr. Williams holds a BA from Harvard University and an MBA from Harvard Business School.

Dr. Neil Cashman is ProMIS' co-founder and chief scientific officer. 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 and ALS. He holds the Canada Research Chair in Neurodegeneration and Protein Misfolding Diseases at the University of British Columbia (UBC) and serves as the director of the UBC ALS Centre. Previous academic postings include the Montreal Neurological Institute and Hospital of McGill University and the University of Toronto.

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.

RISKS

Risks include the standard risks in drug development, such as establishing efficacy and safety in human clinical trials. In addition, we note that the Alzheimer's disease market has been marked by high profile clinical and commercial failures, and improved investor and regulator sentiment will be reliant on the clinical success of newer programs as they advance and readout. Lastly, we expect ProMIS will need to raise additional capital to continue bringing its pipeline to a stage where it can more efficiently partner and secure enhanced downstream economics. Failure to do this would result in higher risk of equity dilution.

RECENT DEVELOPMENTS

In addition to initiating the path to an IND filing for PMN310 in Alzheimer's with the development of its initial producer cell line throughout 2021, ProMIS made significant progress in expanding its executive leadership team, as well as its Scientific Advisory Board and Board of Directors.

Of note, in October 2021, the company appointed Eugene Williams, formerly executive chairman, as chairman and chief executive officer, while Dr. Elliot Goldstein resigned from the CEO role with a transition to a consulting role. In addition, Gavin Malenfant joined the senior management team as chief operating officer, which we view as a key appointment, given his more than 30 years of biopharmaceutical experience and expertise in the oversight of drug development programs. Earlier in the year, Dr. David Wishart, Distinguished University Professor in the Departments of Biological Sciences and Computing Science at the University of Alberta, was appointed as chief physics officer.

In 2021, ProMIS appointed Neil Warma, Josh Mandel-Brehm and Maggie Shafmaster, JD, Ph.D to its Board of Directors, enhancing the company's expertise in matters related to Healthcare Entrepreneurship, Business Development and Operations, and Biopharma Intellectual Property expertise to the Board.

In May 2021, Dr. Rudolph Tanzi, Ph.D., a world-renowned leader in the field, was appointed as the chair of the company's Scientific Advisory Board (SAB). Dr. Tanzi is the Joseph P. and Rose F. Kennedy professor of neurology at Harvard University and vice-chair of neurology, director of the Genetics and Aging Research Unit, and co-director of the Henry and Allison McCance Center for Brain Health at Massachusetts General Hospital. To date in 2022, the company has also appointed Dr. Carsten Korth, Dr. Cheryl Wellington, Dr. Guy Rouleau and Dr. Alain Dagher to its SAB.

Steve Silver,
Argus Research Analyst

INCOME STATEMENT

Growth Analysis ($MIL, CAD)	2019	2020	2021
Revenue	0.0	0.0	0.0
Gross Profit	-4.7	-3.2	-6.3
G&A	2.7	2.5	4.2
R&D	0.0	0.0	0.0
Operating Income	-7.4	-5.7	-10.5
Interest Expense	0.0	0.0	0.5
Pretax Income	-7.4	-5.7	-11.8
Tax Rate (%)	NM	NM	NM
Net income	-7.4	-5.7	-11.8
Diluted Shares	259.8	285.6	347.1
EPS	-0.02	-0.01	-0.02
Dividend	NM	NM	NA
Growth Rates (%)			
Revenue	NM	NM	NM
Operating Income	NM	NM	NM
Net Income	NM	NM	NM
EPS	NM	NM	NM
Valuation Analysis			
Price ($): High, CAD	0.44	0.31	0.28
Price ($):Low, CAD	0.17	0.08	0.08
PE: High	NA	NA	NA
PE: Low	NA	NA	NA
PS: High	NA	NA	NA
PS: Low	NA	NA	NA
Yield: High	NA	NA	NA
Yield: Low	NA	NA	NA
Financial & Risk Analysis ($MIL, CAD)			
Cash	1.7	1.1	21.5
Working Capital	0.3	-1.1	21.2
Current Ratio	1.2	0.5	19.1
LTDebt/Equity (%)	NM	NM	66
Total Debt/Equity (%)	NM	NM	66
Ratio Analysis			
Gross Profit Margin	NM	NM	NM
Operating Margin	NM	NM	NM
Net Margin	NM	NM	NM
Return on Assets (%)	NM	NM	NM
Return on Equity (%)	NM	NM	NM
Op Inc/Int Exp	NM	NM	NM
Div Payout	NM	NM	NM

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