# Zacks Small-Cap Research

*Sponsored – Impartial - Comprehensive*

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## ProMIS Neurosciences Inc (PMN – TSE)

***Natural History Study to Provide Baseline Data***

Based on our DCF model and a 15% discount rate, PMN is valued at approximately $5.50 per share. We apply a 7% probability of eventual sales of portfolio products in global markets.

| | |
|---|---|
| Current Price (3/20/20) | $0.13 |
| **Valuation** | **$5.50** |

### OUTLOOK

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. These allow for precise and efficient target identification.

ProMIS offers a platform that can generate mAbs specific to toxic forms of proteins found in neurodegenerative disease and determine their efficacy quickly and at low cost using biomarkers. ProMIS has identified trials in AD, PD and ALS that can provide proof of concept data and support further development in target indications. We anticipate continued focus on AD and increased partner involvement.

With recent FDA guidance regarding trial design, there is support for the use of fewer endpoints and biomarkers which may accelerate future development in AD. Previous trial results and additional research have refined 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** | **$0.38** |
| **52-Week Low** | **$0.10** |
| **One-Year Return (%)** | **-65.8** |
| **Beta** | **-1.4** |
| **Average Daily Volume (sh)** | **264,629** |
| **Shares Outstanding (mil)** | **275** |
| **Market Capitalization ($mil)** | **$35.8** |
| **Short Interest Ratio (days)** | **0.84** |
| **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 2020 Estimate** | **N/A** |
| **P/E using 2021 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) |
|---|---|---|---|---|---|
| 2018 | $0.0 A | $0.0 A | $0.0 A | $0.0 A | $0.0 A |
| 2019 | $0.0 A | $0.0 A | $0.0 A | $0.0 A | $0.0 A |
| 2020 | | | | | $0.0 E |
| 2021 | | | | | $0.0 E |

| | Q1 (Mar) | Q2 (Jun) | Q3 (Sep) | Q4 (Dec) | Year (Dec) |
|---|---|---|---|---|---|
| 2018 | -$0.01 A | -$0.01 A | -$0.01 A | -$0.01 A | -$0.04 A |
| 2019 | -$0.01 A | -$0.01 A | -$0.01 A | -$0.01 A | -$0.03 A |
| 2020 | | | | | -$0.03 E |
| 2021 | | | | | -$0.05 E |


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## WHAT'S NEW

**Full Year 2019 Operational and Financial Results**

2019 provided a wild ride in the β-amyloid (βA) space. In March 2019, Biogen (NASDAQ: BIIB) announced that its Phase III Alzheimer's Disease (AD) trial for aducanumab failed to reach its endpoints and the drug would be abandoned. Seven months later, Biogen reversed itself itself and decided that it would pursue a Biologics License Application (BLA) for aducanumab based on further analysis of later data that became available. With this shifting environment as a backdrop, ProMIS Neurosciences Inc. (TSE: PMN) adapted its approach by moving efforts away from βA-focused work and shifting resources towards its portfolio of candidates aimed at other neurodegenerative targets. Drug candidates were developed for α-synuclein in multiple system atrophy (MSA), Tau in AD and TDP-43 in amyotrophic lateral sclerosis (ALS) over the last year. This flexibility has allowed the company to remain relevant despite rapidly changing views on the target of choice.

ProMIS has publicized the importance of biomarkers and their value in assessing efficacy and providing the backbone of cost-effective trials. As part of the company's strategy going forward, each program, from α-synuclein to TDP-43 has identified a blood based biomarker that can rapidly and effectively determine whether or not the experimental therapy is working. This effort to develop biomarkers was continued last month with the initiation of a natural history study of blood-based biomarkers in AD. ProMIS will work with Parexel to manage data and detect a treatment sign in early clinical trials. Success here may light the path forward for using a biomarker to support accelerated approval in an FDA sanctioned trial. Accurate, early data will enable the best candidates with the highest likelihood of success to move forward. The data collected from this work will provide valuable reference information for patients with early stage dementia.

Financial results for 2019 were provided in a press release and SEDAR filings released on March 18, 2020. Research and development efforts consumed $4.7 million[1] in 2019 compared to $7.4 million in the prior year, a 36% drop. Lower spending on external contract research organization (CRO) costs and decreased patent expenditures were partially offset by higher contracted research salaries, and external consulting expense. General and administrative expenses were $2.7 million, falling 3.5% over the prior year's $2.8 million. Lower levels of share-based compensation and professional fees were balanced by increased investor and public relations expenses, salaries and foreign exchange loss.

As of December 31, 2019, cash stood at $1.7 million, down from the prior year-end level of $2.4 million. Cash burn for 2019 was ($6.1) million offset by a net $5.4 million in cash from financing. Following the end of the reporting period, ProMIS announced that 6.3 million warrants in the amount of ~$1 million had been exercised

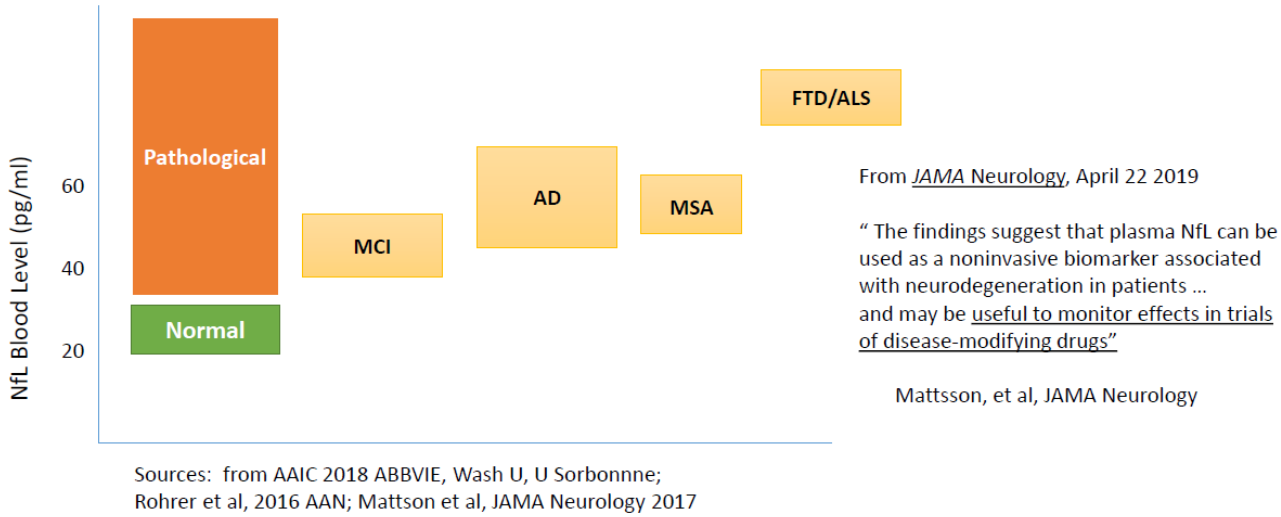
In the constantly changing and uncertain environment of neurodegenerative disease drug development, management has evolved its focus toward its drug discovery platform and highlighted three pillars in the company's value proposition: 1) The root cause of many neurodegenerative diseases is already known, and drugs developed to address the diseases need to focus on the desired target and ignore other proteins. 2) Neurodegenerative diseases are caused by misfolded toxic forms of a protein which can be uniquely identified by ProMIS' proprietary discovery platform. 3) Biomarkers can indicate whether a research program is on the right track early, before substantial capital is spent.

The company is sharing this refined mission with investors and prospective pharmaceutical partners, with whom they are carrying out discussions. While this pushes out our original forecasts for trial launches and ultimate sales, it does open up a wider variety of options that may move forward in the company's portfolio.

Successfully pursuing an indication using biomarkers can be validated with clinical proof of concept trials in enriched populations which can generate meaningful data in six to twelve months for $5 to $10 million. The leading biomarker that ProMIS has identified is neurofilament light chain (NfL), which we discussed in further detail here. Not only has the marker proven itself in the lab, but it has also served as a valuable pharmacodynamic marker in multiple sclerosis and spinal muscular atrophy. We see tremendous value in this tool and anticipate it will support an endpoint in ProMIS' future clinical trials.

[1] Currency is denominated in Canadian Dollars

**Exhibit I – Neurofilament Light Chain Levels in Neurodegenerative Disease[2]**




Sources: from AAIC 2018 ABBVIE, Wash U, U Sorbonnne; Rohrer et al, 2016 AAN; Mattson et al, JAMA Neurology 2017

## MSA, Tau & ALS

In early October, ProMIS announced that it had identified several antibody therapeutics that target toxic forms of α-syneuclein implicated in Multiple System Atrophy (MSA). The antibody candidates demonstrate a high binding coefficient to toxic alpha-synuclein aggregates present in patients diagnosed with MSA.

In a mid-October release, ProMIS demonstrated that several previously identified antibodies that are able to neutralize toxic oligomer forms of Tau protein can block the spread of pathogeic tau aggregate formation in a cellular model. ProMIS employed its discovery platforms to identify unique epitopes of these toxic forms then develop antibodies that can selectively bind to the toxic forms of Tau.

In late October, a set of antibody candidates were created that target the neurotoxic form of TAR DNA-binding protein 43 (TDP-43) This protein is found in all cells and associated with several diseases such as amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). The antibodies are uniquely matched to to misfolded intracellular aggregates of TDP-43 with no binding to normal TDP-43. The binding profile was confirmed in post-mortem brain tissue from FTD patients.

## Partnerships

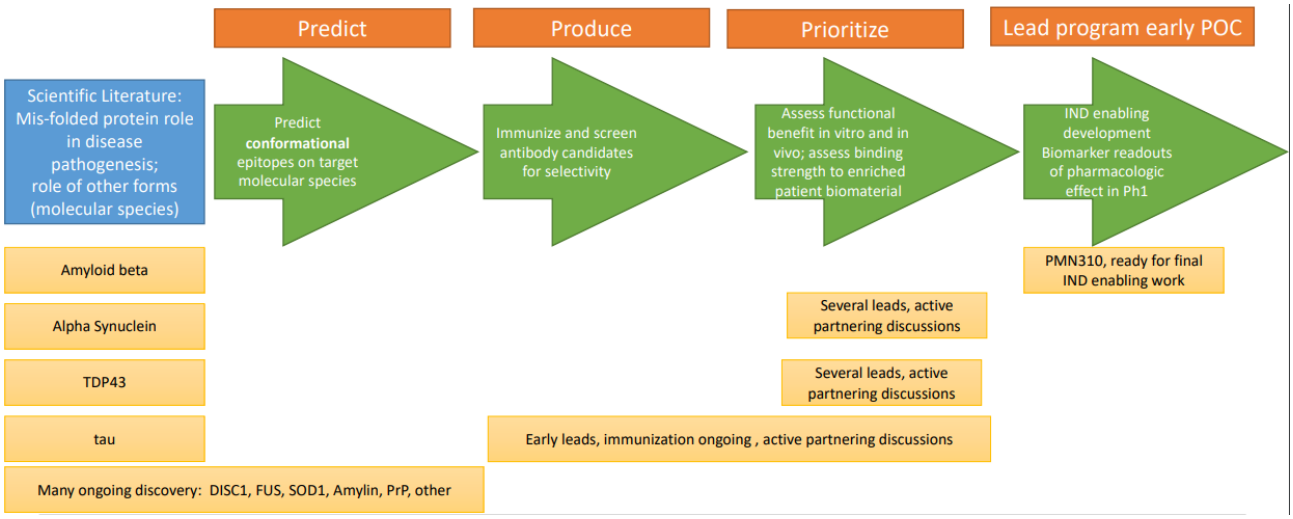
ProMIS is currently in confidential discussions with potential partners for the antibodies associated with the α-synuclein, Tau and TDP-43 targets. Each of these assets has at least two different prospects. If a deal were to take place it would likely enable ProMIS to move the partnered molecule towards the clinic and also provide capital via upfront payments to advance PMN310 into a Phase I trial. An equity capital raise and significant investment from a strategic partner are other mechanisms through which it can raise funds to advance the portfolio.

ProMIS is seeking a partner to help develop the pipeline. The company's unique platform to identify unique epitopes provides data that makes the therapeutic antibodies produced very valuable. Confidential discussions are currently underway with unidentified partners to develop these programs. The company entered into an agreement to raise CAD$6.5 million just prior to the third quarter report and raised funds from warrant exercise in the first quarter of 2020 which will support operations until partnerships can be consummated.

In recent presentations and in the outlook section of the annual results, there have been references to vectorization of antibodies. Using gene therapy, the genetic sequence for intracellular antibodies (intrabodies) can be delivered to cells which can synthesize the desired antibody to address misfolded proteins inside the cytoplasm. This approach has the potential to allow one treatment to have a therapeutic benefit that lasts for years. We hope to hear more detail about this approach in coming quarters.

[2] Source: ProMIS Corporate Presentation August 2019.

**Exhibit II – ProMIS Neurodegenerative Candidate Portfolio**[3]




## Additions to the Team

ProMIS has added several distingushed individuals to its advisory boards and management team over the last year. We see the additions as providing a diverse set of relationships, experiences and competencies to the group that will advance the AD, PD and ALS programs.

Timothy Rothwell was added to the Business Advisory Board in February. He has expierence as former U.S. CEO and Chairman for Sanofi-Aventis, CEO of Sandoz Pharmaceuticals and president of Rhone-Poulenc Rorer Pharmaceuticals. We see his experience and contacts in the industry as indispensable to making introductions to the decision-makers that comprise the opportunity set for partners in the ALS and PD program assets.

In June, C. Warren Olanow joined ProMIS' scientific advisory board (SAB) scientific advisory board with considerable experience in neurodegeneration and PD, an area where he has authored over 300 publications. Dr. Olanow will work with the other members of the board to help guide develop the PD, AD and ALS programs.

Dr. Andre Strydom became a member of the SAB in August. His area of expertise is in Down syndrome where his research has advanced understanding in AD. Specific work includes investigation of biomarkers of cognitive decline including those related to excess amyloid production, oxidative stress, and neurodegeneration. Down syndrome patients show significant levels of amyloid in the brain and are at risk of early onset AD, making this an important population for PMN310 and an area likely to benefit from Dr. Strydom's expertise.

In January 2020, Dr. José Luis Molinuevo ascended to the SAB bringing his experience as a neurologist, researcher, professor, principal investigator and clinician to the post. Dr. Molinuevo has focused on AD and other related diseases such as PD. He is the Scientific Director of the Alzheimer Prevention Program at the BarcelonaBeta Brain Research Center (BBRC) in Barcelona, Spain, which focuses on Alzheimer's disease prevention from a clinical, cognitive, genetic, and biomarker perspective and is an associate professor at the University Pompeu Fabra. His experience and knowledge of biomarkers and relationships throughout Europe are valuable assets that may provide support for later stage clinical trials in ProMIS' portfolio candidates.

[3] Source: ProMIS Corporate Presentation January 2020.

**Significant Event Timeline**

ProMIS has a number of recent and upcoming milestones related to development of its pipeline which we summarize below.

- Confidential discussions with potential partners for platform programs - Ongoing
- PMN310 scale up manufacturing – 2019
- CAD$6.5 million private placement – November/December 2019
- Capital raise or partnership to fund entry into clinic – 2020
- Prepare IND and Phase I trial for PMN310 – 2020
- Pursue a vectorization deal - 2020
- Generate Phase I biomarker data with Toronto Memory Program – 2020
- Launch Phase I trial in PMN310 - 2021

**Summary**

ProMIS has continued to advance its preclinical programs, highlighting three new antibody advancements late last year. Parallel with these endeavors is continued interaction with the scientific, investment and corporate community to present the potential of the company's platform to garner KOL support, financing and partnerships. Management has refined its message highlighting the need to focus on the toxic forms of misfolded proteins that are the root cause of neurodegenerative disease and the importance of biomarkers that can rapidly and inexpensively demonstrate efficacy. We continue to be impressed with ProMIS' discovery platforms and their ability to identify unique features of toxic misfolded proteins. We anticipate that a pharmaceutical partner deal or large investment will allow the company to advance its candidates into the clinic.

ProMIS represents an attractive opportunity to gain exposure to an immense disease area with no other approved disease modifying therapies. There are almost six million persons with AD in the US and over 30 million outside of the US that suffer from it. Additionally, there is a larger population with mild cognitive impairment (MCI) and pre-Alzheimer's which may benefit even more from toxic oligomer sequestering therapy. The path forward is relatively clear with other assets setting the precedent for trial design and potentially accelerated approaches using biomarkers suggested by regulatory agencies. There is also substantial opportunity for drug development in PD, MSA and ALS.

Due to the volatile and uncertain environment following announcements related to aducanumab, the investment community is waiting to put new money to work in βA programs. In the near term we expect to see the BLA submitted for Biogen's drug, which may bring attention back to the βA space. We continued to believe in the potential for PMN310 and the other candidates in development and the tremendous opportunity in AD and other neurodegenerative diseases due to the lack of effective therapies and the magnitude of the need. We maintain our target price of $5.50.

## PROJECTED FINANCIALS

**ProMIS Neurosciences Inc - Income Statement**

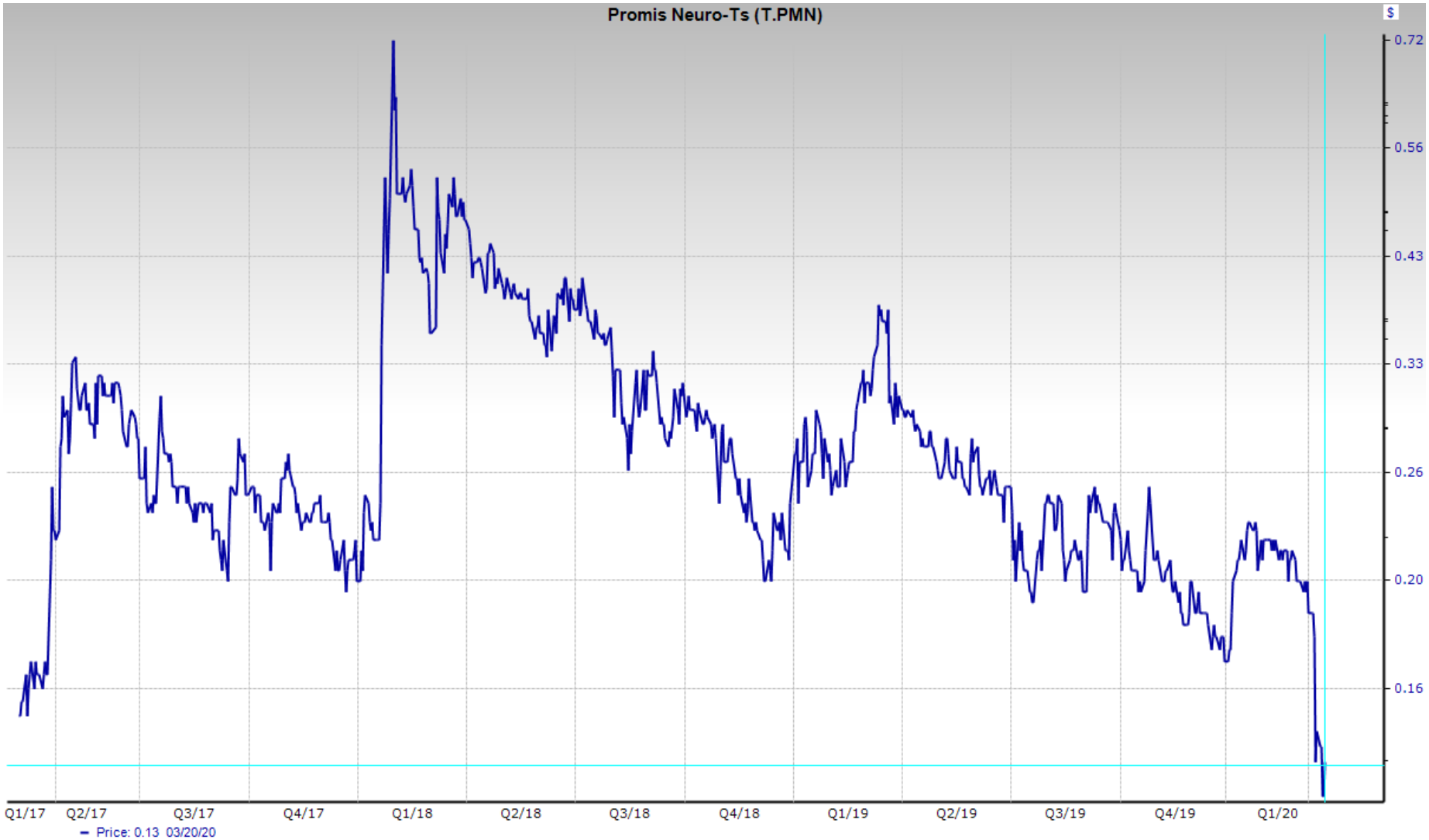
| ProMIS Neurosciences Inc. | 2018 A | Q1 A | Q2 A | Q3 A | Q4 A | 2019 A | 2020 E | 2021 E |
|---|---|---|---|---|---|---|---|---|
| **Total Revenues (CAD$)** | **$0.0** | **$0.0** | **$0.0** | **$0.0** | **$0.0** | **$0.0** | **$0.0** | **$0.0** |
| R&D | $7.4 | $1.8 | $1.0 | $1.1 | $0.9 | $4.7 | $8.2 | $17.5 |
| G&A | $2.8 | $0.7 | $0.8 | $0.6 | $0.6 | $2.7 | $3.1 | $3.3 |
| Operating Income | ($10.2) | ($2.4) | ($1.9) | ($1.6) | ($1.5) | ($7.4) | ($11.3) | ($20.8) |
| *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 | ($10.2) | ($2.4) | ($1.9) | ($1.6) | ($1.5) | ($7.4) | ($11.3) | ($20.8) |
| Taxes & Other | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | $0.0 | |
| *Tax Rate* | | | | | | | | |
| Net Income | ($10.2) | ($2.4) | ($1.9) | ($1.6) | ($1.5) | ($7.4) | ($11.3) | ($20.8) |
| **Reported EPS** | **($0.04)** | **($0.01)** | **($0.01)** | **($0.01)** | **($0.01)** | **($0.03)** | **($0.03)** | **($0.05)** |
| *YOY Growth* | | | | | | | | |
| Shares Outstanding | 239.2 | 254.1 | 256.9 | 261.4 | 266.7 | 259.8 | 345.0 | 400.0 |

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

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## HISTORICAL STOCK PRICE

**ProMIS Neurosciences Inc – Historical Price Chart[4]**




[4] Source: Zacks Research System

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