



**PROMIS NEUROSCIENCES INC.**

**2024 ANNUAL REPORT**



UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

FORM 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2023

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For The Transition Period From To

Commission file number: 001-41429

**PROMIS NEUROSCIENCES INC.**

(Exact name of registrant as specified in its charter)

**Ontario, Canada**

(State of Other Jurisdiction of incorporation or Organization)

**Suite 200, 1920 Yonge Street Toronto, Ontario**

(Address of principal executive offices)

**98-0647155**

(I.R.S. Employer Identification No.)

**M4S 3E2**

(Zip code)

Registrant's telephone number, including area code: (416) 847-6898

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class  
Common Shares, No Par Value per Share

Trading Symbol(s)  
PMN

Name Of Each Exchange  
On Which Registered  
The Nasdaq Capital Market

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act.

Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act.

Yes  No

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

Indicate by check mark whether the Registrant has submitted electronically; every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes  No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer  Accelerated filer  Non-accelerated filer  Smaller reporting company  Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report.

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements.

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b).

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes  No

Based on the closing price as reported on the Nasdaq Capital Market, the aggregate market value of the Registrant's Common Stock held by non-affiliates on June 30, 2023, the last day of its most recent completed second fiscal quarter, was approximately \$29.7 million. Shares of Common Stock held by each executive officer and director and by each shareholder affiliated with a director or an executive officer have been excluded from this calculation because such persons may be deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes. The number of outstanding Common Shares of the Registrant as of March 28, 2024 was 18,961,116.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's definitive proxy statement relating to its 2024 annual meeting of shareholders, or the 2024 Proxy Statement, are incorporated by reference into Part III of this Annual Report on Form 10-K where indicated. The 2024 Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days after the end of the fiscal year to which this report relates.

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## SUMMARY OF THE MATERIAL AND OTHER RISKS ASSOCIATED WITH OUR BUSINESS

Our business is subject to numerous material and other risks and uncertainties that you should be aware of in evaluating our business. These risks are described more fully in Item 1A – “Risk Factors” and include, but are not limited to, the following:

### Risks Related to the Development of Our Product Candidates

- Our product candidates are still in the early stages of development and there is significant uncertainty that any such products will actually be developed.
- We have concentrated a portion of our research and development efforts on the treatment of AD, a field that has seen very limited success in drug development.
- Our business is heavily dependent on the successful development, regulatory approval and commercialization of PMN310 and any future product candidates that we may develop or acquire, including PMN442 and PMN267.
- Nonclinical and clinical drug development involves a lengthy, expensive and uncertain process. The results of nonclinical studies and early clinical trials are not always predictive of future results. PMN310 or any other product candidate that we advance into clinical trials may not achieve favorable results in later clinical trials, if any, or receive marketing approval.
- Interim, “top-line” and preliminary results from our clinical trials that we announce or publish from time to time may change as more data become available and is subject to audit and verification procedures that could result in material changes in the final data.
- We cannot be certain that PMN310, PMN442, PMN267 or any of our future product candidates will receive regulatory approval, and without regulatory approval we will not be able to market our product candidates.

### Risks Related to the Commercialization of Our Product Candidates

- The market opportunities for PMN310, PMN442, PMN267, and future product candidates, if approved, may be smaller than we anticipate.
- Even if our current or future product candidates obtain regulatory approval, they may fail to achieve the broad degree of adoption and use by physicians, patients, hospitals, healthcare payors and others in the medical community necessary for commercial success.
- Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale. In particular, we will need to develop a larger scale manufacturing process to commercialize our potential products, which may not be successful.

### Risks Related to Our Financial Position and Capital Needs

- We have incurred losses since inception, we anticipate that we will incur continued losses for the foreseeable future and there is substantial doubt about our ability to continue as a going concern for the full one-year period following the issuance of the consolidated financial statements. We will require additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our development programs, commercialization efforts or other operations.
- We have no product candidates approved for commercial sale, we have never generated any revenue from product sales and we may never be profitable.

### Risks Related to Our Dependence on Third Parties

- We will rely on third parties to supply components, research, develop, test, and manufacture our product candidates and market, if approved. The loss of any of these third party relationships or the failure of any of them to meet their obligations to us could affect our ability to develop and obtain approval of our product candidates in a timely manner.

#### **Risks Related to Our Intellectual Property**

- If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, and other proprietary technologies we develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates, and other proprietary technologies if approved, may be adversely affected.
- If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties, or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.
- We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through in-licenses.

#### **Risks Related to Legal and Regulatory Compliance Matters**

- Our relationships with customers, healthcare providers, including physicians, and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.
- Even if we obtain regulatory approval for PMN310, PMN442, PMN267 or any future product candidates, they will remain subject to ongoing regulatory oversight, which may result in significant additional expense.

#### **Risks Related to Our Business and Industry**

- We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more effective than ours.
- If we fail to attract and retain senior management and key scientific personnel, our business may be materially and adversely affected.

#### **Risks Related to Ownership of Our Common Shares and Our Status as a U.S. Public Company**

- Investment in our Common Shares is speculative, involves risk, and there is no guarantee of a return.
- The price of our Common Shares may be volatile.
- Our issuance of additional capital stock in connection with financings, acquisitions, investments, our stock incentive plans or otherwise will dilute all other shareholders.
- Our internal controls over financial reporting may not be effective, which could have a material and adverse effect on our business.

#### **General Risk Factors**

- We are subject to the continued listing criteria of Nasdaq and our failure to satisfy these criteria may result in a delisting of our Common Shares.
- The elimination of monetary liability against our directors, officers, and employees under Canadian law and the existence of indemnification rights for our obligations to our directors, officers, and employees may result in substantial expenditures by us and may discourage lawsuits against our directors, officers, and employees.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Annual Report includes statements that express ProMIS' opinions, expectations, beliefs, plans, objectives, assumptions, or projections regarding future events or future results and therefore are, or may be deemed to be, "forward-looking statements." These forward-looking statements can generally be identified by the use of forward-looking terminology, including the terms "believes," "estimates," "anticipates," "expects," "seeks," "projects," "intends," "plans," "may," "will," or "should" or, in each case, their negative or other variations or comparable terminology. These forward-looking statements include all matters that are not historical facts. They appear in a number of places throughout this Annual Report and include statements regarding our intentions, beliefs or current expectations concerning, among other things, results of operations, financial condition, liquidity, our ability to continue as a going concern, patent term expiration dates, prospects, growth, strategies and the markets in which ProMIS operates. Such forward-looking statements are based on available current market material and management's expectations, beliefs and forecasts concerning future events impacting ProMIS. Factors that may impact such forward- looking statements include:

- the anticipated amount, timing and accounting of contingent, milestone, royalty and other payments under licensing or collaboration agreements;
- tax positions and contingencies; research and development costs; compensation and other selling, general and administrative expense;
- amortization of intangible assets;
- foreign currency exchange risk;
- estimated fair value of assets and liabilities; and impairment assessments;
- the potential impact of increased competition in the markets in which we compete;
- patent terms, patent term extensions, patent office actions and expected availability and period of regulatory exclusivity;
- our plans and investments in our portfolio as well as implementation of our corporate strategy;
- the risk that we will maintain enough liquidity to execute our business plan and our ability to continue as a going concern;
- our expected use of proceeds from sales of our common shares in "at-the-market" offerings and the period over which such proceeds, together with existing cash, will be sufficient to meet our operating needs;
- the drivers for growing our business, including our plans and intention to commit resources relating to discovery, research and development programs and business development opportunities as well as the potential benefits and results of, and the anticipated completion of, certain business development transactions;
- the expectations, development plans and anticipated timelines, including costs and timing of clinical trials, filings and approvals, of our products candidates and pipeline programs, including collaborations with third-parties, as well as the potential therapeutic scope of the development and commercialization of our and our collaborators' pipeline product candidates, if approved;
- the timing, outcome and impact of administrative, regulatory, legal and other proceedings related to our patents and other proprietary and intellectual property rights, tax audits, assessments and settlements, pricing matters, sales and promotional practices, product liability and other matters;
- our ability to finance our operations and business initiatives and obtain funding for such activities;

- the direct and indirect impact of health crises on our business and operations, including expenses, reserves and allowances, the supply chain, manufacturing, cyber-attacks or other privacy or data security incidents, research and development costs, clinical trials and employees;
- the impact of global financial, economic, political and health events, such as rising inflation, market volatility and fluctuating interest rates;
- the potential impact of healthcare reform in the United States and measures being taken worldwide designed to reduce healthcare costs and limit the overall level of government expenditures, including the impact of pricing actions and reduced reimbursement for our product candidates, if approved;
- the impact of the continued uncertainty of the credit and economic conditions in certain countries and our collection of accounts receivable in such countries;
- the risk that we become characterized as a passive foreign investment company;
- our ability to prevent and successfully remediate any significant deficiencies or material weaknesses in internal controls over financial reporting;
- lease commitments, purchase obligations and the timing and satisfaction of other contractual obligations; and
- the impact of new laws (including tax), regulatory requirements, judicial decisions and accounting standards.

The forward-looking statements contained in this Annual Report on Form 10-K are based on ProMIS' current expectations and beliefs concerning future developments and their potential effects on ProMIS. There can be no assurance that future developments affecting ProMIS will be those that ProMIS has anticipated. These forward-looking statements involve a number of risks, uncertainties, some of which are beyond ProMIS' control, or other assumptions that may cause actual results or performance to be materially different from those expressed or implied by these forward-looking statements. These risks and uncertainties include, but are not limited to, those factors described under the heading "Risk Factors." Should one or more of these risks or uncertainties materialize, or should any of the assumptions prove incorrect, actual results may vary in material respects from those projected in these forward-looking statements. Moreover, the occurrence of the events described in the "Risk Factors" section and elsewhere in this Annual Report on Form 10-K may adversely affect ProMIS. ProMIS will not undertake any obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required under applicable securities laws.



## PART I

### Item 1. Business

#### *Overview*

ProMIS has in-licensed a patented technology platform with the potential to deliver a portfolio of antibody therapies, therapeutic vaccines, and other therapies derived from antibodies for neurodegenerative diseases and other misfolded protein diseases, which may include Alzheimer's disease, multiple system atrophy, amyotrophic lateral sclerosis, frontotemporal lobar degeneration, progressive supranuclear palsy, corticobasal degeneration (respectively, AD, MSA, ALS, FTL, PSP, CBD) and schizophrenia. A common biologic cause contributes to each of these conditions, in that certain proteins, which normally perform a needed function, when misfolded, can cause neuronal degeneration and death, contributing to morbidity and mortality. ProMIS' technology platform is an example of the advances in drug discovery enabled by computational power, in silico discovery, and/or artificial intelligence. We believe this platform provides a potential advantage by selectively targeting the toxic misfolded proteins with therapeutics.

#### *ProMIS' Platform Technology*

ProMIS' scientific foundation is centered on the growing knowledge base relating to diseases characterized by the presence of abnormal, misfolded proteins. Genetic and experimental research in the neuroscience community has demonstrated that propagating, neurotoxic, misfolded proteins (also referred to as prion-like particles or toxic soluble oligomers) are fundamental drivers of multiple neurodegenerative diseases, including AD, MSA, and ALS. ProMIS' platform technology allows for the identification of conformational epitopes that become exposed on toxic, misfolded forms of a given protein but are not present on the properly folded form of the same protein. Such disease-specific epitopes (DSEs) can then be used to generate therapeutic antibody candidates that selectively target toxic forms of the protein without interfering with essential functions of the healthy protein.

The ability to model protein misfolding in silico to predict target epitopes restricted to toxic, misfolded forms of a protein was a transformational advance for the development of therapeutic antibodies in terms of speed and quality of the antibodies generated. Earlier methods using less defined immunogens, such as synthetic protein aggregates, relied on chance and extensive screening to identify promising antibody clones, and could never quite achieve strict selectivity for the toxic, misfolded protein. The Company first licensed exclusive rights to ProMIS™ target epitope identification technology from the University of British Columbia (UBC) to predict novel DSEs on the molecular surface of misfolded proteins. ProMIS™ is an “in silico” rational selection approach that could be applied to any protein where the normal folding structure is at least partially known. The Company subsequently acquired a worldwide license from UBC to “Collective Coordinates,” a computational algorithm that supersedes ProMIS™, employing thermodynamics and statistical mechanics to model protein misfolding. This proprietary computational discovery platform provides a unique and robust engine to predict DSEs on the molecular surface of misfolded proteins. The amino acid sequence of the toxic, misfolded form and the healthy, properly folded form of a target protein are the same but they differ in their conformation. The ProMIS platform offers the ability to identify targets (epitopes) unique to the toxic, misfolded form. Cyclic peptides containing the conformational epitopes are created and used to immunize mice or rabbits to generate selective monoclonal antibodies (mAbs) that are designed to attack the disease-causing form of the protein without interfering with the healthy form of the same protein. The mAbs raised in animals are humanized (the critical binding regions are inserted into a human antibody framework) for potential use in patients. We believe the ProMIS approach has the potential to produce more effective and safer antibodies compared to traditional methods of immunization with whole proteins/peptides or aggregates which result in pan-reactive antibodies that cross-react with all forms of a target protein. The lack of selectivity of such antibodies dilutes their efficacy by binding to non-toxic forms of the protein and can potentially interfere with the function of the properly folded protein.

#### *Our Pipeline*

We are developing a pipeline of antibodies aimed at selectively targeting misfolded toxic forms of proteins that drive neurodegenerative diseases without interfering with the essential functions of the same properly folded proteins.

Product Candidate	Target Protein	Disease Indication	Discovery	Pre-Clinical	Phase 1	Phase 2	Phase 3
PMN310	Amyloid-Beta	AD	→				
PMN267	TDP-43	ALS	→				
PMN442	Alpha-Synuclein	MSA <sup>1</sup>	→				

<sup>1</sup> The Company may consider additional synucleinopathies, including Parkinson's disease and Lewy Body dementia.

\* Arrows denote the stage of each program

**Additional Development Programs**

Product Candidate	Target Protein	Disease Indication	Discovery	Pre-Clinical	Phase 1	Phase 2	Phase 3
Discovery	RACK1	ALS <sup>2</sup> , HD	→				
Discovery	Tau	Alzheimer's <sup>2</sup> , FTL, PSP, CBD	→				
Discovery	DISC1+Interactome	Schizophrenia	→				
Discovery	Amyloid-Beta Vaccine	Alzheimer's Prevention	→				
Discovery	Alpha-Synuclein Vaccine	Synucleinopathies Prevention	→				

<sup>2</sup> Initial indication

\* Arrows denote the stage of each program

**ProMIS' Objectives for 2024**

The Company plans to pursue the following key objectives for 2024:

- Complete the Phase 1a clinical study with PMN310 in Healthy Volunteers
- Prepare for the Phase 1b clinical study with PMN310 in Alzheimer's patients
- Conduct further preclinical studies to support pipeline candidates

## **PRODUCT CANDIDATES**

### ***Development of a Therapy for the Treatment of Alzheimer's Disease (AD)***

#### ***AD Overview***

AD, a progressive neurodegenerative disease, is the most common type of dementia, accounting for approximately 60 – 80% of all dementia cases. Early symptoms of AD include recent memory loss, as well as apathy and depression. As the disease progresses inexorably, language deterioration, impaired ability to mentally manipulate visual information, poor judgment, confusion, restlessness, and profound mood swings develop. Eventually AD destroys cognition, personality, and the ability to function. The early symptoms of AD, especially at the inaugural stage of mild cognitive impairment (MCI), are often missed because they are frequently and mistakenly taken for natural signs of ageing. In 2020, reports concluded that 50% of primary care physicians believed the medical profession was not prepared to meet the expected increase in demands the projected rise in AD and dementia cases will create.

During 2023, it was estimated there were 6.7 million Americans 65 and older living with AD, and that number is projected to rise to 12.7 million by 2050 ([www.alz.org](http://www.alz.org), Alzheimer's disease Facts and Figures 2023). In the United States, one in three seniors dies of AD or another dementia, which kills more people than breast cancer and prostate cancer combined. AD is the sixth leading cause of death in the United States, according to the Alzheimer's Association. In 2023, AD and other dementias cost the U.S. \$592 billion, and those costs are projected to rise with the increasing number of patients. Approximately 11 million Americans are reported to be unpaid caregivers, who in 2022 provided support for patients valued at \$339 billion, to people with AD and other dementias.

Historically, a major challenge in AD has been diagnosis. Twenty years ago, diagnosis of AD could only be confirmed by autopsy. Consensus guidelines have since been developed that established new diagnostic criteria — A/T/N. The methods used are based on sophisticated approaches to brain imaging: amyloid positron emission tomography (PET) scans measuring amyloid plaque as a proxy for pathology, tau PET scans measuring tau tangles as a proxy for pathology, and cortical magnetic resonance imaging measuring cortical atrophy as a measure of neurodegeneration. Each of these tests costs thousands of dollars, affordable perhaps to diagnose patients for a clinical trial, but not practical for screening millions of people who might be at risk or have pre-symptomatic AD.

There are now blood-based biomarkers (diagnostic assays) that can provide information that correlates with expensive A/T/N imaging. Plasma levels of p217 tau and p181 tau (tau protein phosphorylated at amino acids 217 and 181 respectively) correlate with brain imaging measures, AD diagnosis, and progression (Mattson et al. JAMA 2023, Jack et al. Brain 2023, Therriant et al. JAMA 2023). These advances have implications for ProMIS' strategy. Better diagnostics can facilitate more efficient clinical trials, both in terms of identifying potential subjects for the trial and also detecting a potential treatment effect in early, small trials. Secondly, the ability to diagnose disease prior to symptoms raises the possibility of preventive treatment.

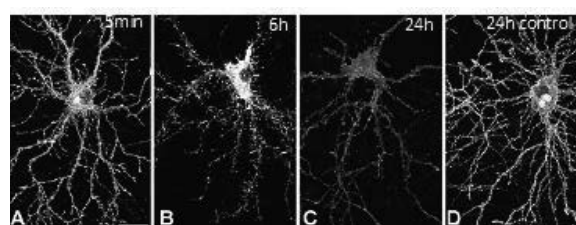
According to the World Alzheimer Report 2022, the current dementia market comprises two product categories, namely, AChE inhibitors and N-methyl-D-aspartate receptor antagonists. AChE inhibitors dominate the market. The overall market is dominated by four leading brands — Aricept, Namenda, Exelon and Ebixa. Aricept, whose active ingredient is an AChE inhibitor, holds the largest market share. North America was the largest market for AD drugs in 2019, accounting for approximately 35% of total worldwide AD pharmaceutical sales in that year. Two mAbs (Aduhelm, Leqembi) were approved in 2021 and 2022 under the U.S. Food and Drug Administration's (the FDA) Accelerated Approval pathway, which creates a third category of marketed AD treatments, and the first to be considered disease modifying. Commercialization of Aduhelm was discontinued in January 2024.

Although there is no scientific consensus on the causation of AD or method of action to treat AD, evidence from some genetic and preclinical studies suggests a causative role for A $\beta$  in the pathogenesis of AD. Published genetic studies support a direct link between increased levels of A $\beta$  and disease susceptibility. Research suggests that genetic mutations in the A $\beta$  precursor protein (APP) and in the presenilin 1 and 2 genes responsible for familial forms of early onset AD all result in increased production of A $\beta$  and A $\beta$  aggregates (*Citron et al, 1992; Borchelt et al, 1996*). Down Syndrome patients with three copies of the APP gene on chromosome 21 also have elevated levels of APP and A $\beta$  deposits and often develop AD

at a premature age (Podlisny *et al.*, 1987). A $\beta$  brain concentration can also increase due to age associated reduction on clearance. Along the same lines, the APOE4 allele, which has been linked to an increased risk of late onset AD, is associated with increased A $\beta$  deposit, while the APOE2 allele, which has been linked to a decreased risk, is associated with decreased A $\beta$  levels (Holtzman *et al.*, 2012). Finally, the only known protective mutation against AD is found in the APP gene and research suggests that this leads to a reduction in the formation of A $\beta$  (Jonsson *et al.*, 2012). In a preclinical study, it was reported that intracerebral injection of A $\beta$ -containing brain extracts from human AD patients into susceptible mice induced cerebral amyloidosis and associated pathology. Depletion of A $\beta$  from the extracts reversed this activity, supporting a link between A $\beta$  and disease induction (Meyer-Luehmann *et al.*, 2006).

While the presence of A $\beta$  plaque is a distinguishing feature of AD, there is a growing body of scientific evidence that the synaptic loss and neurodegenerative spread of AD is primarily mediated by soluble oligomers of misfolded A $\beta$  rather than plaque (Cleary *et al.*, 2004; Jin *et al.*, 2011). Reports from several groups indicate that plaque burden correlates poorly with memory impairment (Cleary *et al.*, 2004; Ferreira *et al.*, 2015) and insoluble A $\beta$  fibrils show little or no demonstrable toxicity *in vitro* or *in vivo* (Balducci *et al.*, 2010; Shankar *et al.*, 2008). In contrast, a significant correlation between disease severity and levels of soluble A $\beta$  in the central nervous system was reported by Lue *et al.* (Lue *et al.*, 1999), and the direct neurotoxicity of soluble A $\beta$  oligomers was demonstrated in neuronal cultures *in vitro* by separate groups (Lauren *et al.*, 2009; Jin *et al.*, 2011). In published reports using rodent models, the injection of soluble oligomeric A $\beta$ , but not soluble monomers or plaque, was shown to induce synaptic damage and cognitive dysfunction (Cleary *et al.*, 2005; Hong *et al.*, 2016).

Figure 1



Synaptotoxicity of A $\beta$  oligomers on hippocampal neurons *in vitro* (Lacor *et al.*, 2007, *J Neuroscience*)

The mechanism by which soluble oligomeric A $\beta$  generates neuronal damage contributing to AD has been elucidated. A convergence of evidence from multiple studies suggests that the progressive nature of AD arises from the formation and spread of a prion-like subset of misfolded oligomers of A $\beta$  that adopt a  $\beta$ -sheet-rich conformation transmissible to native A $\beta$  in a template-like manner. The self-propagation of these prion-like oligomers follows the stereotypical progression of AD, with initial involvement of the entorhinal cortex followed by spreading to the hippocampus and neocortex as described by Khan *et al.* (Khan *et al.*, 2014). The prion-like spread of A $\beta$  oligomers has been well-documented in animal models by different groups following the injection of purified oligomers or brain extracts from AD patients or diseased animals (Cleary *et al.*, 2005; Meyer-Luehmann *et al.*, 2006; Watts *et al.*, 2014; Hong *et al.*, 2016). There is also *in vitro* evidence that such misfolded “A $\beta$  prions” from AD brain can catalyze the misfolding and hyperphosphorylation of tau, another protein involved in the pathogenesis of AD as reported by Jin *et al.* (Jin *et al.*, 2011). Targeting of A $\beta$  oligomers therefore represents an attractive strategy to inhibit progression of the neurodegenerative A $\beta$ -Tau cascade (Choi *et al.*, 2015; Khan *et al.*, 2014).

## PMN310

ProMIS' lead therapeutic program is PMN310, a mAb designed to treat AD by selectively targeting the toxic misfolded form of A $\beta$ . Based on the understanding of A $\beta$  biology described above, PMN310 was designed to be more selective for the toxic oligomer of amyloid than other anti-A $\beta$  antibodies such as aducanumab from Biogen, lecanemab, co-developed by Eisai Co. and Biogen, donanemab from Lilly, ACU193 from Acumen and the Prothena PRX012 antibody. These antibodies bind oligomers, but also plaque. This off-target binding of plaque frequently leads to a side effect, ARIA-E and, potentially, limits the benefit of aducanumab and lecanemab by both limiting the highest dose that can be safely administered and by "wasting" a substantial portion of the administered antibody which binds plaque, reducing what is available to neutralize the toxic oligomers.

Recent clinical trial results show that antibodies that bind A $\beta$  monomers (bapineuzumab, solanezumab, crenezumab, gantenerumab) are not efficacious in AD (Salloway et al, 2014, *NEJM*; Carlson et al, 2016, *Alzheimer's and Dementia*; Ostrowitzki et al, 2022, *JAMA Neurol*; <https://www.roche.com/media/releases/med-cor-2022-11-14>), suggesting that high selectivity for low abundance toxic A $\beta$ O is desirable to prevent mAbs from being consumed by unproductive binding to non-pathogenic, abundant monomers (target distraction). Other antibodies with reduced binding to monomers and more selectivity for aggregated A $\beta$  have produced more promising results, including aducanumab and lecanemab, which have both received Accelerated Approval from the FDA, and donanemab, which showed evidence of a cognitive benefit in Phase 3 trials. However, treatment with all of these antibodies was associated with the dose-limiting adverse events of ARIA-E (brain edema) and ARIA-H (microhemorrhages) correlated with binding to insoluble deposits of A $\beta$  in the vasculature and plaque. We believe that a selective, oligomer-specific antibody that does not bind monomers or plaque could circumvent these issues and potentially provide an improved product profile with enhanced efficacy. In July 2022, we presented results at the Alzheimers' Association International Conference of our analysis of the binding response of A $\beta$ -directed antibodies (aducanumab, lecanemab, donanemab, crenezumab, solanezumab). All antibodies showed some binding signal to toxic A $\beta$ O from human brain extracts but target distraction by monomers abolished or reduced binding. Only the antibodies that retained measurable binding to oligomers (aducanumab, donanemab and lecanemab) in the face of competition by monomers have shown improvement on cognitive endpoints in previous clinical trials, and that improvement was modest. In our analysis, PMN310 avoided monomer target distraction, with the smallest percent inhibition of binding to brain oligomers when compared to other A $\beta$ -directed antibodies. We believe these data support the therapeutic potential of PMN310.

Development of PMN310 began with using the ProMIS computational platform, which produced *in silico* six different conformational epitopes as potential targets exposed on toxic misfolded A $\beta$ O but not A $\beta$  monomers or plaque. The use of A $\beta$ O-restricted epitopes as the immunogen to generate antibodies is drastically different from the conventional immunization methods used by others. Immunization with A $\beta$  peptide or synthetic aggregates used by others to generate A $\beta$ -directed antibodies virtually always results in non-selective antibodies that react not only with oligomers but also to varying degrees with monomers and plaque. In contrast, mAbs raised against cyclic peptides containing our predicted A $\beta$ O conformational epitopes displayed selectivity for A $\beta$  oligomers vs monomers or plaque, and inhibited A $\beta$ O toxicity and propagation *in vitro*. The Company designated the PMN310 antibody as its lead candidate for development in AD. As described in our published preclinical studies (Gibbs et al., 2019, *Scientific Reports*), PMN310 displayed the desired selective profile with binding to synthetic A $\beta$ O and little or no binding to A $\beta$  monomers as determined by surface plasmon resonance (SPR), and no detectable binding to plaque or vascular deposits in AD brain sections as determined by immunohistochemistry (IHC). In SPR studies with brain extracts from multiple individuals who died of AD, PMN310 also showed binding to fractions containing the toxic A $\beta$ O species suggesting that PMN310 can recognize an A $\beta$ O epitope shared across AD brains. *In vitro*, PMN310 inhibited A $\beta$ O propagation in a thioflavin-T (ThT) based assay measuring the formation of A $\beta$  aggregates with a beta-sheet structure over time (Gibbs et al, 2019, *Scientific Reports*). PMN310 also reduced the killing of primary mouse neurons by toxic A $\beta$ O in culture (Fig.1). *In vivo*, the activity of murine PMN310 was tested in two different models. In one model conducted at SynAging (Vandoeuvre-les-Nancy, France), PMN310 and a preparation of toxic A $\beta$ O were co-delivered (mAb:A $\beta$ O ratio of 2:1) by intracerebroventricular (ICV) injection into male, 3-month old, wild-type C57Bl6/J mouse to determine whether PMN310 might improve cognitive performance and molecular markers in this model of A $\beta$ O-induced neurotoxicity. Treatment groups consisted of day 0 ICV injection of vehicle alone, A $\beta$ O alone, vehicle with PMN310 or A $\beta$ O with PMN310, and contained 12 mice per group to achieve statistical significance. Cognitive performance was assessed on days 7 – 8 using the novel object recognition (NOR) assay. Mice were sacrificed and perfused on day 10, the hippocampus was isolated and levels of synaptic (PSD-95, SNAP25)

and inflammation (TNF- $\alpha$ ) markers were measured by ELISA in hippocampal homogenates from individual mice. A $\beta$ O-injected mice failed to recognize a new object and displayed a discrimination index of 0 or less. Co-injection of PMN310 with the toxic oligomers prevented this cognitive deficit. As expected, ICV injection of PMN310 alone had no effect (Fig. 2). The cognitive deficit induced by ICV injection of A $\beta$ O was associated with inflammation and synaptic damage in the hippocampus, a region important in the development of memory. Hippocampal homogenates from A $\beta$ O-treated mice displayed an increase in levels of TNF- $\alpha$  and decreases in PSD-95 and SNAP25. Partial protection from these changes was observed in mice co-injected with synthetic A $\beta$ O and PMN310.

Figure 2

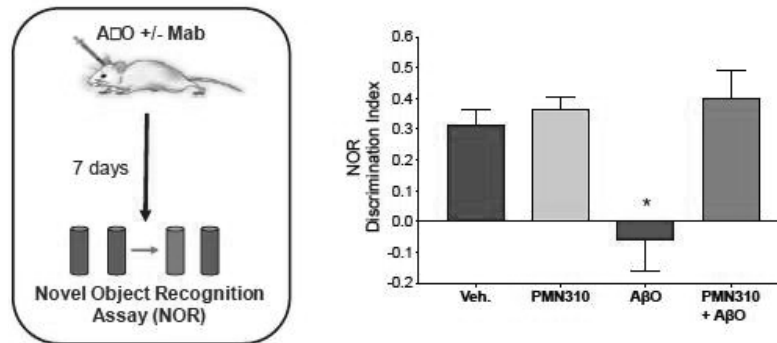


Fig. 2. Administration of PMN310 to mice prevented the loss of short-term memory formation caused by toxic A $\beta$ O.

\* $p < 0.05$  vs Vehicle, # $p < 0.05$  vs A $\beta$ O. Discrimination index = (time exploring new object – time exploring familiar object)/total exploration time.

In a second *in vivo* model conducted at reMYND (Leuven, Belgium), the potential effect of treatment with murine PMN310 (mouse IgG2a) was tested in the transgenic (Tg) hAPP[V717I] mouse model of AD. Characterization of the model indicates that these hAPP-Tg mice display spontaneous, progressive accumulation of A $\beta$  in the brain, eventually resulting in amyloid plaques around 10-11 months of age. In the pre-plaque stage of the pathology, there is a clear cognitive and long-term synaptic potentiation (LTP) deficit in these mice suggesting that impairment is caused by soluble toxic species such as A $\beta$ O rather than plaque. The aim of the study was to assess the impact of seven weekly doses of PMN310 administered intraperitoneally (i.p.) at 30 mg/kg to female mice, beginning at 5.0 months of age. Experimental groups consisted of hAPP-Tg mice treated with vehicle or PMN310, and non-Tg, age-matched littermates treated with vehicle as a control, with 17 mice per group to achieve statistical significance. Spatial learning and memory performance were assessed using the Morris Water Maze task at 6.4 months of age (after seven doses of antibody) which measures the ability of mice to learn and remember the location of a hidden platform in a pool of water. Compared to non-Tg littermates, the hAPP-Tg mice were significantly impaired and showed an increase in both escape latency (time required to find the hidden platform,  $p = 0.0024$ ) and the search path or distance traveled to reach the platform ( $p = 0.0047$ ). Treatment of hAPP-Tg mice with PMN310 significantly improved these outcomes with a decrease in escape latency ( $p = 0.0187$ ) and search path ( $p = 0.0071$ ) (Fig. 3).

Figure 3

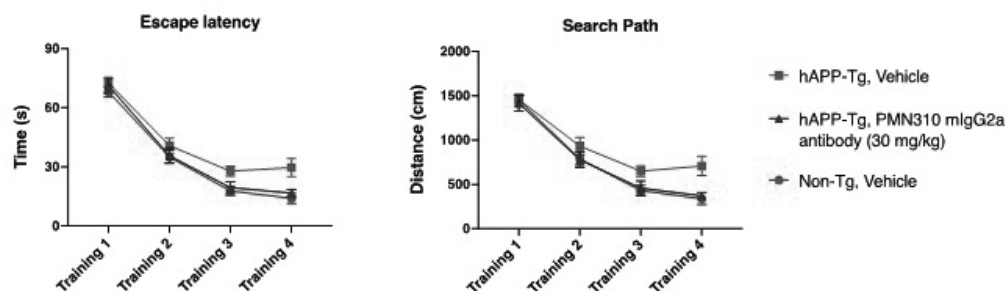


Fig. 3. Systemic administration of PMN310 provides a cognitive benefit in a mouse model of AD (hAPP[V717I] Tg mice)

PMN310 brain exposure and kinetics after systemic i.p. administration were assessed in mice (*Gibbs et al., 2019, Scientific Reports*). In one study conducted by ProMIS, aged 15-17 month old wild type littermates of APP/PS1 mice, received a single 30 mg/kg i.p. injection of humanized PMN310 (n=4), aducanumab (n=3) or PBS as a negative control (n=2). Levels of human IgG present in the plasma and perfused brains were measured 24 hours later by ELISA. Equivalent amounts of PMN310 and aducanumab were detected in plasma and brain demonstrating a comparable degree of CNS penetrance (p=0.28) in the range of ~0.3%. As expected, no human IgG was detected in mice injected with PBS alone. Additionally, a study was conducted by ProMIS in aged (13-17 months old) transgenic APP/PS1 mice in order to assess the time course of CNS exposure to PMN310. Plasma and brain levels of human IgG were measured by ELISA on days 1, 7, 14 and 21 after i.p. administration of 30 mg/kg PMN310 (n=4-6 per time point). In spite of declining plasma levels (p=0.0016 for day 1 vs day 7, p<0.0001 for day 1 vs days 14 and 21), CNS levels of PMN310 were detectable out to the study endpoint at day 21, with no significant difference in brain levels at the different time points. These results suggest that PMN310 is comparable to other therapeutic mAbs and is able to cross the blood-brain barrier to reach its target. The Company believes that the greater selectivity of PMN310 for A $\beta$ O may result in greater neutralization of this disease-causing species (no target distraction) compared with A $\beta$  antibodies derived from immunization with synthetic aggregates. By avoiding plaque binding, PMN310 may also lower the risk of the ARIA adverse events that have been reported associated with plaque-binding antibodies and allow for higher doses to treat the dementia.

The Company has conducted a GLP toxicology study in cynomolgus monkeys. PMN310 was administered as a 30-minute IV infusion, on a weekly basis (Days 1, 8, 15, 22, and 29), at dose levels of 0, 200, 500, and 1,200 mg/kg/day. Administration of PMN310 was not associated with any adverse effects on clinical observations (local or systemic), body weight, food consumption, ECG, or hematology, coagulation, or urinalysis endpoints. No organ weight effects, macroscopic observations, or microscopic observations were attributed to PMN310 treatment at any doses. PMN310-related changes in clinical chemistry parameters were limited to mildly to moderately increased globulins (1.31x-2.00x) at 1200 mg/kg on Days 2 and 30 likely resulting from circulating PMN310 given one day prior. Based on the results of this study, the PMN310 NOAEL was considered to be 1,200 mg/kg/day in nonhuman primates when administered as a weekly 30-minute IV infusion over four weeks, which is five times higher than the comparable dose in humans that will be used in our Phase 1 trials.

#### Clinical Development Plan

The Company successfully manufactured PMN310 clinical supply under cGMP conditions and received clearance on its IND application with the FDA in May 2023 to initiate a Phase 1a clinical trial of PMN310. The Phase 1a trial was initiated in November 2023 as a placebo-controlled single ascending dose (SAD) trial in healthy volunteers testing single intravenous doses of PMN310 escalating from 2.5 to 40 mg/kg in 2-fold increments, and potentially up to 60 mg/kg in adults. Each dosing cohort consists of 6 drug-treated and 2 placebo-treated subjects. Results of the Phase 1a trial will provide a safety and tolerability assessment across a wide dose range and enable dose selection for a Phase 1b, multiple

ascending dose (MAD) study in AD patients. Assessment of PMN310 levels in CSF will also be leveraged to determine well-tolerated dose(s) that achieve concentrations required for target engagement. Phase 1a data are expected in mid-2024.

Pending review by the FDA of the trial design, the planned Phase 1b MAD trial will consist of two phases. The first phase is a 6-month double-blind, placebo-controlled monthly intravenous dosing of PMN310 in the 5-40 mg/kg range with approximately 3 dosing cohorts at a 2:1 ratio of drug- to placebo-treated patients and a total of approximately 80 patients. Dose selection will be informed by results from the Phase 1a SAD study. The second phase is a 6-month open label extension (OLE) phase at the same dose levels. Safety will be a primary outcome with particular emphasis on assessing the expectation that, as a non-plaque binder, PMN310 will have a reduced risk of ARIA. The study will be powered to provide 95% confidence for detection of ARIA. Plasma and CSF biomarkers which have been reported to reflect treatment effects in the timeframe of the planned study (p-tau, GFAP, neurogranin, etc) will be measured as early indicators of potential efficacy. Cognition endpoints will also be measured and could potentially reveal trends for a treatment effect. Subject to feedback from the FDA and securing the necessary capital, initiation of the Phase 1b trial is expected in 2H'24.

### ***Development of a Therapy for the Treatment of Amyotrophic Lateral Sclerosis***

#### ***ALS Overview***

Amyotrophic lateral sclerosis (ALS), commonly known as Lou Gehrig's Disease, is a progressive neurodegenerative disease that causes muscle weakness, paralysis and, ultimately, respiratory failure leading to death. ALS attacks randomly, and occurs throughout the world with no racial, ethnic or socioeconomic boundaries. It is estimated there are currently 30,000 people in the United States and 450,000 people worldwide, suffering from ALS, with approximately 5,000 new cases arising in the United States annually. Patients with ALS present symptoms such as progressive weakness, muscle atrophy and spasticity. These neurodegenerative and neuromuscular symptoms arise due to the ultimate degeneration of motor neurons in the spinal cord, the brain stem and in the brain cortex. Incurable and usually fatal within five years, ALS gradually robs a patient of the ability to walk, talk and breathe. Currently, there is no confirmatory test for ALS and many people go undiagnosed at early phases of the disease. Approximately two-thirds of those afflicted by ALS are currently undergoing some form of symptomatic treatment. There are no therapies approved that halt or significantly slow progression.

The biological mechanisms that cause ALS are only partially understood. Misfolded, aggregated TDP-43 forming inside neurons has been implicated in the pathogenesis of ALS (as well as frontotemporal lobe dementia or FTL, and limbic-predominant age-related TDP-43 encephalopathy or LATE) through direct toxicity, loss of function of normal TDP-43, induction of misfolding of other neuronal proteins, and prion-like, cell-to-cell propagation of disease.

Experimentally, misfolded aggregates of TDP-43 are toxic to neural cells, and the prion-like propagation of TDP-43 aggregates has been demonstrated in cell culture and animal models. Importantly, misfolded TDP-43 has been found to induce the misfolding of other proteins into pathogenic aggregates (e.g., SOD1, nuclear pore proteins and transport proteins, DISC1), such that targeting misfolded TDP-43 potentially represents an opportunity to not only neutralize TDP-43 pathology but also interrupt this pathogenic interactome.

#### ***PMN267***

Using the ProMIS discovery platform, we identified epitopes present on misfolded TDP-43 and generated high affinity antibodies (Fig. 4) that selectively recognized misfolded cytoplasmic aggregates of TDP-43 with no detectable interaction with normal TDP-43. Normal TDP-43 is located in the nucleus and is important for normal cell function (Fig. 5). The antibodies recognized and stained pathogenic TDP-43 aggregates in spinal cord sections from ALS patients and brain sections from FTL patients (immunohistochemistry) indicating that they have the potential to target disease-causing TDP-43. *In vitro* data showed that such antibodies can inhibit the cell-to-cell transmission of misfolded TDP-43 in the extracellular space thereby offering the potential to inhibit spreading of pathology (Fig. 6).



Figure 4

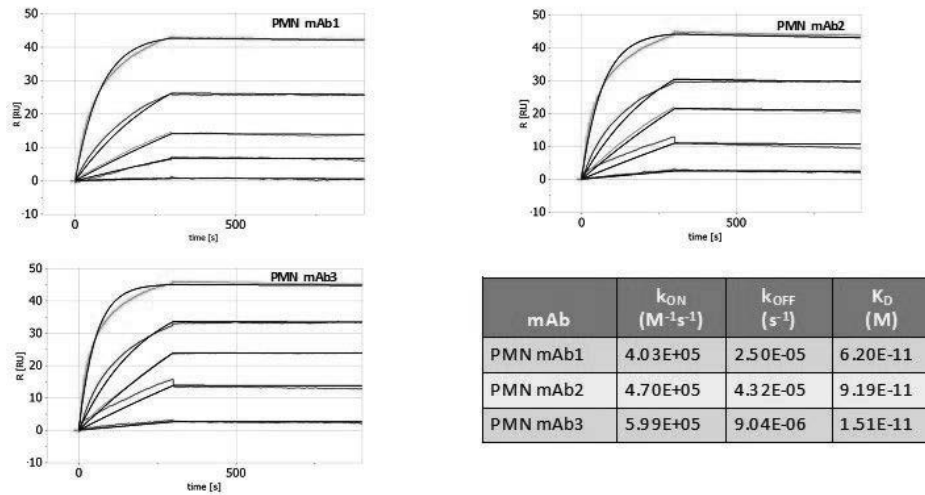


Fig. 4. High affinity mAbs. In SPR studies, serial dilutions of test mAbs were flowed over the target epitope immobilized on sensorchips to assess the binding kinetics and affinity. Binding curves were fitted to a Langmuir 1:1 interaction model.

Figure 5

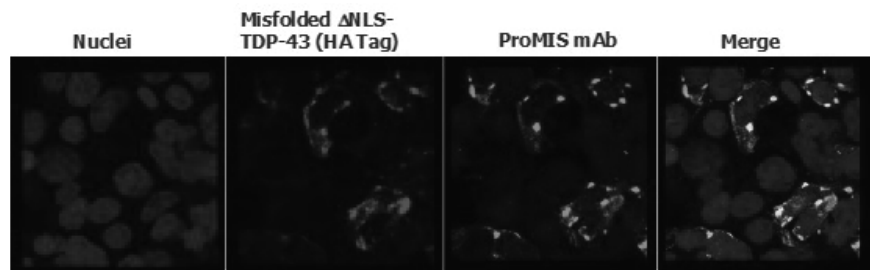


Fig. 5. Selective binding of mAb to misfolded, cytoplasmic aggregates of TDP-43. Staining of HEK293 cells transfected with mutant TDP-43 shows cytoplasmic aggregates of misfolded TDP-43 (red). Staining of the same cells with a PMN mAb (green) shows co-localization with TDP-43 aggregates with no staining of endogenous, normal TDP-43 in the nucleus (nuclei stained blue).

Figure 6

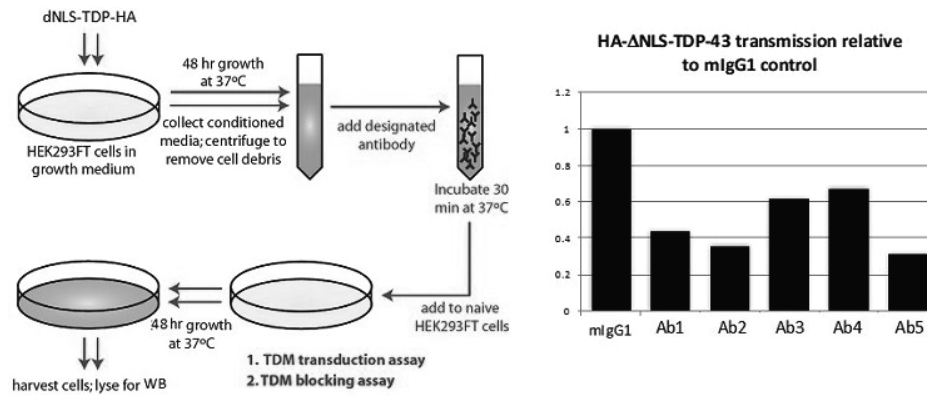


Fig. 6. Inhibition of cell-to-cell transmission of misfolded TDP-43 by mAbs. Supernatant from HEK293 cells transfected with misfolding mutant TDP-43 was incubated with test antibodies and added to naïve recipient cells to assess transmission of misfolding TDP-43 (HA-tagged). Compared to a mouse IgG1 negative control (mIgG1), several mAbs inhibited transmission to recipient cells as determined by a reduction in the density of the HA band on a Western blot of recipient cell lysate.

A complementary approach is to target intracellular TDP-43 to reduce toxic gains-of-function within the cell by generating intrabody versions of the TDP-43 antibodies. Intrabodies (from intracellular and antibody) are expressed from within the cell and were designed to target intracellular aggregates of TDP-43. Testing indicated that intrabodies expressed inside HEK293 cells associated selectively with pathogenic aggregates of TDP-43 in the cytoplasm (Fig. 7) and promoted degradation of the aggregates without affecting normal TDP-43 function or harming the cells (Fig. 8).

Figure 7

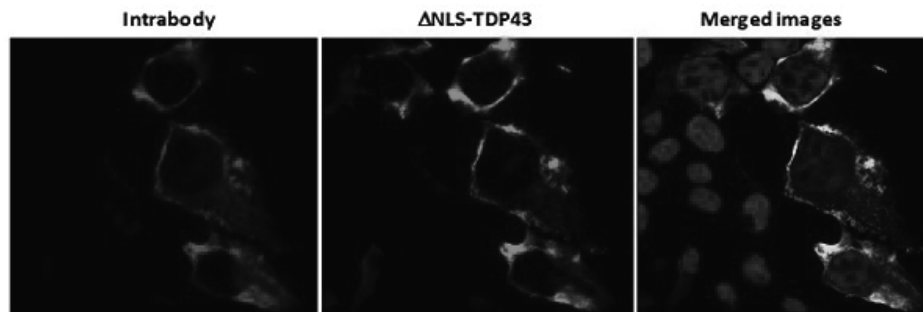


Fig. 7. Co-localization of intrabody with misfolded, cytoplasmic aggregates of TDP-43. Staining of HEK293 cells co-transfected with mutant TDP-43 (green) and plasmid encoding a PMN intrabody (red) shows co-localization of the two. There was no interaction of the intrabody with endogenous, normal TDP-43 in the nucleus (nuclei stained blue).

Figure 8

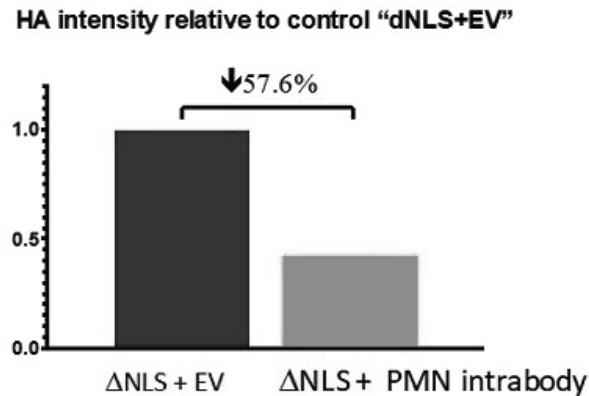


Fig. 8. Clearance of TDP-43 aggregates by intrabody. Transfection of HEK293 cells with a ProMIS intrabody results in degradation of HA-tagged mutant TDP-43 ( $\Delta$ NLS) aggregates as measured by reduction in the density of the HA band on a Western blot of cell lysate compared to an empty vector (EV) control.

These results support the potential for using this mAb to selectively target and protect against pathogenic TDP-43. We believe the extracellular antibody could be used to interfere with the cell-to-cell spread of misfolded aggregates of TDP-43 in the extracellular space and slow disease progression, or it could be combined with intrabody constructs delivered inside the cells via viral vectors to degrade intracellular aggregates and prevent further propagation.

The mAbs for TDP-43 generated using the ProMIS platform were tested for selective reactivity with misfolded TDP-43 aggregates and protective activity. Screening of multiple mAbs yielded PMN267 as the lead candidate exhibiting the desired properties. PMN267 bound its target epitope with high affinity in the 10E-11M range. In a cell system, PMN267 showed selective recognition of misfolded, cytoplasmic TDP-43 aggregates and no detectable interaction with endogenous normal TDP-43 in the nucleus. Similarly, PMN267 did not react with TDP-43 in stress granules, which are important in protection against oxidative stress. PMN267 also showed binding to exosomes derived from the brains of deceased FTL D individuals. Systemic IP delivery of PMN267 was tested in a transgenic mouse model of ALS/FTLD. In this model, doxycycline-regulated expression of human  $\Delta$ NLS-TDP-43 is under control of the neurofilament heavy chain promoter such that progression of disease is driven by intracellular expression of aggregating  $\Delta$ NLS-TDP-43 in all neurons, with little or no contribution of cell-to-cell spread of aggregates. In this aggressive model, a trend for improvement was observed with PMN267 treatment (30 mg/kg/week for 9 weeks) in the majority of motor function read-outs evaluated, including hind limb clasping, hind limb paralysis, grill test of agility, paw coordination, and footfall pattern. We believe the results suggest evidence of protection against motor function deficits by systemic, extracellular delivery of PMN267.

An intrabody version of PMN267 (single chain antibody sequence encoded into a plasmid) expressed from within cells showed co-localization with cytoplasmic aggregates of TDP-43 and no detectable binding to normal, nuclear TDP-43. Expression of the intrabody promoted degradation of misfolded TDP-43 aggregates in the HEK293 cell system by approximately 58% (Fig. 7). *In vitro* studies were also performed in collaboration with Dr. Gene Yeo at University of California, San Diego using iPSC-derived motor neurons from ALS patients, the cell type predominantly affected in ALS. In these studies, neurons transduced with vectorized PMN267 intrabody or a control protein (luciferase) were subjected to prolonged stress by puromycin-induced suppression of protein synthesis for 24 hours, giving rise to TDP-43 aggregates that persisted after another 24 hours of recovery. Neurons expressing PMN267 intrabody compared to control protein showed a 30-60% reduction in the amount of stress-induced TDP-43 aggregates as quantitated by high-content imaging. The Company believes that the observed selectivity of PMN267 for misfolded TDP-43 and avoidance of normal TDP-43 has the potential to allow for inhibition of disease without compromising essential TDP-43 function. PMN267 has been

humanized in a human IgG1 framework for IND-enabling studies to support the systemic, extracellular administration form. Development of the intrabody form would involve collaboration with a partner with expertise in viral vectorization.

### **Development of a Therapy for the Treatment of Multiple System Atrophy**

#### **MSA Overview**

Multiple system atrophy (MSA) is a rare neurodegenerative disease with an estimated prevalence of 3.4 – 4.9 cases per 100,000 population. MSA is characterized by rapidly progressive autonomic failure and motor symptoms with predominant parkinsonian features (MSA-P) or dominant cerebellar features (MSA-C). There is no effective treatment and the mean survival from the onset of symptoms is 6 – 10 years. Histologically, the disease is characterized by alpha-synuclein (a-syn) aggregates in the cytoplasm of oligodendrocytes and, to a lesser extent, in neurons and other glial cells. Published research shows that misfolded toxic a-syn aggregates can trigger the misfolding of normal a-syn into aggregated forms in a prion-like manner. This process can propagate within cells and then spread to other cells that are local or synaptically connected. A-syn aggregates from MSA brain homogenates have been demonstrated to cause MSA-like neurodegeneration in mice. The characteristics of MSA, although devastating for the patients, present several advantages for clinical development: disease progression is rapid allowing for earlier detection of therapeutic potential; high levels of neurofilament light chain (NFL) in serum represent a potential biomarker for inhibition of neuronal damage; and no placebo effects have been observed in clinical trials to date. Even though MSA is a rare disease, recruitment for clinical trials of other candidates has been facilitated by the unmet need and existence of a global MSA Registry (GLOMAR), along with supporting organizations.

Toxic aggregates of misfolded a-syn are also believed to be involved in the pathogenesis of Parkinson's disease (PD) and Lewy body dementia (DLB).

PD is a progressive neurodegenerative disorder characterized by loss of dopaminergic neurons located in the midbrain and the presence of intraneuronal inclusions (Lewy bodies/Lewy neurites) consisting mainly of aggregates of a-syn. Accumulation of insoluble a-syn fibrils in the brain is also observed in LBD. While these insoluble a-syn deposits are characteristic of the disease, recent evidence suggests that a-syn toxicity resides primarily with soluble oligomers and small seeding fibrils (*Fusco et al, 2017, Science; Westphal & Chandra, 2013, J Biol Chem*). Our candidate antibody against misfolded a-syn could also be directed towards these disorders.

#### **PMN442**

Multiple studies indicate that pathogenic aggregates of a-syn can propagate from cell-to-cell in a prion-like manner causing progressive neuronal damage and disease symptoms. Using the ProMIS platform, several conformational epitopes were identified as likely to become exposed on misfolded, pathogenic forms of a-syn (toxic oligomers and soluble seeding fibrils). MAbS were raised against these epitopes and were tested for the desired binding profile and ability to protect neurons against toxic a-syn species *in vitro*. Traditional methods are unable to generate antibodies with adequate precision to selectively target these neurotoxic forms of a-syn. ProMIS is using its proprietary technology platform for generating and developing antibodies that can uniquely and precisely target these specific toxic forms. As illustrated in figure 9, ProMIS mAbS showed the ability to selectively bind the pathogenic forms of a-syn (toxic oligomers and small soluble fibrils) but not a-syn monomers that play an important functional role in the brain.

Figure 9

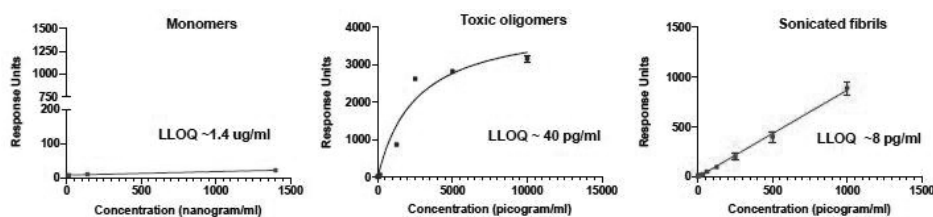


Fig. 9. Selectivity of mAbs for pathogenic species of a-syn. The binding response of a representative mAb to various concentrations of a-syn monomers, toxic oligomers and soluble fibrils (sonicated PFFs) measured in a Millipore immunoassay. Mean  $\pm$  SD of triplicates shown with the calculated lower limit of quantitation (LLOQ) for each species.

Multiple mAbs were screened and PMN442 emerged as the lead candidate and PMN411 as a back-up with the desired characteristics for this program. As measured by surface plasmon resonance (SPR), PMN442 showed robust binding to toxic a-syn oligomers and seeding fibrils, with negligible binding to a-syn monomers and physiologic tetramers which are required for normal neuronal function (Figure 10). PMN442 also reacted with native toxic a-syn present in brain homogenates from individuals with MSA and DLB (Figure 11).

Figure 10

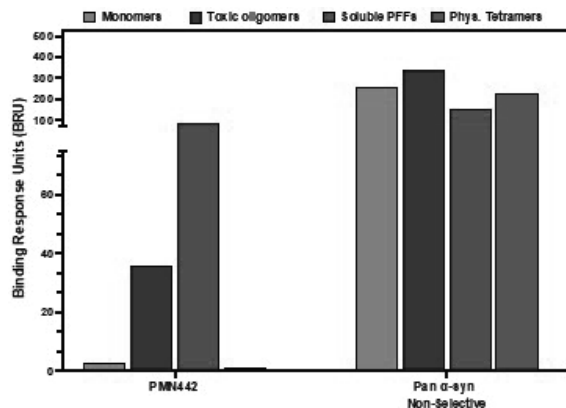


Fig. 10. Selective binding of PMN442 to pathogenic species of a-syn by SPR. The binding response of immobilized PMN442 to a-syn monomers, toxic oligomers, soluble (seeding) preformed fibrils (PFFs) and physiologic (Phys.) tetramers was measured by SPR. The same pattern of binding was observed in 4 independent experiments.

Figure 11

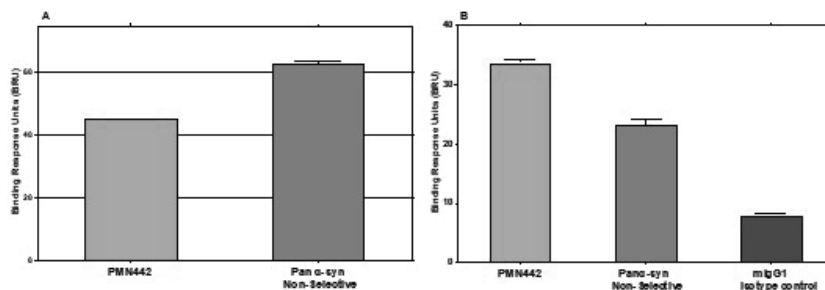


Fig. 11. Binding to native pathogenic a-syn species in patient brain extract. The binding response of immobilized PMN442 to a-syn in brain extract from dementia with Lewy bodies (DLB) (A) and MSA (B) patients was measured by SPR. A pan a-syn reactive antibody and mouse IgG1 (mIgG1) were used as controls. Results shown are the mean  $\pm$  SEM of two (A) or four (B) independent studies.

In activity assays, PMN442 protected rat dopaminergic neurons against neuronal death by a-syn toxic oligomers (Figure 12). In separate assays, PMN442 also inhibited the processes involved in the cell-to-cell propagation of a-syn aggregates: it reduced the uptake of human a-syn seeding fibrils by neurons and the subsequent formation of intracellular aggregates, as well as the recruitment of endogenous normal a-syn into those aggregates (Figure 13). Taken together, these results support the potential of PMN442 to selectively target and protect against a-syn pathogenic species in patients with MSA and other synucleinopathies. PMN442 has been humanized in a human IgG1 framework for advancement to IND-enabling studies. In addition to PMN442, ProMIS is evaluating other antibodies that have shown favorable selectivity and in vitro data.

Figure 12

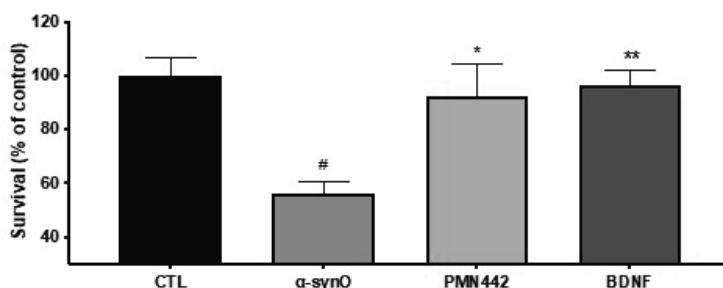


Fig. 12. Protection against neurotoxicity. PMN442 inhibition of oligomer toxicity for dopaminergic neurons. Cultures of primary rat dopaminergic neurons were exposed to toxic a-syn oligomers with or without PMN442. Survival is expressed as the percentage of viable neurons compared to a control culture with vehicle only (CTL). Results shown are the mean  $\pm$  SEM of 6 replicate cultures. BDNF was used as a positive control. #  $p = 0.0004$  vs. CTL, \* $p \leq 0.002$  vs. a-synO, \*\* $p \leq 0.003$  vs. a-synO.

Figure 13

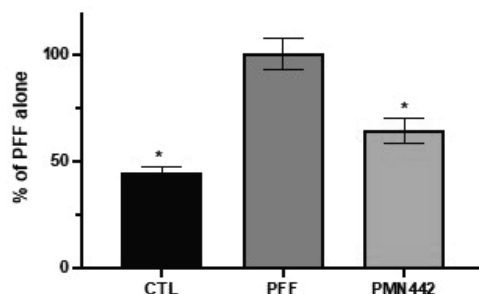


Fig. 13. Inhibition of seeding activity. PMN442 inhibition of the recruitment of endogenous rat a-syn into phosphorylated aggregates. Cultures of primary rat hippocampal neurons were exposed to soluble human a-syn preformed fibrils (PFF) with or without PMN442. CTL = neurons incubated with vehicle alone. Results are expressed as a percentage of the phosphorylated rat a-syn staining area with PFF alone and show the mean  $\pm$  SEM of 6 replicate cultures. \* $p < 0.02$  vs PFF.

## DEVELOPMENT PROGRAMS

### Expansion to Include Other Neurodegenerative and Misfolded Protein Diseases

The ProMIS discovery platform is being applied to other toxic misfolded proteins that drive disease including tau in AD, FTL, PSP, and CBD, HD, DISC1 in schizophrenia, and RACK1 in ALS in order to potentially generate antibody therapies for these disorders. Under disease conditions, misfolding of each of these proteins leads to the formation of toxic aggregates inside brain cells that can spread damage by propagating from cell-to-cell. Disease-associated conformational epitopes identified through ProMIS' computational platform are being used to generate potentially therapeutic antibodies. Additionally, we are using the epitopes identified in the amyloid-beta discovery program to generate a vaccine candidate that potentially could be used for prophylactic treatment of Alzheimer's disease. The Discovery phase of the process comprises two distinct stages: (1) computational modeling to predict and construct conformational peptide epitopes present on the misfolded, toxic form of a protein, followed by either immunization with the peptide epitopes to generate antibodies/ intrabodies, or incorporation of the peptide antigen into a therapeutic vaccine and (2) screening and validation of multiple candidates in vitro and in vivo to select a lead for preclinical development.

### Alzheimer's disease

#### Tau

Propagation of misfolded, pathogenic aggregates of tau has also been implicated in the progression of AD and other tauopathies such as PSP, CBD, CTE, and FTL-tau.

Pan-tau antibodies and relatively non-selective sequence-specific antibodies have failed to show clinical benefit in PSP and AD. The ProMIS platform was used to identify misfolding-specific epitopes and raise mAbs against pathogenic forms of tau (toxic oligomers and small soluble fibrils). A set of mAbs has been generated that preferentially bind pathogenic tau aggregates as opposed to physiologic tau monomers. In binding assays, the ProMIS mAbs recognized toxic species of tau in brain homogenates from individuals with AD (Fig. 14).

Misfolded tau aggregates can form aggregation seeds that spread through anatomically connected pathways and form toxic fibrillar tau aggregates ultimately leading to the formation of neurofibrillary tangles. Preclinical data suggest that inhibition of seeding by misfolded tau can inhibit this spread (Sandusky-Beltran & Sigurdsson Neuropharmacology 2020). In activity assays, the mAbs were able to inhibit the seeding activity of AD brain homogenate resulting in decreased induction of tau aggregation in a cell system. (Fig. 15). These results suggest that these mAbs may be useful in targeting pathogenic tau in AD and potentially other tauopathies. Therefore, the Company believes that selectivity of antibodies for tau pathogenic species that promote formation of toxic aggregates, as opposed to pan-tau reactivity (binding to all forms of tau), is needed both to preserve normal tau function and to minimize the diversion of active antibody from the target through unproductive binding to more abundant non-toxic forms of tau.

Figure 14

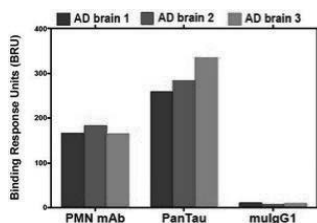


Fig. 14. Binding to native pathogenic tau species in the brain extracts of individuals with AD. The binding response of a representative immobilized mAb to tau in brain extract from 3 different individuals with AD was measured by SPR. Mouse IgG1 (muIgG1) was used as a negative control.

Figure 15

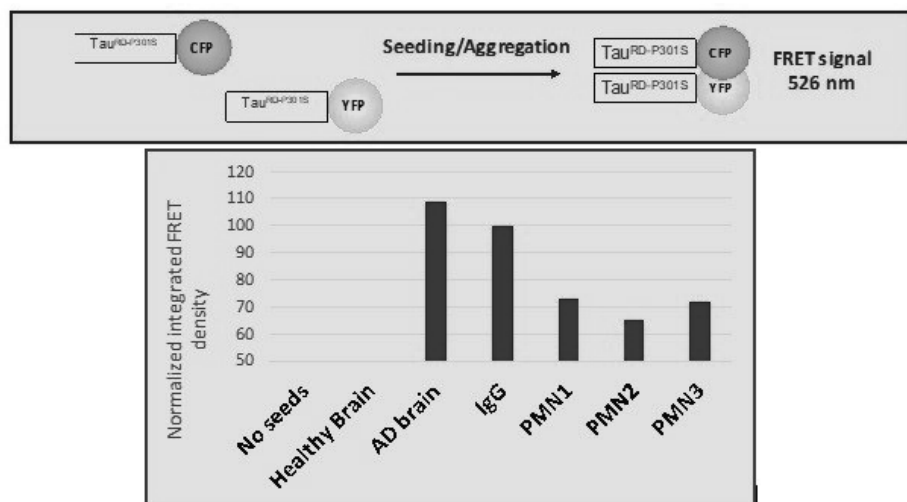


Fig. 15. Inhibition of seeding activity of AD brain homogenate. Brain homogenate +/- mAbs was transduced into Biosensor cells with Lipofectamine 200. FRET signal was measured 48 hours later by flow cytometry. Results are expressed as Normalized Integrated FRET density defined as the percent of FRET positive cells multiplied by the Median Fluorescence Intensity of those FRET positive cells and normalized to cells treated with IgG.

### Schizophrenia

#### DISC1

Protein misfolding and proteostasis defects have been found to play a role in neurodevelopmental diseases, but until recently, the proteins implicated in these disease processes were not known. Just such a protein was first identified in a Scottish family with an autosomal dominant neurodevelopmental syndrome including schizophrenia, and was subsequently named “disrupted in schizophrenia,” or DISC1 (Soares et al. 2011). DISC1 is an important hub protein participating in neurogenesis, mitochondrial transport and dynamics in dendrites, cytoskeletal function, and protein translation in adults, especially at the synapse and under conditions of oxidative stress. DISC1 has been shown to misfold and aggregate in schizophrenia, as indicated by impaired detergent solubility in brains of individuals dying with sporadic (non-genetic) schizophrenia (Leliveld et al. 2008), and the induced co-aggregation of DISC1 by TDP-43 inclusions in human frontotemporal dementia (Endo et al. 2018). In addition, many genetic variants in interactors of DISC1 show significant association with schizophrenia and cognitive decline. Finally, misfolded DISC1 has been shown to exhibit prion-like attributes with transmission from cell-to-cell that can trigger misfolding of healthy DISC1 in the recipient cell (Korth 2012). Thus, DISC1 can be designated a misfolding protein in schizophrenia, just like amyloid and tau are misfolded proteins in AD. We believe application of the PromIS platform to DISC1 and its interactome offers the potential to generate selective antibodies to selectively degrade toxic misfolded DISC1 while sparing normally folded DISC1 to perform its physiological function. Immunizations have been performed with epitopes predicted by Collective Coordinates to be present specifically on misfolded DISC1 and the resulting mAbs are being characterized.



## ***Amyotrophic Lateral Sclerosis***

### ***RACK1***

RACK1 is a core ribosomal protein of the eukaryotic small (40S) ribosomal subunit. It is a scaffold protein that interacts with several other proteins thereby regulating a variety of signaling pathways critical for cell proliferation, transcription and protein synthesis. It is essential for proper neuronal function. In ALS, our own findings and those of others indicate that misfolded RACK1 co-localizes into cytoplasmic aggregates in motor neurons of the spinal cord which may play a role in disease pathology. For example, in a cell system, we and others have found that mutant TDP-43 suppresses global protein synthesis by co-aggregating with RACK1 on polyribosomes. Our recent work indicates that the same observations also apply to the interaction between RACK1 and Fused in sarcoma/translocated in sarcoma (FUS), another protein associated with ALS pathogenesis.

To investigate RACK1 as a potential target for ALS, ProMIS explored the impact of RACK1 knock-down (KD) (i.e., what happens in the absence of RACK1). Our findings were recently published in *Acta Neuropathologica Communications* (<https://doi.org/10.1186/s40478-023-01705-8>). In a cell system, RACK1 was observed to co-aggregate with misfolded mutant TDP-43 or mutant FUS in the cytoplasm. Knock-down of RACK1 expression resulted in disaggregation of cytoplasmic TDP-43 or FUS and even relocation to the nucleus (normal location) in some of the cells, accompanied by a reversal of the suppression of protein synthesis. In fruit flies (*Drosophila melanogaster*) experiencing neurodegeneration as a result of human TDP-43 expression, RACK1 KD alleviated degeneration of neurons in the retina and improved the climbing ability of the flies.

Results from the literature and ProMIS' proof of concept data using RACK1 KD support targeting of RACK1 as a potential therapeutic approach for ALS. The ProMIS platform identified epitopes present on misfolded RACK1 and generated antibodies selective for pathogenic, aggregated RACK1.

ProMIS has generated five mAbs with the desired selectivity and intrabody versions have been generated for testing. These mAbs recognize diseased tissue (ALS and FTD) but not normal tissue, suggesting that RACK1 is misfolded and aggregated in disease. Research is ongoing to continue to characterize the mAbs and select a candidate.

### ***Alzheimer's Vaccine Program***

We believe that the same peptide antigens that generate a mAb infusion therapy can be used to create a vaccine. The goal of a therapeutic vaccine is to spur the human immune system to generate antibodies that neutralize toxic oligomers, just as the infusion antibodies will hopefully do. The advantage is that a single course of therapy, usually an initial vaccination followed by a booster, can potentially provide years of therapeutic benefit, eliminating the need for frequent costly infusions. Progress in the reliability of blood-based biomarkers of neurodegeneration will likely increase screening to identify individuals in the early stages of AD or at risk of developing the disease. A vaccine capable of inducing an effective antibody response against A $\beta$ O could be administered prophylactically to at-risk individuals to potentially prevent development of symptomatic disease; and the vaccine could also be given therapeutically to individuals living with a diagnosis of AD to potentially inhibit disease progression. Initial results obtained with peptide 301 (the conformational A $\beta$ O epitope of PMN310) in a vaccine configuration showed robust induction of antibodies selective for A $\beta$ O with no binding to monomers or plaque. There was also no induction of a potentially deleterious T cell response as observed previously with other A $\beta$  vaccines. ProMIS performed studies to optimize adjuvant formulation and dosing regimen as well as to explore multivalent vaccine configurations containing additional A $\beta$ O-restricted epitopes identified by the ProMIS discovery platform. Results from these studies have been submitted for presentation at the 2024 Alzheimer's Association International Conference.

In previous studies reported in the literature, a first-generation vaccine consisting of aggregated human A $\beta$  protein with QS1 adjuvant induced antibody production in AD patients but elicited meningoencephalitis (brain inflammation) and had to be discontinued for safety reasons. Subsequent studies indicated that T helper (Th) cell epitopes in the A $\beta$  vaccine gave rise to a pro-inflammatory Th1-type response against the same A $\beta$  epitopes in the brain). The Company believes it can avoid this issue with a vaccine candidate consisting of its A $\beta$ O B cell epitopes (no A $\beta$  Th epitopes) conjugated to keyhole limpet hemocyanin (KLH) as a carrier protein. KLH has been used in humans and provides Th cell epitopes that are needed

to help the development of an antibody response by B cells. Since KLH is a foreign protein not present in human brain, immunization is expected to result in an antibody response against A $\beta$ O without a potentially detrimental Th cell inflammatory response (Fig. 16). This premise is supported by initial preclinical studies that we conducted in collaboration with the University of Saskatchewan's Vaccine and Infectious Disease Organization-International Vaccine Centre (VIDO-InterVac), a global leader in vaccine research and development. The results were presented at the AD/PD conference in 2022.

In these studies, 5-6 week old Balb/c mice (n=6/group) received two intramuscular (IM) injections (days 0 and 28) of a vaccine candidate construct containing ProMIS' A $\beta$ O 301 peptide epitope linked to KLH and formulated with different adjuvants. Analysis of serum samples collected on day 0 and after 1 or 2 vaccinations on days 28 and 48 showed induction of a robust antibody response against the A $\beta$ O epitope as measured by ELISA (Fig. 17). ELISPOT analysis of spleen cells (immune cells) collected from immunized mice at the end of the study on day 48 showed a lack of Th cell cytokine production in response to stimulation with the A $\beta$ O epitope thereby indicating that the peptide only contains a B cell epitope. As expected, T cell help was provided by the carrier protein and stimulation with KLH gave rise to the production of Th cytokines. These results support the premise that a vaccine consisting of A $\beta$ O-restricted conformational B cell epitopes conjugated to KLH for T cell help may successfully induce a protective antibody response against A $\beta$ O without eliciting a potentially inflammatory A $\beta$ -directed Th response. Characterization of immune sera from the mice also showed the desired antibody binding profile: selective binding to A $\beta$ O compared to A $\beta$  monomers as determined by SPR, and no binding to plaque in brain sections from AD patients as determined by IHC.

Figure 16

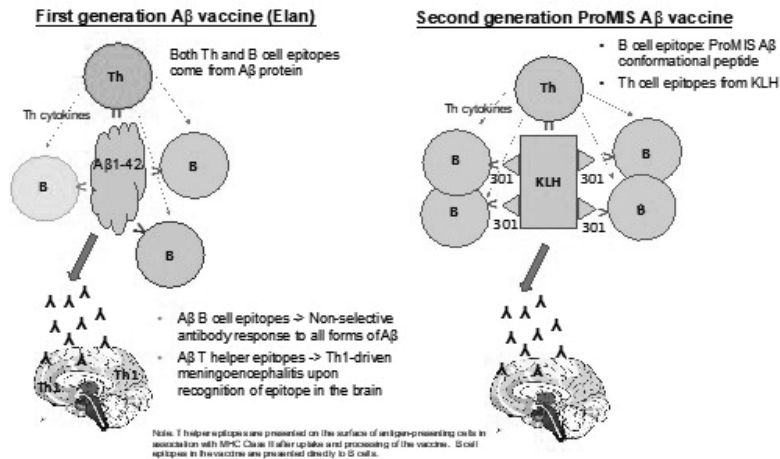


Fig. 16. Illustration of vaccine concept

Figure 17

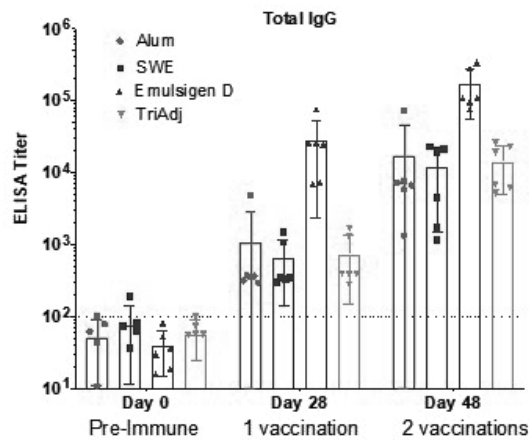


Fig. 17. Induction of robust antibody response against AβO epitope. Titers of IgG antibodies against the 301 peptide epitope were measured by ELISA. Values for individual mice at baseline and on days 28 and 48 post-immunization are shown.

Using the ProMIS discovery platform, our aim is to devise a safe and effective vaccine to induce a specific immune response against toxic AβOs. We have identified different peptide epitopes selectively exposed on toxic AβOs that can induce antibodies that selectively bind AβOs. The immediate goal for this program is to progress an amyloid vaccine into preclinical development.

### ***Alpha-Synuclein Vaccine Program***

The same principle of immunization with conformational peptide epitopes of misfolded toxic proteins was applied to alpha-synuclein (a-syn) for vaccination against synucleinopathies such as MSA, PD and LBD. Potential conformational epitopes (misfolded portions) unique to toxic alpha-synuclein were identified by the ProMIS platform. Formulations of several of these epitopes were tested in mouse vaccination studies leading to the selection of a lead vaccine candidate for testing in mouse models replicating cognitive and motor deficits of human disease. This pioneering work was made possible through a C\$1.16 million research grant by the Weston Family Foundation to the University of British Columbia to support the research of the team led by Neil Cashman, M.D., ProMIS Chief Scientific Officer and Professor Emeritus at the University of British Columbia. The team also includes Scott Napper, Ph.D., from the Vaccine and Infectious Disease Organization (VIDO) and Professor of Biochemistry, Microbiology, and Immunology at the University of Saskatchewan, Marco Prado, Ph.D., the Canada Research Chair in Neurochemistry of Dementia and Professor of Anatomy & Cell Biology / Physiology and Pharmacology, at the University of Western Ontario, and Joel Watts, Ph.D., Canada Research Chair in Protein Misfolding Disorders and Associate Professor within the Department of Biochemistry and the Tanz Centre for Research in Neurodegenerative Diseases at the University of Toronto.

Results from the vaccination studies have been submitted for presentation at the 2024 meeting of the American Academy of Neurology (AAN).

### **ProMIS' Technology Platform and Intellectual Property Portfolio**

The basis of ProMIS' proprietary technology platform is the ability to identify small regions of toxic proteins, including their specific shape or "conformation" that are displayed only on the toxic forms of that protein. We have developed patented methods and know-how combining biology and physics, to identify these small regions of proteins which can be the targets for antibodies. When displayed on the toxic protein, these small regions are known as "epitopes." ProMIS makes copies of these epitopes, in a precisely defined shape. These drug development tools are called peptide antigens and we believe they are the key to our ability to create antibody therapies, vaccines, and diagnostics.

The ProMIS computational platform is based on the Collective Coordinates algorithm that combine physics and biology to simulate the folding, or misfolding of proteins. ProMIS has successfully applied this computational algorithm to several misfolded protein categories, looking for epitopes exposed only on a misfolded toxic form which can be used as an antigen to generate an antibody.

Peptide antigens are the key to creating selective antibodies that target toxic misfolded proteins, like our lead therapeutic antibody candidate (PMN310 for AD). PMN310 was created using a peptide antigen that we correctly predicted to be exposed only on toxic A $\beta$ O<sub>s</sub>, not the monomeric or plaque forms of A $\beta$ . ProMIS has generated a portfolio of over 20 peptide antigens that have led to selective antibodies against toxic misfolded forms of A $\beta$  for AD, a-syn for MSA and PD, tau for AD, FTL, PSP, and CBD, TDP-43 and SOD1 for ALS, RACK1 for ALS and HD, and DISC1 for schizophrenia. Those peptide antigens, and the corresponding selective antibodies, represent proprietary reagents that potentially can be used to create proprietary diagnostic tests in neurodegenerative diseases.

Finally, peptide antigens are also a potential key to making vaccines. Therapeutic vaccines are designed to treat a disease by causing the patient's immune system to make antibodies (or T-Cells, in some areas like cancer) that neutralize the toxic disease driver. The potential advantage of a therapeutic vaccine, if effective, is that a single course of therapy might provide benefit for many years, not requiring frequent, expensive and inconvenient infusions. In preventive therapy, we believe such an approach may be particularly valuable.

### ***Overview of ProMIS' Intellectual Property (IP) Portfolio***

The ProMIS IP program consists of a three-layered strategy. The first layer of protection comprises two computational algorithms, ProMIS™ and Collective Coordinates, obtained under worldwide exclusive license from the UBC. These algorithms are used to predict the specific site and shape (conformation) of epitopes on misfolded proteins implicated in the development of neurodegenerative diseases and on other complex proteins. PCT applications for these disease specific epitopes have been submitted and comprise the second layer of IP protection. Finally, the third layer of protection consists

of the composition of matter for the antibodies targeting these disease related epitopes, including use(s) thereof. The second and third layers of this strategy may be in the same patent application.

### ***License Agreements and Patents***

#### *License Agreement with the University of British Columbia (UBC)*

On February 4, 2009, ProMIS (under its previous name, Amorfix Life Sciences Ltd.) entered into an exclusive license agreement with UBC in which ProMIS gained exclusive worldwide rights to develop and commercialize certain intellectual property rights belonging to UBC, based on its technology relating to misfolded proteins. Such agreement was amended and restated effective October 6, 2015 (as amended and restated, the “UBC License Agreement”). Under the terms of the UBC License Agreement, ProMIS has a worldwide exclusive license to UBC’s rights in existing and future intellectual property (Improvements as defined in the UBC License Agreement) related to misfolded protein technology, with the right to sublicense. ProMIS is also responsible for managing the filing, maintenance and prosecution of the licensed patents and applications and is responsible for costs associated with the same. The UBC License Agreement expires on a product by product and country by country basis upon the expiration of ProMIS’ obligation to pay royalties to UBC under the terms thereof (unless terminated earlier pursuant to the terms of the UBC License Agreement). The Company’s obligation to pay royalties under the UBC License Agreement expires upon the longer of the life of the Patents (as defined in the UBC License Agreement), including those identified in Schedule A thereto (as amended from time to time), and ten years following the First Commercial Sale of a Product (as those terms are defined in the UBC License Agreement) in any country. Since the Company has not made commercial sales under the UBC License Agreement to date, the UBC License Agreement is currently expected to expire no earlier than February 19, 2044. However, this date may be adjusted upon the Company’s First Commercial Sale of a Product or upon an amendment to Schedule A to the UBC License Agreement to add additional patents. The UBC License Agreement may also be terminated by UBC, at its option, upon the occurrence of certain events including, but not limited to, our insolvency, winding up, liquidation, if the subject technology becomes subject to a security interest that is not released, if ProMIS or any of its directors or officers have materially breached or failed to comply with securities laws, in the event of certain breaches of, or our failure to perform obligations under, the UBC License Agreement or other agreements between ProMIS and UBC or other terminations of existence. Either party may terminate the license for breaches pursuant to the terms thereof, unless remedied within a certain period specified in the UBC License Agreement. ProMIS also has the right, in its sole discretion, to terminate the UBC License Agreement upon written notice to UBC. The UBC License Agreement calls for certain customary payments such as an annual license fee and payment to UBC of a low to high single digit royalty on revenues. As of December 31, 2023, the Company has paid a total of C\$225,000 to UBC pursuant to the terms of the UBC License Agreement.

The foregoing description of the UBC License Agreement is qualified in its entirety by reference to the UBC License Agreement.

#### *The UBC Patents*

The UBC patent license includes a patent family directed toward systems and methods for predicting therapeutic targets in misfolding proteins. This patent family (referred to as Collective Coordinates target identification technology) includes an issued U.S. patent, seven issued foreign patents and two pending foreign applications. Issued patents from this family are expected to expire in November 2036, absent any disclaimers or extensions available.

The UBC patent license also includes several patent families directed to biologics including antibodies targeting neurological disease related toxic misfolded proteins and methods related thereto, many of which targets were identified using their proprietary prediction systems and methods, including several families related to immunogens, antibodies and methods directed to various misfolded A $\beta$  and Tau targets relevant in AD and related diseases (AD family), several families related to immunogens, antibodies and methods directed to various misfolded TDP-43 targets relevant in ALS and related diseases (ALS disease family), a patent family related to antisense molecules and biologics directed at RACK1 relevant in ALS and Huntington’s (ALS disease family), and a patent family related to immunogens and antibodies directed to a-syn targets relevant in PD, MSA, LBD and related diseases (PD family).

The AD family includes patent families related to three A $\beta$  epitope targets. The first A $\beta$  epitope target patent family, includes several patent subfamilies and includes specifically one issued and one allowed U.S. patent, four pending U.S. applications, seven issued or allowed foreign patents and 15 foreign pending patent applications. Issued patents from this family are expected to expire in November 2036, July 2037 or July 2038, depending on the subfamily and absent any disclaimers or extensions available. The second A $\beta$  epitope target patent family includes one issued U.S. patent and one pending U.S. application, two issued foreign patents and five foreign pending applications. Issued patents from this family are expected to expire in November 2036, absent any disclaimers or extensions available. The third A $\beta$  epitope target patent family includes one issued and one allowed U.S. patent, one issued and one allowed foreign patent and five foreign pending applications. Issued patents from this family are expected to expire in November 2036, absent any disclaimers or extensions available. The AD family also includes one issued U.S. patent directed to combinations of the three A $\beta$  epitope target antibodies and an issued U.S. patent directed to combinations of the three A $\beta$  epitope target immunogens. Issued patents from this family are expected to expire in November 2036, absent any disclaimers or extensions available. Also included is an issued U.S. patent to a fourth A $\beta$  epitope target which is expected to expire March 2031 absent any disclaimers or extensions available.

The AD family includes a patent family for a Tau epitope target. The Tau epitope target patent family includes one pending U.S. patent application and six foreign pending patent applications. Issued patents from this family are expected to expire in May 2040, absent any disclaimers or extensions available.

The ALS disease family includes patent families directed to two TDP-43 epitope targets. The first TDP-43 epitope target family includes one issued U.S. patent, one pending U.S. application, and 4 pending foreign applications. Issued patents from this family are expected to expire in May 2038, absent any disclaimers or extensions available. The second TDP-43 epitope target family includes two patent subfamilies, the earlier of which includes one pending U.S. patent application and 6 pending foreign applications, and a later patent subfamily directed more specifically to intrabodies, that includes one pending U.S. application and 5 foreign patent applications. Issued patents from this family are expected to expire in December 2039 and April 2041, respectively, absent any disclaimers or extensions available.

The ALS disease family includes a patent family related to a SOD1 epitope target. The patent family includes a PCT application. Issued patents from this PCT application are expected to expire in February 2044, absent any disclaimers or extensions available.

The ALS disease family also includes a patent family related to RACK1 nucleic acid targets. The RACK1 nucleic acid target family includes one pending U.S. patent application and five pending foreign applications. Issued patents from this family are expected to expire April 2041, absent any disclaimers or extensions available.

The PD disease family includes a patent family related to alpha-synuclein epitope target. The a-syn patent family includes one pending U.S. patent application and six foreign pending patent applications. Issued patents from this family are expected to expire in October 2039, absent any disclaimers or extensions available.

#### *Other Patents*

We are the current owner of two U.S. patents related to SOD1 epitope targets that were co-owned and then acquired from University Health Network (UHN) by assignment. These patents expire on August 2024 and December 2026, absent any disclaimers or further extensions available. We also own three U.S. patents related to SOD-1 immunogens and/or antibodies. Issued patents from this family are expected to expire August 2024 to June 2026, absent any disclaimers or extensions available. We also own two U.S. patents directed to detecting misfolded disease associated proteins. These patents are expected to expire August 2024 and June 2025, absent any disclaimers or further extensions available.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In the countries in which we file, the patent term is 20 years from the earliest non-provisional filing date, subject to any disclaimers or extensions. The term of a patent in the United States can be adjusted due to any failure of the U.S. Patent Office (USPTO) following certain statutory deadlines for issuing a patent.

In the United States, the patent term of a patent that covers an FDA-approved drug may also be eligible for patent term extension, which permits patent term restoration as compensation for a portion of the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the original expiration of the patent. The protection provided by a patent varies from country to country, and is dependent on the type of patent granted, the scope of the patent claims, and the legal remedies available in a given country.

For a discussion of the risks we face relating to our intellectual property, see *“Risk Factors — Risks Related to our Intellectual Property — If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, and other proprietary technologies we develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates, and other proprietary technologies if approved, may be adversely affected.”*

## **Industry Overview**

### ***Markets***

ProMIS is applying its in-licensed patented technology platform to build a portfolio of antibody therapies and therapeutic vaccines, for neurodegenerative diseases such as AD, ALS, MSA, FTL, PSP, CBD, and schizophrenia. A common biologic cause contributes to each of these conditions, in that misfolded versions of proteins which normally perform a needed function can cause neuronal degeneration and death when misfolded, contributing to morbidity and mortality. ProMIS’ technology platform is an example of the advances in drug discovery enabled by computational power, in silico discovery, and artificial intelligence. We believe this platform provides a potential advantage by allowing us to selectively target the toxic misfolded proteins with therapeutics.

### **Marketing Plans and Milestones**

Marketing and commercial launch of any products in the ProMIS portfolio which successfully progress in development must be planned in relation to its available resources. ProMIS intends to out-license the marketing and sales of its products, should they progress successfully in development, to strategic partners for commercialization.

### **Government Regulations**

Government authorities in the United States at the federal, state and local level and in other countries regulate, among other things, the research, development, manufacture, testing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of drug and biological products, as well as diagnostics. Generally, before a new drug, biologic or diagnostic can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved, authorized, or cleared by the applicable regulatory authority.

### ***Regulatory Approval and Certification***

All commercial applications of ProMIS’ technology will be subject to substantial regulation and certification in the jurisdictions in which ProMIS or its strategic partners intend to sell its therapeutic products. The initial markets for ProMIS’ product candidates are expected to be the U.S. and Canada and, because the Canadian healthcare marketplace is regulated in a similar manner as in the United States, ProMIS intends to conform its regulatory and certification scheme to the more rigorous standards imposed by the FDA.

### ***Human Therapeutic Products***

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act (FD&C Act) and its implementing regulations and biologics under the FD&C Act and the Public Health Service Act (PHS Act) and their implementing regulations. Both drugs and biologics also are subject to other federal, state and local statutes and

regulations, such as those related to competition. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or following approval may subject an applicant to administrative actions or judicial sanctions. These actions and sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, license revocation, a clinical hold, untitled or warning letters, voluntary or mandatory product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal fines or penalties. Any agency or judicial enforcement action could have a material adverse effect on our business, the market acceptance of our product candidates, if approved, and our reputation.

Our product candidates must be approved by the FDA through either a New Drug Application (NDA) or a Biologics License Application (BLA) process before they may be legally marketed in the United States. The process generally involves the following:

- completion of extensive preclinical studies in accordance with applicable regulations, including studies conducted in accordance with Good Laboratory Practices (GLP) requirements;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval by an Institutional Review Board (IRB) or independent ethics committee (EC) at each clinical trial site before each human trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, Good Clinical Practices (GCP) requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- submission to the FDA of an NDA or BLA;
- a determination by the FDA within 60 days of its receipt of an NDA or BLA to accept the filing for review;
- satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the drug or biologic will be produced to assess compliance with Current Good Manufacturing Practices (cGMP) requirements to assure that the facilities, methods and controls are adequate to preserve the drug or biologic's identity, strength, quality and purity;
- potential FDA audit of the clinical trial sites that generated the data in support of the NDA or BLA;
- payment of user fees for FDA review of the NDA or BLA; and
- FDA review and approval of the NDA or BLA, including consideration of the views of any FDA advisory committee, prior to any commercial marketing or sale of the drug or biologic in the United States.

The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and the regulatory scheme for drugs and biologics is evolving and subject to change at any time. We cannot be certain that any approvals for our product candidates will be granted on a timely basis, or at all.

#### ***Preclinical and Clinical Development***

ProMIS' human therapeutic product applications will be subject to rigorous preclinical and clinical testing and other approval procedures by the FDA and similar regulatory agencies in other countries. First, preclinical testing of human therapeutics is conducted in nonclinical models and on animals in the laboratory to evaluate the potential efficacy, safety



and toxicity of a pharmaceutical product candidate. The conduct of preclinical studies is subject to federal and state regulations and requirements, including GLP regulations for safety/toxicology studies.

The results of these studies, along with applicable chemistry, manufacturing, and controls information are submitted to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans, and must become effective before human clinical trials may begin. An IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, notifies the applicant of safety concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence. Additionally, the review of information in an IND submission may prompt FDA to, among other things, scrutinize existing INDs or any marketed products and could generate requests for information or clinical holds on other product candidates or programs.

The clinical stage of development involves the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control, in accordance with GCP requirements, which include the requirements that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol, and any subsequent amendments to the protocol must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable related to the anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative, and must monitor the clinical trial until completed. The FDA, the IRB or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the patients are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There also are requirements governing the reporting of ongoing clinical trials and completed clinical trials to public registries. Information about applicable clinical trials, including clinical trial results, must be submitted within specific timeframes for publication on the [www.clinicaltrials.gov](http://www.clinicaltrials.gov) website.

Typically, the clinical evaluation process involves three phases. In Phase 1, clinical trials are conducted with a small number of healthy human subjects, or in a small number of patients to determine the early safety profile, the pattern of therapeutic drug distribution and metabolism. The total number of subjects included in Phase 1 clinical trials varies but is generally in the range of 20 to 80. In Phase 2, clinical trials are conducted with groups of patients who have the disease being evaluated to determine preliminary evidence of efficacy, the optimal dosages, and more extensive evidence of safety. Phase 2 clinical trials are typically controlled and conducted in a limited population, usually involving no more than several hundred subjects. In Phase 3, large scale, statistically-driven multi-center, well-controlled clinical trials are conducted with patients afflicted with a target disease in order to provide enough data to demonstrate the efficacy and safety required by the FDA. Phase 3 clinical trials usually involve several hundred to several thousand subjects. In most, though not all, cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to support approval of a drug.

Data from clinical trials conducted outside the U.S. may be accepted by the FDA subject to certain conditions. For example, the clinical trial must be conducted in accordance with Good Clinical Practices (GCP) requirements and/or the FDA must be able to validate the data from the clinical trial through an onsite inspection if it deems such inspection necessary. Where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will not approve the application on the basis of foreign data alone unless those data are considered applicable to the U.S. patient population and U.S. medical practice, the clinical trials were performed by clinical investigators of recognized competence, and the data is considered valid without the need for an on-site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means.

Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA. Written IND safety reports must be submitted to the FDA and the investigators fifteen days after the trial sponsor determines the information qualifies for reporting for serious and unexpected suspected adverse events, findings from other studies or animal or *in vitro* testing that suggest a significant risk for human volunteers and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must also notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as possible but in no case later than seven calendar days after the sponsor's initial receipt of the information.

Phase 1, Phase 2, Phase 3 and other types of clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug or biologic has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated check points based on access to certain data from the trial. Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the drug or biologic as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidates do not undergo unacceptable deterioration over their shelf life.

### ***Marketing Approval***

Assuming successful completion of the required clinical testing, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA or BLA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA or BLA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act (PDUFA) guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA or BLA, for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA or BLA is submitted to the FDA because the FDA has approximately two months to make a "filing" decision.

The FDA conducts a preliminary review of all NDAs or BLAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA or BLA to determine, among other things, whether the drug or biologic is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality, and purity.

The FDA may refer an application for a novel drug or biologic to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, which reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA or BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to ensure consistent production of the product within required specifications. Additionally, before approving an NDA or BLA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA or BLA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA or BLA and may require additional clinical or preclinical testing in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's or biologic's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a Risk Evaluation and Mitigation Strategy (REMS) which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

#### ***Orphan Drug Designation and Exclusivity***

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or 200,000 or more individuals in the United States and for which there is no reasonable expectation that the cost of developing and making the product available in the United States for this type of disease or condition will be recovered from sales of the product.

Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years from the date of such approval, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity by means of greater effectiveness, greater safety or providing a major contribution to patient care or in instances of drug supply issues. Competitors, however, may receive approval of either a different product for the same indication or the same product for a different indication but that could be used off-label in the orphan indication. Orphan drug exclusivity also could block the approval of our products for seven years if a competitor obtains approval before we do for the same product, as defined by the FDA, for the same indication we are seeking approval, or if our product is determined to be contained within the scope of the competitor's product for the same indication or disease. If we pursue marketing approval for an indication broader than the orphan drug designation we have received, we may not be entitled to orphan drug exclusivity.

#### ***Expedited Development and Review Programs***

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs or biologics to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval, and the purpose of these programs is to expedite the development and review of new products that are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. While these programs are intended to expedite product development and approval, they do not alter the standards for FDA approval.

A drug may be eligible for Fast Track designation if it is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast Track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed. Rolling review means that the agency may review portions of the marketing application before the sponsor submits the complete application. In addition, a drug may be eligible for Breakthrough Therapy designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough Therapy designation provides all the features of Fast Track designation in addition to intensive guidance on an efficient drug development program, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

A product submitted to the FDA for approval, including a product with Fast Track or Breakthrough Therapy designation, may also be eligible for additional FDA programs intended to expedite the review and approval process, including Priority Review designation and Accelerated Approval. A product is eligible for Priority Review designation, once an NDA or BLA is submitted, if the drug that is the subject of the marketing application has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. Under priority review, the FDA's goal date to take action on the marketing application is six months compared to ten months for a standard review. Products are eligible for Accelerated Approval if they are in development for a serious or life-threatening condition and can be shown to have an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, which is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

Accelerated Approval is usually contingent on a sponsor's agreement to conduct additional post-approval studies to verify and describe the product's clinical benefit. The FDA may withdraw approval of a drug or an indication approved under Accelerated Approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product, other evidence demonstrates that the product is not shown to be safe and effective under conditions of use, or required post-approval studies are not conducted with due diligence. Under the Food and Drug Omnibus Reform Act of 2022 (FDORA), the FDA is now permitted to require, as appropriate, that such trials be underway prior to approval or within a specific time period after the date of approval for a product granted Accelerated Approval. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under Accelerated Approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. In addition, the FDA generally requires, unless otherwise informed by the Agency, that all advertising and promotional materials intended for dissemination or publication within 120 days of marketing approval be submitted to the agency for review during the pre-approval review period. After the 120-day period has passed, all advertising and promotional materials must be submitted at least 30 days prior to the intended time of initial dissemination or publication.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval do not change the scientific or medical standards for approval or the quality of evidence necessary to support approval, though they may expedite the development or review process.

#### ***Pediatric Information and Pediatric Exclusivity***

Under the Pediatric Research Equity Act (PREA), certain NDAs and BLAs and certain supplements to an NDA or BLA must contain data to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of pediatric data or full or partial waivers. The Food and Drug Administration Safety and Innovation Act (FDASIA) amended the FD&C Act to require that a sponsor who is planning to submit a marketing application for a drug that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration, unless the drug is for an indication for which orphan designation has been

granted and is not for a molecularly targeted cancer indication, submit an initial Pediatric Study Plan (PSP) within 60 days of an end-of-Phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 study. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach an agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials and/or other clinical development programs.

A drug or biologic product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and, for drugs, patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or, for drugs, patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

### ***Post-approval Requirements***

Drugs or biologics manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There are continuing, annual user fee requirements for any marketed products and the establishments where such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA or BLA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs or biologics may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, drug and biologic manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics, and those supplying products, ingredients, and components of them, are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with ongoing regulatory requirements, including cGMP requirements. Manufacturers and other parties involved in the drug supply chain for prescription drug products must also comply with product tracking and tracing requirements and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or products that are otherwise unfit for distribution in the United States. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Failure to comply with statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution.

Once an approval of a drug or biologic is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety

risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- fines, warning letters or untitled letters or holds on post-approval clinical trials;
- refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs or mandated modification of promotional materials and labeling and issuance of corrective information.

In many foreign countries, drugs and biologics are subject to regulatory requirements in addition to and sometimes different than the U.S. requirements described herein.

#### ***Companion Diagnostics***

The FDA defines an *in vitro* companion diagnostic (IVD) device as an *in vitro* diagnostic device that provides essential information for the safe and effective use of a corresponding therapeutic product. The use of an IVD companion diagnostic device with a therapeutic product is stipulated in the instructions for use in the labeling of both the diagnostic device and the corresponding therapeutic product, including the label. Applications for an IVD companion diagnostic device and its corresponding therapeutic product will be reviewed and approved according to applicable regulatory requirements. The IVD companion diagnostic device application will be reviewed and approved or cleared under the device authorities of the FD&C Act and relevant medical device regulations; the therapeutic product application will be reviewed and approved under section 505 of the FD&C Act (i.e., drug products) or section 351 of the Public Health Service Act (i.e., biological products) and relevant drug and biological product regulations. The FDA intends to review each IVD companion diagnostic device submission within the context of, or in conjunction with, its corresponding therapeutic product, and FDA review of the IVD companion diagnostic device and the therapeutic product will be carried out collaboratively among relevant FDA offices.

Ideally, a therapeutic product and its corresponding IVD companion diagnostic device should be developed contemporaneously, with the clinical performance and clinical significance of the IVD companion diagnostic device established using data from the clinical development program of the corresponding therapeutic product. Some of our current and future product development candidates may depend upon co-development of accurate genetic and potentially other IVDs. Thus, we will likely need to comply with both FDA drug and medical device regulations. This adds additional cost and complexity to our development programs. The availability of IVD companion diagnostics can allow more efficient development programs and more appropriate use of products in the marketplace with more predictable outcomes for patients and higher value medicines. Ultimately FDA approval of the IVD will be required to allow approval of some of our products. However, technical difficulties or other issues could delay or disrupt the development of our products.

#### ***U.S. Patent Term Extension and Marketing Exclusivity***

Depending upon the timing, duration and specifics of FDA approval of a drug or biologic, some U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984,

commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits extension of a patent term of up to five years beyond the normal expiration date of the patent as compensation for patent term lost during the FDA regulatory review process. Patent term extension, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension. An NDA or BLA applicant may apply for extension of patent term for its currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Marketing exclusivity provisions under the FD&C Act also can delay the submission or the approval of certain applications. The FD&C Act provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (ANDA), or a 505(b)(2) NDA submitted by another Company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FD&C Act also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

#### ***Biosimilars and Exclusivity***

Certain of our product candidates are regulated as biologics. An abbreviated approval pathway for biological products shown to be similar to, or interchangeable with, an FDA-licensed reference biological product was created by the Biologics Price Competition and Innovation Act of 2009 (BPCI Act), as part of the ACA. This amendment to the PHS Act, in part, attempts to minimize duplicative testing. Biosimilarity, which requires that the biological product be highly similar to the reference product notwithstanding minor differences in clinically inactive components and that there be no clinically meaningful differences between the product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical trial or trials. Interchangeability requires that a biological product be biosimilar to the reference product and that the product can be expected to produce the same clinical results as the reference product in any given patient and, for products administered multiple times to an individual, that the product and the reference product may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product without such alternation or switch. Complexities associated with the larger, and often more complex, structure of biological products as compared to small molecule drugs, as well as the processes by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

A reference biological product is granted four and twelve year exclusivity periods from the time of first licensure of the product. The FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product, and the FDA will not approve an application for a biosimilar or interchangeable product based on the reference biological product until twelve years after the date of first licensure of the reference product. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity, and potency of the other company's product. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for

a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity, or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the “first licensure” of a biological product is determined on a case-by-case basis with data submitted by the sponsor. The law is complex and is still being interpreted and implemented by the FDA.

#### ***U.S. Healthcare Fraud and Abuse Laws and Compliance Requirements***

We are subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales and marketing programs for drugs and biologics. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect such operations include:

- the federal Anti-Kickback Statute is a criminal statute which prohibits, among other things, persons from soliciting, receiving, offering or paying remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs. The term “remuneration” has been broadly interpreted to include anything of value. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. A person does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil monetary penalties;
- federal false claims and civil monetary penalties laws, including the federal civil False Claims Act, which can be enforced by private citizens through civil whistleblower or qui tam actions, and civil monetary penalty laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment or approval from the federal government, including Medicare, Medicaid and other government payors, that are false or fraudulent or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim or to avoid, decrease or conceal an obligation to pay money to the federal government. A claim includes “any request or demand” for money or property presented to the U.S. federal government. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. The federal False Claims Act also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies’ marketing of products for unapproved, and thus non-reimbursable, uses. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act which prohibits anyone from, among other things, knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services that are false or fraudulent;
- HIPAA which created additional federal criminal statutes that prohibit, among other things, a person from knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program,



including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false or fraudulent statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH) and its implementing regulations, impose certain requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates, independent contractors or agents of covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- federal transparency laws, including the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, medical devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the State Children's Health Insurance Program, with specific exceptions, to report annually to CMS, information related to: (i) payments or other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other licensed healthcare practitioners, and teaching hospitals, and (ii) ownership and investment interests held by physicians and their immediate family members);
- the FCPA which prohibits U.S. businesses and their representatives from offering to pay, paying, promising to pay or authorizing the payment of money or anything of value to a foreign official in order to influence any act or decision of the foreign official in his or her official capacity or to secure any other improper advantage in order to obtain or retain business; and
- analogous state and foreign laws and regulations; state laws that require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or that otherwise restrict payments that may be made to healthcare providers; and state and local laws that require the registration of pharmaceutical sales representatives.

Because of the breadth of these laws and the narrowness of the statutory exceptions and regulatory safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant penalties, including, without limitation, civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in federal and state funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, contractual damages, diminished profits and future earnings, reputational harm and the curtailment or restructuring of our operations, any of which could harm our business.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it,

could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance and reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

### ***Environmental Regulation***

The Company may also be subject to foreign and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control and disposal of hazardous or potentially hazardous substances. There can be no assurance that the Company will not incur significant costs to comply with laws and regulations in the future or that such laws or regulations will not have a material adverse effect upon the Company's business, financial condition and results of operations.

### ***Pricing and Reimbursement***

Precision therapeutic products and their accompanying companion diagnostic are largely paid for based on third party payor reimbursement. In the United States., concurrent with approval for commercialization of such therapeutic products by the FDA, each therapeutic product is assigned a product code, and its associated companion diagnostic assigned a similar code, or CPT. Each product code and CPT is then assigned a reimbursement level by CMS. Third party insurance payors typically establish a specific fee to be paid for each code submitted. Third party payor reimbursement policies are generally determined with reference to the reimbursement for CPT codes for Medicare patients which themselves are determined on a national basis by CMS.

No uniform policy for coverage and reimbursement for products exists among third-party payors in the U.S. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases on short notice, and we believe that changes in these rules and regulations are likely.

In recent years, Congress has considered reductions in Medicare reimbursement levels for drugs administered by physicians. CMS, the agency that administers the Medicare and Medicaid programs, also has authority to revise reimbursement rates and to implement coverage restrictions for some drugs. Cost reduction initiatives and changes in coverage implemented through legislation or regulation could decrease utilization of and reimbursement for any approved products. While Medicare regulations apply only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from federal legislation or regulation may result in a similar reduction in payments from private payors.

The U.S. government, state legislatures, and foreign governments have continued implementing cost- containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Increasingly, third-party payors are also requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any products that we commercialize and, if reimbursement is available, the level of reimbursement.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain

product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Parallel to this regulatory reimbursement scheme in the United States., other countries also regulate reimbursement similarly to the United States. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amounts that we are able to charge for our product candidates. Accordingly, in markets outside the United States., the reimbursement for our product candidates may be reduced compared with the United States and may be insufficient to generate commercially-reasonable revenue and profits. Therefore, it is important that ProMIS establish for its human diagnostic and therapeutic products reimbursement schemes, which provide ultimate financial payment for ProMIS' products consistent with its business plan.

### ***Healthcare Reform Measures***

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system. The U.S. government, state legislatures and foreign governments also have shown significant interest in implementing cost-containment programs to limit the growth of government- paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs.

The Affordable Care Act (ACA) substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. Among other things, the ACA subjected biologic products to potential competition by lower-cost biosimilars; increased the minimum Medicaid rebates owed by most manufacturers; ; extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations; subjected manufacturers to new annual fees and taxes for certain branded prescription drugs; created a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and provided incentives to programs that increase the federal government's comparative effectiveness research.

Other legislative changes have been proposed and adopted since passage of the ACA.

- The Budget Control Act of 2011, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee did not achieve its targeted deficit reduction of an amount greater than \$1.2 trillion for the fiscal years 2012 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions included aggregate reductions to Medicare payments to healthcare providers of up to 2.0% per fiscal year. These reductions went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2031 unless additional action is taken by Congress.
- On January 2, 2013, the American Taxpayer Relief Act was signed into law, which, among other things, reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.
- On April 13, 2017, CMS published a final rule that gives states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.
- On May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the

FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

- On May 23, 2019, CMS published a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020.
- In August 2022, the United States Inflation Reduction Act of 2022, or the IRA, was signed into law. The IRA contains substantial drug pricing reforms, including the establishment of a drug price negotiation program within the U.S. Department of Health and Human Services that would require manufacturers to charge a negotiated “maximum fair price” for certain selected drugs or pay an excise tax for noncompliance, the establishment of rebate payment requirements on manufacturers of certain drugs payable under Medicare Parts B and D to penalize price increases that outpace inflation, and requires manufacturers to provide discounts on Part D drugs. Substantial penalties can be assessed for noncompliance with the drug pricing provisions in the Inflation Reduction Act of 2022. Under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one orphan designation and for which the only approved indication is for that disease or condition. If a product receives multiple orphan designations or has multiple approved indications, it may not qualify for the orphan drug exemption. The implementation of the IRA is currently subject to ongoing litigation challenging the constitutionality of the IRA’s Medicare drug price negotiation program. The IRA could have the effect of reducing the prices we can charge and reimbursement we receive for our products, if approved, thereby reducing our profitability, and could have a material adverse effect on our financial condition, results of operations and growth prospects. The effect the IRA on our business and the pharmaceutical industry in general is not yet known.

Further legislative and regulatory changes under the Affordable Care Act remain possible, although the Biden Administration has signaled that it plans to build on the Affordable Care Act and expand the number of people who are eligible for subsidies under it. It is unknown what form any such changes or any law would take, and how or whether it may affect our business in the future. We expect that changes or additions to the Affordable Care Act, the Medicare and Medicaid programs, allowing the federal government to directly negotiate drug prices and changes stemming from other healthcare reform measures, especially with regard to healthcare access, financing or other legislation in individual states, could have a material adverse effect on the healthcare industry.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

We expect that additional federal, state and foreign healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in limited coverage and reimbursement and reduced demand for our products, if approved, or additional pricing pressures.

#### ***Regulation Outside of the United States***

In addition to regulations in the United States, we may be subject to a variety of regulations in foreign jurisdictions that govern, among other things, clinical trials and any commercial sales and distribution of our products, if approved, either directly or through our distribution partners. Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign jurisdictions prior to the commencement of clinical trials or marketing and sale of the product in those countries. The foreign regulatory approval process and the time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA

approval. Some foreign jurisdictions have a drug product approval process similar to that in the U.S., which requires the submission of a clinical trial application much like the IND prior to the commencement of clinical studies. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others. Moreover, some nations may not accept clinical studies performed for U.S. approval to support approval in their countries or require that additional studies be performed on natives of their countries. In addition, in certain foreign markets, the pricing of drug products is subject to government control and reimbursement may in some cases be unavailable or insufficient. We face the risk that the resulting prices would be insufficient to generate an acceptable return to us or any future partner of ours. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions, and criminal prosecution.

### **Commercial Marketing Plans and Strategies**

ProMIS currently does not intend to market its therapeutic products or any companion diagnostics it develops that require extensive distribution channels. Instead, ProMIS expects to license to, or enter into strategic alliances with, pharmaceutical entities that are equipped to manufacture and/or market ProMIS' products through their distribution networks. ProMIS may license some or all of its patent rights to more than one company to achieve the fullest development, marketing and distribution of its products. To this end, ProMIS intends to continue to develop and improve its proprietary technologies and to expand the applications of its technologies in the healthcare markets.

### **Generate Product Revenues**

Revenues, if any, from its precision therapeutics pipeline and companion diagnostics are expected to be generated from research funding, license fees, milestone payments, co-development funding, and royalties from partnerships to be completed by ProMIS with selected third-party, multi-national health care firms. As of the date of this form, ProMIS has not generated any significant product revenues.

### **Develop Collaborative Customer-Funded Commercialization Agreements**

In order to increase market exposure of its products and to capitalize on a partner's clinical development competencies, market position, and distribution capabilities, ProMIS intends to develop its projects with collaborative commercial partners who will fund further product development projects incorporating ProMIS' technology. These collaborative arrangements typically will provide for a jointly funded development project and contemplate a licensing arrangement (which may be entered into at the same time as the development project or at a later date) under which, if a project is commercialized by the collaborative partner, ProMIS would potentially receive license fees, royalty payments from product sales and manufacturing revenue. ProMIS believes that such arrangements with major commercial partners will serve to validate its proprietary technologies in human healthcare areas and thereby assist ProMIS in attracting additional licensing arrangements on favorable terms.

### **Enhance Out-licensing of ProMIS Requirements**

Where practical, ProMIS will outsource its product manufacturing and has explored and will continue to evaluate the possibility of entering into strategic manufacturing alliances with appropriate third parties.

### **Competition**

#### ***Human Healthcare Products Competition***

ProMIS will compete with many large and small pharmaceutical companies that are developing and/or marketing therapeutic compounds for AD, ALS and/or PD. Many large pharmaceutical companies and smaller biotechnology companies maintain well-funded research departments concentrating on therapeutic approaches to neurodegenerative diseases. ProMIS expects substantial competition from these companies as they develop different and/or novel approaches

to the treatment of these diseases. Some of these approaches may directly compete with the technology that ProMIS is currently developing.

Although we believe PMN310 currently is differentiated to other products on the market or in development, if approved, PMN310 will compete with therapies currently approved for the treatment of patients with AD, which have primarily been developed to treat the symptoms of AD rather than the underlying cause of the disease, such as memantine and cholinesterase inhibitors. PMN310 may also compete with one or more potentially disease-modifying therapeutics that target A $\beta$  or amyloid plaques. Biogen's aducanumab (Aduhelm) was approved by the FDA in June 2021 under the Accelerated Approval pathway, but commercialization was discontinued in January 2024.

Eisai and Biogen announced that the Phase 3 confirmatory AD trial of lecanemab met the primary endpoint (Clinical Dementia Rating-Sum of Boxes) and all key secondary endpoints with statistically significant results in September 2022, and lecanemab received Accelerated Approval from FDA in January 2023. Results from Phase 3 trials of Roche's gantenerumab were announced in November 2022, while results from Phase 3 trials of Lilly's donanemab were announced in May 2023. In many therapeutic categories, after initial approvals validate a general mechanistic approach, competitive dynamics are driven by relative safety, efficacy, convenience, and cost effectiveness. We expect this will be the case in the anti-amyloid immunotherapy category.

Other companies known to be developing therapies with A $\beta$ /amyloid plaque-related targets include Alzheon, Inc., Alzinova AB, Chugai Pharmaceutical Co. Ltd., Cognition Therapeutics, Inc., Eisai Co., Ltd., Eli Lilly and Company, Grifols, S.A., KalGene Pharmaceuticals, Inc., Neurimmune AG, Novartis AG, Acumen Pharmaceuticals Inc., Prothena Biosciences, Inc., Roche Holding AG (including Genentech, its wholly owned subsidiary) and Wren Therapeutics, Inc. Additionally, PMN310, if approved, may also compete with other potential therapies intended to address underlying causes of AD that are being developed by several companies, including AbbVie Inc., AC Immune SA, Alektor, Inc., Anavex Life Sciences Corp., Annovis Bio, Inc., Athira Pharma, Inc., Biohaven Pharmaceuticals, Inc., Cassava Sciences, Inc., Cortexyme, Inc., Denali Therapeutics, Inc., Johnson & Johnson (including Janssen, its wholly-owned subsidiary) and Takeda Pharmaceutical Co. Ltd. Some of these competitors are developing therapies that either seek to block the aggregation of amyloid oligomers (for example, Alzheon, Inc.), or mitigate the toxicity of amyloid oligomers (for example, Cognition Therapeutics, Inc.). These and other therapies may end up being used as complementary therapies in clinical practice, in addition to antibodies targeting aggregated amyloid.

In the intense competitive environment that is the human pharmaceutical industry, those companies that complete clinical trials, obtain regulatory approval and commercialize their therapeutic products first may enjoy competitive advantages. ProMIS believes that it will develop compounds with characteristics that may enable them, if fully developed, to have a market impact. A number of major human pharmaceutical companies have significant programs to develop drugs for the treatment of neurodegenerative disease. These companies include Eisai/Pfizer, Novartis, Merck, Genentech, Lilly, Biogen, Amgen and Johnson & Johnson.

#### **Proprietary Protection**

ProMIS has acquired the rights to certain proprietary discovery platforms for the identification of proteins involved in misfolding diseases embodied in various national and international patent applications. ProMIS has also filed international patent applications related to immunotherapy targeting toxic forms of SOD1 and TDP-43 for ALS, toxic oligomers of A $\beta$  for AD and toxic aggregates for a-syn for PD to further protect its intellectual property rights related to its therapeutic programs. In addition, the Company has obtained proprietary rights to a computational algorithm (Collective Coordinates) for identification of DSEs in protein misfolding diseases as well as predicted DSEs against multiple disease targets. ProMIS intends to aggressively protect the commercial applications for diagnostic, therapeutic and prophylactic applications of these discoveries. In addition, ProMIS has developed know-how, which it may elect to keep as trade secrets and not publicly disclose in patent applications.

## **Human Capital Management**

ProMIS seeks to hire qualified scientists and key employees as needed. As of December 31, 2023, the Company employed six full-time employees and one part-time employee. The remainder of the scientists and key personnel had consulting agreements with ProMIS.

Our future success depends on our ability to attract, develop and retain key personnel, maintain our culture, and ensure diversity and inclusion in our board, management and broader workforce. Our human resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards. As these areas directly impact our ability to compete and innovate, they are key focus areas for our board of directors and senior executives.

## **Corporate Structure**

ProMIS Neurosciences Inc. was incorporated on January 23, 2004 under the name 4203801 Canada Inc. pursuant to the Canada Business Corporations Act (CBCA). The Company changed its name to Amorfix Life Sciences Ltd. on August 24, 2004 and to ProMIS Neurosciences Inc. effective July 8, 2015. On July 13, 2023, the Company continued its existence from a corporation incorporated under the CBCA into the Province of Ontario under the Business Corporations Act (Ontario) (OBCA) (Continuance). The Continuance was approved by the Company's shareholders at the Company's 2023 Annual Meeting of Shareholders held on June 29, 2023.

On June 21, 2022, the directors of the Company authorized a reverse share split of the issued and outstanding Common Shares in a ratio of 60:1, effective June 28, 2022 (the Reverse Share Split). All information included in this Annual Report on Form 10-K has been adjusted to reflect the Reverse Share Split. Unless otherwise stated herein, all share and per share numbers relating to the Company's Common Shares prior to the effectiveness of the Reverse Share Split have been adjusted to give effect to the Reverse Share Split, including the consolidated financial statements and notes thereto. The Company's Common Shares are listed on the Nasdaq Capital Market (Nasdaq) under the symbol, "PMN."

Our head office is located at 1920 Yonge Street, Suite 200, Toronto, Ontario, Canada M4S 3E2 and our registered and records office is located at 1055 West Georgia Street, Vancouver, British Columbia, Canada V6E 4N7. Our telephone number is (416) 847-6898 and our website address is [www.promisneurosciences.com](http://www.promisneurosciences.com). The information provided on our website is not part of this Annual Report on Form 10-K.

We own or have rights to various trademarks, service marks and trade names that we use in connection with the operation of our business. This Annual Report on Form 10-K may also contain trademarks, service marks and trade names of third parties, which are the property of their respective owners. Our use or display of third parties' trademarks, service marks, trade names or products in this Annual Report on Form 10-K is not intended to, and does not imply a relationship with, or endorsement or sponsorship by us. Solely for convenience, the trademarks, service marks and trade names referred to in this Annual Report on Form 10-K may appear without the ®, ™ or SM symbols, but the omission of such references is not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the right of the applicable owner of these trademarks, service marks and trade names.

Unless the context indicates otherwise, references in this prospectus to the "Company," "ProMIS," "we," "us," "our," and similar terms refer to ProMIS Neurosciences Inc. and its consolidated subsidiary.

Unless otherwise indicated, all references to "\$" or "US\$" in this Annual Report on Form 10-K refer to U.S. dollars, and all references to "C\$" refer to Canadian dollars. Following the Company's voluntary delisting from the Toronto Stock Exchange in July 2023, the Company reassessed its functional currency and determined that, as of July 1, 2023, its functional currency had changed from the C\$ to the US\$.

## **Available Information**

We will make available on our website, free of charge, our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the

SEC. The SEC maintains an Internet site, <http://www.sec.gov>, containing reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC.

#### **Item 1A. Risk Factors**

*Investors should carefully consider the following risk factors, together with all of the other information included in this Annual Report on Form 10-K, before making an investment decision. The occurrence of one or more of the events or circumstances described in these risk factors, alone or in combination with other events or circumstances, may have an adverse effect on our business, cash flows, financial condition and results of operations. You should also carefully consider the following risk factors in addition to the other information included herein, including matters addressed in the section entitled "Cautionary Note Regarding Forward-Looking Statements," and all other information in the Company's other public filings prior to making an investment decision. We may face additional risks and uncertainties that are not presently known to us or that we currently deem immaterial, which may also impair our business or financial condition. Additionally, investors should not interpret the disclosure of a risk to imply that the risk has not already materialized. The following discussion should be read in conjunction with the financial statements and notes to the financial statements included herein.*

#### **Risks Related to the Development of Our Product Candidates**

***Our product candidates are still in the early stages of development and there is significant uncertainty that any such products will actually be developed.***

Our product candidates are at an early stage of development. Significant additional investment in research and development, product validation, technology transfer to manufacturing, production scale-up, manufacturing, clinical testing, and regulatory submissions of such product candidates is required prior to commercialization. There can be no assurance that any such product candidates will actually be developed and, if developed, will be approved. The development and regulatory processes may require access to rare biofluid and tissue samples from people and animals which may not be available to us in sufficient amounts or in a timely fashion to allow us to complete the development or receive regulatory approval of any product candidate or process. A commitment of substantial time and resources is required to conduct research and clinical trials if we are to complete the development of any product candidate. It is not known whether any of these product or process candidates will meet applicable health regulatory standards and obtain required regulatory approvals, or whether such products, if approved, can be produced in commercial quantities at reasonable costs and be successfully marketed, or if our investment in any such products will be recovered through sales or royalties.

We expect to incur substantial capital expenditures in connection with the development of our product candidates. If we fail to successfully develop and sell all or any of our product candidates, if approved, then we will not earn any return on our investment in these future products, which will adversely affect our results of operations and could adversely affect the market price of the Common Shares. Our success in developing and selling new products will depend upon multiple factors, including:

- our ability to develop safe and effective products;
- our serology assays and vaccines achieving the desired sensitivity for antibody-based immunity and immune response, as applicable;
- acceptance of the product by the medical community and by patients and third-party payors;
- inherent development risks, such as the product proving to be unsafe or unreliable, or not having the anticipated effectiveness; and
- our ability to develop repeatable processes to manufacture new products in sufficient quantities.



If any of these factors cannot be overcome, we may not be able to develop and introduce our products in a timely or cost-effective manner, which could adversely affect our future growth and results of operations. Our failure to develop and obtain approval of our product candidates could adversely affect the market price of the Common Shares.

***Our business is heavily dependent on the successful development, regulatory approval and commercialization of PMN310 and any future product candidates that we may develop or acquire, including PMN442 and PMN267.***

We currently have no products approved for sale, and our lead product candidate is in early stages of development. The success of our business, including our ability to finance our company and generate revenue in the future, will primarily depend on the successful development, regulatory approval and commercialization of our product candidates and, in particular, the advancement of PMN310. However, given our stage of development, it may be many years, if we succeed at all, before we have demonstrated the safety and efficacy of a product candidate sufficient to warrant approval for commercialization. We cannot be certain that our product candidates will receive regulatory approval or be successfully commercialized even if we receive regulatory approval.

The clinical and commercial success of PMN310 and any future product candidates that we may develop or acquire will depend on a number of factors, including the following:

- our ability to raise any additional required capital on acceptable terms, or at all;
- our ability to complete IND enabling studies and successfully submit INDs or comparable applications;
- timely completion of our preclinical studies and clinical trials, which may be significantly slower or cost more than we currently anticipate and will depend substantially upon the performance of third-party contractors;
- delays or difficulties in enrolling and retaining patients in our clinical trials;
- whether we are required by the FDA or similar foreign regulatory agencies to conduct additional clinical trials or other studies beyond those planned to support the approval and commercialization of our product candidates or any future product candidates;
- acceptance of our proposed indications and primary endpoint assessments relating to the proposed indications of our product candidates by the FDA and similar foreign regulatory authorities;
- our ability to demonstrate to the satisfaction of the FDA and similar foreign regulatory authorities the safety, efficacy and acceptable risk to benefit profile of our product candidates or any future product candidates;
- the prevalence, duration and severity of potential side effects or other safety issues experienced with our product candidates or future approved products, if any;
- achieving and maintaining, and, where applicable, ensuring that our third-party contractors achieve and maintain, compliance with our contractual obligations and with all regulatory requirements applicable to our product candidates or any future product candidates or approved products, if any;
- the ability of third parties with whom we contract to manufacture adequate clinical trial and commercial supplies of our product candidates or any future product candidates remain in good standing with regulatory agencies and develop, validate and maintain commercially viable manufacturing processes that are compliant with cGMPs;
- the convenience of our treatment or dosing regimen;
- the timely receipt of necessary marketing approvals from the FDA and similar foreign regulatory authorities;

- acceptance by physicians, payors and patients of the benefits, safety and efficacy of our product candidates or any future product candidates, if approved, including relative to alternative and competing treatments;
- the willingness of physicians, operators of clinics and patients to utilize or adopt any of our product candidates or any future product candidates, if approved;
- our ability to achieve sufficient market acceptance, coverage and adequate reimbursement from third-party payors and adequate market share and revenue for any approved products;
- our ability to successfully develop a commercial strategy and thereafter commercialize our product candidates or any future product candidates in the U.S. and internationally, if approved for
- marketing, reimbursement, sale and distribution in such countries and territories, whether alone or in collaboration with others;
- patient demand for our product candidates, if approved, including patients' willingness to pay out-of-pocket for any approved products in the absence of coverage and/or adequate reimbursement from third-party payors;
- our ability to establish and enforce intellectual property rights in and to our product candidates or any future product candidates;
- our ability to avoid third-party patent interference, intellectual property challenges or intellectual property infringement claims; and
- our current clinical development plans for PMN310 may change as a result of clinical trial outcomes and future interactions with the FDA.

These factors, many of which are beyond our control, could cause us to experience significant delays or an inability to obtain regulatory approvals or commercialize our product candidates. Even if regulatory approvals are obtained, we may never be able to successfully commercialize any of our product candidates. Accordingly, we cannot provide assurances that we will be able to generate sufficient revenue through the sale of our product candidates or any future product candidates to continue our business or achieve profitability.

***Our approach to the potential treatment of AD is based on a novel therapeutic approach, which exposes us to unforeseen risks.***

There is no current scientific or general consensus on the causation of AD or method of action to treat AD. We have discovered and are developing PMN310, a humanized antibody that selectively targets A $\beta$ O, or A $\beta$ Os, to treat AD. Our approach is based on research on A $\beta$ Os, globular assemblies of the A $\beta$  peptide that are distinct from other forms of amyloid. A $\beta$ Os have gained scientific acceptance as primary toxins involved in the initiation and propagation of AD pathology. Based on the results of our nonclinical studies to date, we believe PMN310 is different from current and prior clinical-stage anti-amyloid drugs and product candidates based on its selectivity for A $\beta$ Os. We believe that this is a novel mechanism which has the potential to provide more favorable outcomes, as compared to approved therapies and product candidates in development and may potentially slow disease progression. However, we may ultimately discover that PMN310 does not possess properties required for therapeutic effectiveness. We have no evidence regarding the efficacy, safety or tolerability of PMN310 in humans. We may spend substantial funds attempting to develop PMN310 or other product candidates and never succeed in doing so.

The market for any products that we successfully develop, if any, will also depend on the cost of the product. We do not yet have sufficient information to reliably estimate what it would cost to commercially manufacture PMN310, if approved, and the actual cost to manufacture PMN310 or any drug we develop in the future could materially and adversely affect the commercial viability of the drug. We may also find that the manufacture of our product candidates is more difficult than anticipated, resulting in an inability to produce a sufficient amount of our product candidates for our clinical trials or, if

approved, commercial supply. If we do not successfully develop PMN310 or any other drug we develop with drug product that can be reliably and economically manufactured at scale, we will not become profitable, which would materially and adversely affect the value of our Common Shares.

***We may not successfully expand our pipeline of product candidates, including by pursuing additional indications for PMN310 or by in-licensing or acquiring additional product candidates for other diseases.***

A key element of our strategy is to build and expand our pipeline of product candidates, including by developing PMN310 for the treatment AD, and by identifying other product candidates. In addition, we may in-license or acquire additional product candidates for other diseases. We may not be able to identify or develop additional product candidates that are safe, tolerable and effective. Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify, in-license or acquire may not be suitable for clinical development. For example, our research methodology may be unsuccessful in identifying potential drug candidates or those we identify may be shown to have harmful side effects or other characteristics that make them unmarketable or unlikely to receive regulatory approval. We cannot guarantee that we will be successful in identifying additional potential drug candidates, or that we will be able to successfully identify and in-license new and valuable product candidates from other parties.

***Nonclinical and clinical drug development involves a lengthy, expensive and uncertain process. The results of nonclinical studies and early clinical trials are not always predictive of future results. PMN310 or any other product candidate that we advance into clinical trials may not achieve favorable results in later clinical trials, if any, or receive marketing approval.***

The research and development of product candidates is extremely risky. Only a small percentage of product candidates that enter the development process ever receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete nonclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain.

The results of nonclinical studies and early clinical trials are not necessarily predictive of future results and PMN310, or any other product candidate that we may develop, may not be further developed or have favorable results in later studies or trials. Clinical trial failure may result from a multitude of factors including, but not limited to, flaws in study design, dose selection, placebo effect, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. As such, failure in clinical trials can occur at any stage of testing. A number of companies in the pharmaceutical industry have suffered setbacks in the advancement of their product candidates into later-stage clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding results in earlier nonclinical studies or clinical trials. In addition, the results of clinical trials in one set of patients or disease indications may not be predictive of those obtained in another. In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial protocols and the rate of dropout among clinical trial participants. This is particularly true in AD, where failure rates historically are higher than in most other disease areas.

In the event of negative or inconclusive results, we may decide, or regulatory authorities may require us, to conduct additional clinical trials or nonclinical studies. In addition, data obtained from clinical trials and nonclinical studies is susceptible to varying interpretations, and regulatory authorities may not interpret our data as favorably as we do, which may further delay, limit or prevent development efforts, clinical trials or marketing approval. Furthermore, as more competing product candidates within a particular class of drugs proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change.

If we are unable to complete nonclinical studies or clinical trials of PMN310 or future product candidates, due to safety concerns or otherwise, or if the results of these trials are not sufficient to convince regulatory authorities of their safety or efficacy, we will not be able to obtain marketing approval for commercialization on a timely basis or at all. Even if we are able to obtain marketing approval for PMN310 or any future product candidates, those approvals may be for indications or dose levels that deviate from our desired approach or may contain other limitations that would adversely affect our

ability to generate revenue from sales of those product candidates. Moreover, if we are not able to differentiate our product candidate against other approved product candidates within the same class of drugs, or if any of the other circumstances described above occur, our business would be harmed and our ability to generate revenue from that class of drugs would be severely impaired.

***Clinical failure can occur at any stage of clinical development and our Company has never completed a clinical trial or submitted a BLA.***

We are early in our development efforts for PMN310 and will need to successfully complete our ongoing and planned clinical trials, including pivotal clinical trials, in order to obtain FDA approval to market PMN310 or any other product candidate we seek to develop. Carrying out clinical trials and the submission of a successful BLA is a complicated process. Although members of our team have significant experience in clinical development of drugs through regulatory approval, as an organization, we have limited experience in conducting any clinical trials with PMN310, we have limited experience in preparing regulatory submissions with PMN310 and we have not previously submitted a BLA.

In addition, we have had limited interactions with the FDA and cannot be certain how many clinical trials of PMN310 will be required or how such trials should be designed. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to BLA submission and approval of PMN310 or any other product candidate. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our current or planned clinical trials, could prevent us from or delay us in commercializing PMN310 or any future product candidates we may develop, and failure to successfully complete any of these activities in a timely manner could have a material adverse impact on our business and financial performance.

***We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.***

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- regulatory authorities, Institutional Review Boards (IRBs) or Ethics Committees (ECs), may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site or we may fail to reach a consensus with regulatory authorities on trial design;
- regulatory authorities in jurisdictions in which we seek to conduct clinical trials may differ from each other on our trial design, and it may be difficult or impossible to satisfy all such authorities with one approach;
- we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- we may be unable to add or be delayed in adding a sufficient number of clinical trial sites and obtaining IRB or independent EC approval at each clinical trial site;
- clinical trials of our product candidates may fail to show safety or efficacy or otherwise produce negative or inconclusive results, and we may decide, or regulatory authorities may require us, to conduct additional clinical trials or abandon drug development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate;
- enrollment in our clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;

- difficulties in having subjects complete a clinical trial or returning for post-treatment follow-up;
- changes to clinical trial protocols;
- our third-party contractors, including clinical investigators, contract manufacturers and vendors may fail to comply with applicable regulatory requirements, lose their licenses or permits, or otherwise fail, or lose the ability to, meet their contractual obligations to us in a timely manner, or at all;
- we might have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- regulatory authorities or IRBs may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements, a finding that our product candidates have undesirable side effects or other unexpected characteristics, or that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate, and we may lack adequate funding to continue one or more clinical trials;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- clinical trial sites may deviate from clinical trial protocol or drop out of a clinical trial; and
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies.

***Adverse side effects, properties or other safety risks associated with PMN310, PMN267, PMN442 or any future product candidates could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon further development, limit the commercial profile of an approved label or result in significant negative consequences following marketing approval, if any.***

As is the case with pharmaceuticals generally, it is possible that there may be side effects and adverse events associated with the use of PMN310, PMN267, PMN442 or any future product candidates we may develop. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics as the clinical trials progress to greater exposures and a larger number of patients. Undesirable side effects caused by, or unexpected or unacceptable characteristics associated with, PMN310, PMN267, PMN442 or any future product candidates we may develop, could result in the delay, suspension or termination of clinical trials by us, the FDA or other regulatory authorities, or IRBs for a number of reasons. We may also elect to limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for such product candidate if approved. If we elect or are required to further delay, suspend or terminate any clinical trial of any product candidates we may develop, the commercial prospects of such product candidates will be harmed and our ability to generate drug revenues from any such product candidates will be delayed or eliminated.

It is possible that, as we test our product candidates in clinical trials, or as the use of a product candidate becomes more widespread if it receives regulatory approval, we may identify additional adverse events that were not identified or not considered significant in our earlier trials. If such side effects become later known in development or upon approval, if any, such findings may harm our business, financial condition, results of operations and prospects significantly. If we or others later identify undesirable side effects, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw, suspend or limit approval of a product candidate;

- we may be required to recall a drug or change the way such drug is administered to patients;
- regulatory authorities may require additional warnings or statements in the labeling, such as a boxed warning or a contraindication or issue safety alerts, press releases or other communications containing warnings or other safety information about the product candidate, for example, field alerts to physicians and pharmacies;
- regulatory authorities may require us to implement a REMS to ensure that the benefits of the drug outweigh its risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools;
- we may be required to change the way a drug is distributed or administered, conduct additional clinical trials or be required to conduct additional post-marketing studies or surveillance;
- we may be subject to regulatory investigations and government enforcement actions;
- we may decide to remove such product candidates, if approved, from the market;
- we could be sued and held liable for harm caused to patients;
- sales of the drug may decrease significantly or become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of a product candidate, if approved, and could significantly harm our business, financial condition, results of operations and prospects.

***We may experience delays or difficulties in the enrollment and retention of patients in clinical trials, which could delay or prevent our receipt of regulatory approvals.***

Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients. Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors, including the size and nature of the patient population and competition for patients eligible for our clinical trials with competitors which may have ongoing clinical trials for product candidates that are under development to treat the same indications as one or more of our product candidates or approved products for the conditions for which we are developing our product candidates.

Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, EMA or foreign regulatory authorities. We cannot predict how successful we will be at enrolling subjects in future clinical trials. Subject enrollment is affected by other factors including:

- the severity and difficulty of diagnosing the disease under investigation;
- the eligibility and exclusion criteria for the trial in question;
- the size of the patient population and process for identifying patients;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- the design of the trial protocol;
- the perceived risks and benefits of the product candidate in the trial, including relating to cell therapy approaches;

- the availability of competing commercially available therapies and other competing therapeutic candidates' clinical trials for the disease or condition under investigation;
- the willingness of patients to be enrolled in our clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- potential disruptions caused by any global health crisis, including difficulties in initiating clinical sites, enrolling and retaining participants, diversion of healthcare resources away from clinical trials, travel or quarantine policies that may be implemented, and other factors;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment; and
- the proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Furthermore, we expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and we will have limited influence over their performance. Even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials.

***Interim, "top-line" and preliminary results from our planned clinical trials that we may announce or publish from time to time may change as more data become available and is subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, as we continue existing and initiate new clinical trials, we may publish interim, top-line or preliminary results from our clinical trials. Interim results from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are reported. Differences between preliminary, top-line or interim data and final data could significantly harm our business prospects and may cause the trading price of our Common Shares to fluctuate significantly. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated.

Further, others, including regulatory agencies may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular development program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure. Any information we determine not to disclose may ultimately be deemed meaningful by you or others with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product candidate or our business. If the interim, top-line or preliminary data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, product candidates may be harmed, which could significantly harm our business prospects.

***We cannot be certain that PMN310, PMN267, PMN442 or any of our future product candidates will receive regulatory approval, and without regulatory approval we will not be able to market our product candidates.***

We currently have no product candidates approved for sale and we cannot guarantee that we will ever have marketable product candidates. Our ability to generate revenue related to sales of PMN310, PMN267 and PMN442, if ever, will depend on the successful development and regulatory approval of such product candidates.

The development of a product candidate and its approval and commercialization, including the product candidate's design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale, distribution, import and export are subject to extensive regulation by the FDA, the EMA and regulatory authorities in other countries, with regulations differing from country to country. We are not permitted to market our product candidates in the U.S., Europe or other countries until we receive approval of a BLA from the FDA or MAA from the EMA, respectively. We have not submitted any marketing applications for any product candidate.

BLAs and MAAs, and other foreign equivalents must include extensive nonclinical and clinical data and supporting information to establish the product candidate's safety and effectiveness for each desired indication. BLAs and MAAs must also include significant information regarding the chemistry, manufacturing and controls for the drug. Obtaining approval of a BLA or a MAA is a lengthy, expensive and uncertain process, and we may not be successful in obtaining approval. The FDA and the EMA review processes can take years to complete and approval is never guaranteed. If we submit a BLA to the FDA, the FDA must decide whether to accept or reject the submission for filing. We cannot be certain that any submissions will be accepted for filing and review by the FDA. Regulators of other jurisdictions, such as the EMA, have their own procedures for approval of product candidates.

Even if a drug is approved, the FDA or the EMA, or other foreign equivalent, as the case may be, may limit the indications for which the drug may be marketed, require extensive warnings on the drug labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the U.S. and Europe also have requirements for approval of product candidates with which we must comply prior with marketing in those countries. Obtaining regulatory approval for marketing of a product candidate in one country does not ensure that we will be able to obtain regulatory approval in any other country. In addition, delays in approvals or rejections of marketing applications in the U.S., Europe or other countries may be based upon many factors, including regulatory requests for additional analyses, reports, data, nonclinical studies and clinical trials, regulatory questions regarding different interpretations of data and results, changes in regulatory policy during the period of drug development and the emergence of new information regarding PMN310, PMN267, PMN442 or other product candidates we may develop in the future. Also, regulatory approval for any of our product candidates may be withdrawn.

Before we submit a BLA to the FDA or a MAA to the EMA for a product candidate, we will be required to successfully complete our clinical trials. The FDA generally requires two pivotal clinical trials to support approval. In addition, we must scale up manufacturing and complete other standard nonclinical and clinical studies. We cannot predict whether clinical trials will be successful or whether regulators will agree with our conclusions regarding the nonclinical studies and the clinical trials we conduct.

***Our lead product candidate, PMN310, is being developed for the treatment of AD, a disease that has seen limited success in drug development.***

Efforts by biopharmaceutical and pharmaceutical companies in treating AD have seen limited success in drug development. Only two disease-modifying therapeutic options have been approved by the FDA. Biogen's Aduhelm, a mAb administered via infusion, received Accelerated Approval from the FDA on June 7, 2021 but commercialization was discontinued in January 2024. Eisai's and Biogen's Leqembi (lecabemab), also a mAb administered via infusion, received Accelerated Approval on January 6, 2023. We cannot be certain that our approach will lead to the development of approvable or marketable products. With the exception of Aduhelm and Leqembi, the only drugs approved by the FDA to treat patients with AD address the symptoms of the disease. Since 2003, over 500 clinical studies have been completed and only Aduhelm and Leqembi have been approved by the FDA as disease-modifying therapeutic options. As a result, the FDA has a limited set of products to rely on in evaluating PMN310. This could result in a longer than expected



regulatory review process, increased expected development costs or the delay or prevention of commercialization of PMN310 for the treatment of AD.

In addition to the significant uncertainty related to insurance coverage and reimbursement of all newly- approved products, there is greater uncertainty for products approved for the treatment of AD. For example, the yearly wholesale acquisition out of pocket cost of the maintenance dose of Aduhelm was \$28,200. CMS issued a draft determination that proposes to cover the cost of anti-amyloid monoclonal antibodies, including Aduhelm, only in the context of clinical trials approved by CMS or by the National Institutes of Health. These include only randomized controlled trials conducted in hospital-based outpatient settings, and require patient diversity reflecting that of the U.S. population diagnosed with AD. In April 2022, CMS confirmed this determination and announced that it would deny routine payment for Aduhelm and finalized a strict policy to require patients to enroll in clinical trials for the government to cover the drug. Biogen announced discontinuation of Aduhelm commercialization in January 2024. In contrast, Leqembi was priced at \$26,500 and is covered by Medicare Part B and some private insurers.

***We may in the future conduct clinical trials for our product candidates outside the U.S., and the FDA, EMA and other foreign regulatory authorities may not accept data from such trials.***

We may in the future choose to conduct one or more of our clinical trials outside the U.S. The acceptance of study data from clinical trials conducted outside the U.S. by FDA, or of data collected outside the jurisdiction by any foreign regulatory body, may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to cGCP, regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory bodies have similar approval requirements. There can be no assurance that the FDA, EMA or any other foreign regulatory authority will accept data from trials conducted outside of their jurisdiction. If the FDA, EMA or any applicable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which would be costly and time-consuming and delay aspects of our business plan, and which may result in our product candidates not receiving approval or clearance for commercialization in the applicable jurisdiction.

***If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed.***

From time to time, we may estimate the timing of the accomplishment of various scientific, clinical, regulatory, manufacturing and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of nonclinical studies and clinical trials and the submission of regulatory filings, including BLA submissions. From time to time, we may publicly announce the expected timing of some of these milestones. All of these milestones are, and will be, based on a variety of assumptions. The actual timing of these milestones can vary significantly compared to our estimates, in some cases for reasons beyond our control. We may experience numerous unforeseen events during, or as a result of, any future clinical trials that we conduct that could delay or prevent our ability to receive marketing approval or commercialize our product candidates.

***We may develop PMN310, PMN442, PMN267 and future product candidates for use in combination with other therapies, which could expose us to additional regulatory risks.***

We may develop PMN310, PMN442, PMN267 and future product candidates for use in combination with one or more other approved therapies for the disease state being studied. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risk that the FDA, EMA or comparable foreign regulatory authorities could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. This could result in our own products being removed from the market or being less successful commercially.

Further, we will not be able to market and sell any product candidate we develop in combination with an unapproved therapy for a combination indication if that unapproved therapy does not ultimately obtain marketing approval either alone or in combination with our product. In addition, unapproved therapies face the same risks described with respect to our product candidates currently in development, including the potential for serious adverse effects, delay in their clinical trials and lack of FDA approval.

***Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.***

As product candidates proceed through nonclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and product characteristics.

Such changes carry the risk that they will not achieve our intended objectives. Any such changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue. In addition, we may be required to make significant changes to our upstream and downstream processes across our pipeline, which could delay the development of our future product candidates.

**Risks Related to the Commercialization of Our Product Candidates**

***Successful commercialization of our product candidates, if approved, will depend on a number of factors and we cannot guarantee that we will be able to successfully commercialize our products.***

Successful commercialization of our products, if at all, will depend on a number of factors, including our ability to:

- raise sufficient capital to fund future commercialization efforts;
- build a commercial team and supporting organizational infrastructure;
- obtain necessary licenses, on commercially reasonable terms, for certain offerings we may contemplate;
- establish partnerships and alliances with third parties to secure commercial capabilities that we may not wish to build;
- market and distribute our products;
- distinguish our products from others available on the market;
- obtain any necessary regulatory approvals for our facilities, product candidates and processes;
- gain reimbursement by third-party payors, such as private health insurers, managed-health organizations, and state-sponsored health insurance plans for each jurisdiction in which our products are offered;
- educate physicians and change physician behavior to secure clinical adoption of our products;
- promote awareness of our products to increase market penetration; and
- publish in peer-reviewed journals.

There is no assurance that we will be successful in these areas. Any failure or delay in such areas could have a material adverse impact on our business, financial condition, results of operations and prospects.

***The market opportunities for PMN310, PMN267, PMN442 and future product candidates, if approved, may be smaller than we anticipate.***

We expect to seek approval for product candidates for various neurodegenerative diseases and other misfolded protein diseases. Our estimates of market potential have been derived from a variety of sources, including scientific literature, patient foundations and market research and may prove to be incorrect. Even if we obtain significant market share for our product candidates after FDA approval, the potential target populations may be too small to consistently generate revenue, and we may never achieve profitability without obtaining marketing approval for additional indications.

***Even if our current or future product candidates obtain regulatory approval, they may fail to achieve the broad degree of adoption and use by physicians, patients, hospitals, healthcare payors and others in the medical community necessary for commercial success.***

Even if one or more of our product candidates receive FDA or other regulatory approvals, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. Most of our product candidates target mechanisms for which there are limited or no currently approved products, which may result in slower adoption by physicians, patients and payors. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the clinical indications for which the product is approved and patient demand for approved products that treat those indications;
- the safety and efficacy of our product as compared to other available therapies;
- the availability of coverage and adequate reimbursement from governmental healthcare plans or third party payors for any of our product candidates that may be approved;
- acceptance by physicians, operators of clinics and patients of the product as a safe and effective treatment;
- physician and patient willingness to adopt a new therapy over other available therapies to treat approved indications;
- overcoming any biases physicians or patients may have toward particular therapies for the treatment of approved indications;
- proper training and administration of our product candidates by physicians and medical staff;
- public misperception regarding the use of our therapies, if approved for commercial sale;
- patient satisfaction with the results and administration of our product candidates and overall treatment experience, including, for example, the convenience of any dosing regimen;
- the cost of treatment with our product candidates in relation to alternative treatments and reimbursement levels, if any, and willingness to pay for the product, if approved, on the part of insurance companies and other third-party payors, physicians and patients;
- the revenue and profitability that our products may offer a physician as compared to alternative therapies;
- limitations or warnings contained in the FDA-approved labeling for our products;

- any FDA requirement to undertake a REMS;
- the effectiveness of our sales, marketing and distribution efforts;
- adverse publicity about our products or favorable publicity about competitive products; and
- potential product liability claims.

We cannot assure that our current or future product candidates, if approved, will achieve broad market acceptance among physicians, patients, healthcare payors and others in the medical community. Even if we receive regulatory approval to market any of our product candidates, we cannot assure that any such product candidate will be more effective than other commercially available alternatives or successfully commercialized. Any approval we may obtain could be for indications or patient populations that are not as broad as intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We may also be required to perform additional or unanticipated clinical trials to obtain approval or be subject to additional post-marketing testing requirements to maintain approval. In addition, regulatory authorities may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a REMS. Any failure by our product candidates that obtain regulatory approval to achieve market acceptance or commercial success would adversely affect our reputation, ability to raise additional capital, financial condition, results of operations and business prospects.

***Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale. In particular, we will need to develop a larger scale manufacturing process to commercialize our potential products, which may not be successful.***

Our product candidates have never been manufactured on a commercial scale, and there are risks associated with scaling up manufacturing to commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, lot consistency and timely availability of raw materials. There is no assurance that our third-party manufacturers will be successful in establishing a larger-scale commercial manufacturing process for our product candidates which achieves our objectives for manufacturing capacity and cost of goods. In addition, there is no assurance that any third-party manufacturers will be able to manufacture our product candidates to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of such products or to meet potential future demand. Our failure to properly or adequately scale up manufacturing for commercial scale would adversely affect our business, results of operations and financial condition.

***The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish adequate coverage, reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those drugs and decrease our ability to generate revenue.***

The availability and adequacy of coverage and reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as our product candidates, if approved. Our ability to achieve acceptable levels of coverage and reimbursement for products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize our product candidates. For more information regarding the risks related to insurance coverage and reimbursement please see “*Business — Government Regulation — Pricing and Reimbursement.*”

Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which drugs and treatments they will cover and the amount of reimbursement. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor’s determination that use of a product is:

- a covered benefit under its health plan;

- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Even if we obtain coverage for our product candidates by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the U.S., the European Union or elsewhere will be available for our product candidates or any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

There is significant uncertainty related to the insurance coverage and reimbursement of newly-approved products. In the U.S., third-party payors, and governmental healthcare plans, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs and biologics will be covered. The Medicare and Medicaid programs increasingly are used as models in the U.S. for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs and biologics. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse healthcare providers who use such therapies. We cannot predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our product candidates. Outside the U.S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other foreign jurisdictions have and will continue to put pressure on the pricing and usage of our product candidates.

Moreover, increasing efforts by governmental and third-party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products, and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of our product candidates due to the trend toward managed health care, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and biologics and surgical procedures and other treatments, has become intense. As a result, increasingly high barriers are being erected to the entry of new products.

***We currently have no sales organization. If we are unable to establish sales capabilities on our own or through third parties, we may not be able to market and sell our product candidates effectively in the U.S. and foreign jurisdictions, if approved, or generate product revenue.***

We currently do not have a marketing or sales organization. In order to commercialize our product candidates in the U.S. and foreign jurisdictions, if approved, we intend to make arrangements with third parties to perform these services, and we may not be successful in doing so. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize our product candidates, if approved. If we are not successful in commercializing our product candidates or any future product candidates, if approved, either on our own or through arrangements with third parties, we may not be able to generate any product revenue and we would incur significant additional losses.

## **Risks Related to Our Financial Position and Capital Needs**

***We have incurred losses since inception, we anticipate that we will incur continued losses for the foreseeable future and there is substantial doubt about our ability to continue as a going concern for the full one-year period following the issuance of the consolidated financial statements. We will require additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our development programs, commercialization efforts or other operations.***

The development of biopharmaceutical therapeutic candidates is capital-intensive. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct our ongoing and planned preclinical studies of our development programs, conduct existing and initiate new clinical trials for our therapeutic candidates and seek regulatory approval for our current therapeutic candidates and any future therapeutic candidates we may develop. If we obtain regulatory approval for any of our therapeutic candidates, we also expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Because the outcome of any preclinical study or clinical trial is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our therapeutic candidates. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. We had working capital of approximately \$4.3 million as of December 31, 2023. Management believes its working capital position raises substantial doubt about the Company's ability to continue as a going concern within the next twelve months from the date of the issuance of the consolidated financial statements. We will require substantial additional funds for further research and development, current and planned clinical testing, regulatory approvals, establishment of manufacturing capabilities and, if necessary, the marketing and sale of our products. Our ability to raise additional financing and maintain operations in the future could be at substantial risk and there can be no assurance that additional funding or partnerships will be available on acceptable terms that would foster successful commercialization of our products. Failing to raise capital when needed or on attractive terms could force us to delay, reduce or eliminate our research and development programs or any future commercialization efforts. We may attempt to raise additional funds for these purposes through public or private equity or debt financing, use of "at-the-market" offerings, collaborations with other biopharmaceutical companies and/or from other sources.

***We have no product candidates approved for commercial sale, we have never generated any revenue from sales and we may never be profitable.***

We have no product candidates approved for sale, have never generated any revenue from sales, have never been profitable and do not expect to be profitable in the foreseeable future. We have not recorded any revenues from the sale of biopharmaceutical products. As of December 31, 2023, we had a deficit of \$93.5 million. The cumulative deficit incurred from when we changed our name and focus in July 2015, through December 31, 2023 was \$63.2 million. We expect to incur additional losses during the periods of research and development, clinical testing, and application for regulatory approval of its product candidates. We also expect to incur losses unless and until such time as payments from corporate collaborations, product sales and/or royalty payments generate sufficient revenues to fund its continuing operations.

We have devoted most of our financial resources to research and development of PMN310, including our clinical and nonclinical development activities of PMN310, and corporate overhead. We expect that it will be several years, if ever, before we have a product candidate approved and ready for commercialization. We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, PMN310 and any other product candidate we may develop in the future, prepare for and begin the commercialization of any approved product candidates and add infrastructure and personnel to support our drug development efforts and operations as a public company. We anticipate that any such losses could be significant for the next several years. These net losses and negative cash flows have had, and will continue to have, an adverse effect on our shareholders' equity and working capital. Further, these net losses may fluctuate significantly from quarter-to-quarter or year-to-year. To become and remain profitable, we must develop and eventually commercialize PMN310 or another drug with significant revenue.

We may never succeed in developing a commercial drug and, even if we succeed in commercializing one or more product candidates, we may never generate revenues that are large enough to achieve profitability. In addition, we may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown challenges. Because of these

numerous risks and uncertainties, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to generate revenues or achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis, and we will continue to incur substantial research and development costs and other expenditures to develop and market additional product candidates.

#### **Risks Related to Our Dependence on Third Parties**

***We will rely on third parties to supply components, research, develop, test, and manufacture our product candidates and market these product candidates, if approved. The loss of any of these third party relationships or the failure of any of them to meet their obligations to us could affect our ability to develop and obtain approval of our product candidates in a timely manner.***

Our activities will require us to enter into various arrangements with corporate and academic collaborators, licensors, licensees and others for the research, development, clinical testing, manufacturing, marketing and commercialization of our products. We intend to attract corporate partners and enter into additional research collaborations. There can be no assurance, however, that we will be able to establish such additional collaborations on favorable terms, if at all, or that our current or future collaborations will be successful. Failure to attract commercial partners for our products may result in substantial clinical testing, manufacturing and commercialization costs prior to realizing any revenue from product sales or result in delays or program discontinuance if funds are not available in sufficient quantities.

Should any collaborative partner fail to develop, manufacture, or successfully commercialize any product to which we have rights, or any partner's product to which we will have rights, our business may be adversely affected. Failure of a collaborative partner to continue to participate in any particular program could delay or halt the development or commercialization of products generated from such program. In addition, there can be no assurance that the collaborative partners will not pursue other technologies or develop alternative products either alone or in collaboration with others, including our competitors, as a means for developing treatments for the diseases targeted by our programs.

Furthermore, we will hold licenses for certain technologies and there can be no assurance that these licenses will not be terminated, or that they will be renewed on acceptable conditions. We intend to negotiate additional licenses in respect of technologies developed by other companies and academic institutions. Terms of license agreements to be negotiated may include, *inter alia*, a requirement to make milestone payments, which may be substantial. We will also be obligated to make royalty payments on the sales, if any, of products resulting from licensed technology and, in some instances, may be responsible for the costs of filing and prosecuting patent applications.

***We intend to rely on CROs and other third parties to conduct, supervise and monitor a significant portion of our research and nonclinical testing and clinical trials for our product candidates, and if those third parties do not successfully carry out their contractual duties, comply with regulatory requirements or otherwise perform satisfactorily, we may not be able to obtain regulatory approval or commercialize product candidates, or such approval or commercialization may be delayed, and our business may be substantially harmed.***

We intend to engage CROs and other third parties to conduct our planned nonclinical studies or clinical trials, and to monitor and manage data. We expect to continue to rely on third parties, including clinical data management organizations, medical institutions and clinical investigators, in the future. Any of these third parties may terminate their engagements with us, some in the event of an uncured material breach and some at any time for convenience. If any of our relationships with these third parties terminate, we may not be able to timely enter into arrangements with alternative third parties or to do so on commercially reasonable terms, if at all. Switching or adding CROs involves substantial cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we intend to carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

In addition, any third parties conducting our clinical trials will not be our employees, and, except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and

resources to our clinical programs. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Consequently, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

We plan to rely on these parties for execution of our nonclinical studies and clinical trials and generally do not control their activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with Good Clinical Practices, or GCPs, which are standards for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. If we or any of our CROs or other third parties, including trial sites, fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMPs conditions. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process, or may result in fines, adverse publicity and civil and criminal sanctions.

We also are required to register certain ongoing clinical trials and post the results of certain completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the trial. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval for PMN310 or any other product candidate we develop.

We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, producing additional losses and depriving us of potential revenue.

***If any of our third-party manufacturers encounter difficulties in production of PMN310, PMN267, PMN442 or any future product candidate we develop, or fail to meet rigorously enforced regulatory standards, our ability to provide supply of our product candidates for clinical trials or, if approved, for commercial sale could be delayed or stopped, or we may be unable to maintain a commercially viable cost structure.***

The processes involved in manufacturing PMN310, PMN267, PMN442 and any other product candidate we may develop are highly-regulated and subject to multiple risks. As product candidates are developed through nonclinical studies to late-stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives, and any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials. When changes are made to the manufacturing process, we may be required to provide preclinical and clinical data showing the comparable identity, strength, quality, purity or potency of the products before and after such changes. If microbial, viral or other contaminations are discovered at the facilities of our third-party manufacturers, such facilities may need to be



closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm our business.

In order to conduct clinical trials of our product candidates, or supply commercial product candidates, if approved, we will need to manufacture them in both small and large quantities. We currently rely on third parties to manufacture our product candidates, and our manufacturing partners will have to modify and scale-up the manufacturing process when we transition to commercialization of our product candidates, if approved. Our manufacturing partners may be unable to successfully modify or scale-up the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities. If our manufacturing partners are unable to successfully scale-up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed or become infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business. In addition, building internal manufacturing capacity would carry significant risks in terms of being able to plan, design and execute on a complex project to build manufacturing facilities in a timely and cost-efficient manner.

In addition, the manufacturing process for any product candidates that we may develop will be subject to FDA, EMA and foreign regulatory requirements, and continuous oversight, and we will need to contract with manufacturers who can meet all applicable FDA, EMA and foreign regulatory authority requirements, including complying with cGMPs on an ongoing basis. If we or our third-party manufacturers are unable to reliably produce product candidates in accordance with the requirements of the FDA, EMA or other regulatory authorities, we may not obtain or maintain the approvals we need to commercialize such product candidates. Even if we obtain regulatory approval for any of our product candidates, there is no assurance that either we or our third party contract manufacturers will be able to manufacture the approved product in accordance with the requirements of the FDA, EMA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product, or to meet potential future demand. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates, impair commercialization efforts, increase our cost of goods and have an adverse effect on our business, financial condition, results of operations and growth prospects. Significant non-compliance could also result in the imposition of sanctions, including warning or untitled letters, fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could damage our reputation and our business.

***We will likely seek collaborations with third parties for the development or commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates, including PMN310, PMN267 and PMN442. Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our future products.***

We will likely seek third-party collaborators for the commercialization of PMN310, PMN267, PMN442 and any of our future product candidates, in the U.S. and may enter into collaboration agreements for the development and commercialization of any of our product candidates outside the U.S. In the U.S., commercialization partners are likely to include large biotechnology or pharmaceutical companies. Our likely collaborators outside the U.S. would most likely include regional and national pharmaceutical companies and biotechnology companies. If we enter into such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates would pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;

- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or drugs, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;
- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If any future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program could be delayed, diminished or terminated.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for any collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA, EMA or similar regulatory authorities outside the U.S., the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business

combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate revenue.

#### **Risks Related to Our Intellectual Property**

***If we are unable to obtain and maintain sufficient intellectual property protection for our product candidates, and other proprietary technologies we develop, or if the scope of the intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our product candidates, and other proprietary technologies if approved, may be adversely affected.***

Our commercial success will depend in part on our ability to obtain and maintain a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates, and other proprietary technologies we develop. If we are unable to obtain or maintain patent protection with respect to our product candidates, and other proprietary technologies we may develop, our business, financial condition, results of operations, and prospects could be materially harmed.

The patent position of biotechnology and pharmaceutical companies is highly uncertain and involves complex legal, scientific, and factual questions and has been the subject of frequent litigation in recent years.

As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights are highly uncertain. Our patent applications may not result in patents being issued that protect our product candidates and other proprietary technologies we may develop or that effectively prevent others from commercializing competitive technologies and products. Further, no consistent policy regarding the breadth of claims allowed in pharmaceutical patents has emerged to date in the U.S. or in many jurisdictions outside of the U.S. Changes in either the patent laws or interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be enforced in the patents that may be issued from the applications we may own or license from third parties. Further, if any patents we obtain or license are deemed invalid and unenforceable, our ability to commercialize or license our technology could be adversely affected.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our actual or potential future collaborators will be successful in protecting our product candidates and other proprietary technologies and their uses by obtaining, defending and enforcing patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- issued patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable, or may otherwise not provide any competitive advantage;

- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with, or eliminate our ability to make, use and sell our product candidates;
- other parties may have designed around our claims or developed technologies that may be related or competitive to ours, may have filed or may file patent applications and may have received or may receive patents that overlap or conflict with our patent applications and/or patents, either by claiming the same composition of matter, methods or formulations or by claiming subject matter that could dominate our patent position;
- any successful opposition to any patents owned by or licensed to us could deprive us of rights necessary for the practice of our technologies or the successful commercialization of any product candidate that we may develop;
- because patent applications in the U.S. and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates and other proprietary technologies and their uses;
- an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of any application with an effective filing date before March 16, 2013;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the U.S. for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the U.S. may have patent laws less favorable to patentees than those upheld by

U.S. courts, allowing foreign competitors a better opportunity to create, develop, and market competing product candidates in those countries.

The patent prosecution process is expensive, time-consuming, and complex, and we may not be able to file, prosecute, or maintain all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection for such output. In addition, our ability to obtain and maintain valid and enforceable patents depends on whether the differences between our inventions and the prior art allow our inventions to be patentable over the prior art. Furthermore, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the U.S. and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. If we do not adequately protect our intellectual property and proprietary technology, competitors may be able to use our product candidates and other proprietary technologies and erode or negate any competitive advantage we may have, which could have a material adverse effect on our financial condition and results of operations. For example:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of our patents;
- we might not have been the first to file patent applications for these inventions;

- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- any patents that we obtain may not provide us with any competitive advantages;
- we may not develop additional proprietary technologies that are patentable;
- our competitors might conduct research and development activities in countries where we do not have patent rights or where patent protection is weak and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we cannot ensure that we will be able to successfully commercialize our product candidates on a substantial scale, if approved, before the relevant patents that we own or license expire; or
- the patents of others may have an adverse effect on our business.

Others have filed, and in the future are likely to file, patent applications covering products and technologies that are similar, identical or competitive to ours or important to our business. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed or in-licensed by us, or that we or our licensors will not be involved in interference, opposition or invalidity proceedings before U.S. or non-U.S. patent offices.

We cannot be certain that claims in an issued patent covering our product candidates will be considered patentable by the USPTO, courts in the U.S., or by patent offices and courts in foreign countries. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property internationally.

The strength of patents in the biotechnology and pharmaceutical fields involves complex legal and scientific questions and can be uncertain. Patent applications that we file or in-license may fail to result in issued patents with claims that cover our product candidates in the U.S. or in foreign countries. Even if such patents do successfully issue, third parties may challenge the ownership, validity, enforceability, or scope thereof, which may result in such patents being narrowed, invalidated, or held unenforceable. Any successful opposition to our patents could deprive us of exclusive rights necessary for the successful commercialization of our product candidates. Furthermore, even if they are unchallenged, our patents may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. If the breadth or strength of protection provided by our patents with respect to our product candidates is threatened, it could dissuade companies from collaborating with us to develop, or threaten our ability to commercialize our product candidates.

For U.S. patent applications in which claims are entitled to a priority date before March 16, 2013, an interference proceeding can be provoked by a third party or instituted by the USPTO to determine who was the first to invent any of the subject matter covered by the patent claims of our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our participation in an interference proceeding may fail and, even if successful, may result in substantial costs and distract our management and other employees.

For U.S. patent applications containing a claim not entitled to priority before March 16, 2013, there is greater level of uncertainty in the patent law. In September 2011, the Leahy-Smith America Invents Act, or America Invents Act, was signed into law. The America Invents Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The USPTO is developing regulations and procedures to govern the administration of the America Invents Act, and many of the substantive changes to patent law associated with the America Invents Act, and in particular, the “first to file” provisions, were enacted on March 16, 2013. This will require us to be cognizant going forward of the time from invention to filing of a patent application and be diligent in filing patent applications, but circumstances could prevent us from promptly filing patent applications on our inventions. It remains unclear what impact the America Invents Act will have on the operation of our

business. As such, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

***Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.***

The term of any individual patent depends on applicable law in the country where the patent is granted. In the U.S., provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non-provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. When the terms of all patents covering our product candidates expire, our business may become subject to competition from competitive products, including biosimilar version of our products.

Our product candidates are protected by certain patents or patent applications, which expire at varying times. We cannot be certain that we will file and, if filed, obtain patent protection for our product candidates beyond our rights in our current patent portfolio. If we are unable to obtain additional patent protection on our product candidates, our primary protection from biosimilar market entries will be limited to regulatory biologic exclusivity.

***If we do not obtain patent term extension for our product candidates our business may be materially harmed.***

Depending upon the timing, duration, and specifics of any FDA marketing approval of our product candidates, one or more of patents issuing from U.S. patent applications that we file or license may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term, or PTE, of up to five years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it or a method for manufacturing it may be extended. Similar patent term restoration provisions to compensate for commercialization delay caused by regulatory review are also available in certain foreign jurisdictions, such as in Europe under Supplemental Protection Certificate, or SPC. If we encounter delays in our development efforts, including our future clinical trials, the period of time during which we could market our product candidates under patent protection would be reduced. Additionally, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents, or otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration, or the term of any such extension is less than we request, the period during which we will have the right to exclusively market our product will be shortened and our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced.

***If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties, or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.***

Licensing of intellectual property rights is of critical importance to our business and involves complex legal, business and scientific issues. Disputes may arise between us and our licensors regarding intellectual property rights subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property rights of the licensor that are not subject to the license agreement;
- our right to sublicense intellectual property rights to third parties under collaborative development relationships;

- our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our product candidates, and what activities satisfy those diligence obligations; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners.

If disputes over intellectual property rights that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms and/or to secure our rights to the licensed intellectual property, our business, results of operations, financial condition, and prospects may be adversely affected. We may enter into additional licenses in the future and if we fail to comply with obligations under those agreements, we could suffer adverse consequences.

***Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.***

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on any issued patents and/or applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we employ outside counsel to pay these fees due to foreign patent agencies. While an inadvertent lapse may sometimes be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market with similar or identical products or technology earlier than should otherwise have been the case, which would have a material adverse effect on our business, financial condition, results of operations, and prospects.

***Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.***

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property, particularly on obtaining and enforcing patents. Our patent rights may be affected by developments or uncertainty in United States or foreign patent statutes, patent case law, USPTO rules and regulations or the rules and regulations of foreign patent offices. Obtaining and enforcing patents in the biotechnology and pharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States may, at any time, enact changes to its patent law and regulations, including by legislation, by regulatory rule-making, or by judicial precedent, that adversely affect the scope of patent protection available and weaken the rights of patent owners to obtain patents, enforce patent infringement and obtain injunctions and/or damages. For example, the scope of patentable subject matter under 35 U.S.C. 101 has evolved significantly over the past several years as the Court of Appeals for the Federal Circuit and the Supreme Court issued various opinions, and the USPTO modified its guidance for practitioners on multiple occasions. Other countries may likewise enact changes to their patent laws in ways that adversely diminish the scope of patent protection and weaken the rights of patent owners to obtain patents, enforce patent infringement, and obtain injunctions and/or damages.

Further, the United States and other governments may, at any time, enact changes to law and regulation that create new avenues for challenging the validity of issued patents. For example, the America Invents Act created new administrative post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings that allow third parties to challenge the validity of issued patents. This applies to all of our U.S. patents, even those issued before March 16, 2013. Because of a lower evidentiary standard in USPTO proceedings compared to the evidentiary standard in U.S. federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could

change in unpredictable ways that could weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

***We may not be able to protect our intellectual property rights throughout the world.***

Patents are of national or regional effect. Filing, prosecuting, and defending patents on our product candidates, and other proprietary technologies we develop in all countries throughout the world would be prohibitively expensive. In addition, the laws of some foreign countries do not protect intellectual property rights in the same manner and to the same extent as laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement of such patent protection is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The requirements for patentability may differ in certain countries. For example, unlike other countries, China has a heightened requirement for patentability, and specifically requires a detailed description of medical uses of a claimed drug. In India, unlike the United States, there is no link between regulatory approval for a drug and its patent status. In addition to India, certain countries in Europe and developing countries, including China, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors.

In those countries, we may have limited remedies if patents are infringed or if we are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets, and other intellectual property protection, particularly those relating to biotechnology or pharmaceutical products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***We may become subject to claims challenging the inventorship or ownership of our patents and other intellectual property.***

We may be subject to claims that former employees (including former employees of our licensors), collaborators or other third parties have an interest in our patents rights, trade secrets, or other intellectual property as an inventor or co-inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. For example, we may have inventorship disputes arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co-ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and/or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business, financial condition, results of operations and prospects. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.



***We may not be successful in obtaining or maintaining necessary rights to product components and processes for our development pipeline through in-licenses.***

Presently we have intellectual property rights to our product candidates through a license from the UBC. Assuming this agreement remains in place, we could be required to pay a low to high single digit royalty on revenues to UBC in the future. Because our program may require the use of additional proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license, on reasonable terms, proprietary rights related to any compositions, formulations, methods of use, processes or other intellectual property rights from third parties that we identify as being necessary for our product candidates. Even if we are able to obtain a license to such proprietary rights, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In that event, we may be required to expend significant time and resources to develop or license replacement technology.

Where we obtain licenses from or collaborate with third parties, we may not have the right to control the preparation, filing, and prosecution of patent applications, or to maintain or enforce the patents, covering technology that we license from third parties, or such activities, if controlled by us, may require the input of such third parties. If any of our licensors or collaboration partners fail to prosecute, maintain and enforce such patents and patent applications in a manner consistent with the best interests of our business, including by payment of all applicable fees for patents covering our product candidates, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, our ability to develop and commercialize those product candidates may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products. In addition, even where we have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors and their counsel that took place prior to the date upon which we assumed control over patent prosecution. We may also require the cooperation of our licensors and collaborators to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business, or in compliance with applicable laws and regulations, which may affect the validity and enforceability of such patents or any patents that may issue from such application.

Moreover, we will likely have obligations under our current or future licenses, including making royalty and milestone payments, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license, or expiration of licensed patents or patent applications, could have a material adverse impact on our business. Our business would suffer if any such licenses terminate, if the licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter into necessary licenses on acceptable terms. Furthermore, if any licenses terminate, or if the underlying patents fail to provide the intended exclusivity, competitors or other third parties may gain the freedom to seek regulatory approval of, and to market, products identical or similar to ours. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

The licensing and acquisition of third-party proprietary rights is a competitive area, and companies, which may be more established, or have greater resources than we do, may also be pursuing strategies to license or acquire third-party proprietary rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we have collaborated and may in the future collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate an exclusive license to any of the institution's proprietary rights in

technology resulting from the collaboration. Regardless of such option to negotiate a license, we may be unable to negotiate a license within the specified time-frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer, on an exclusive basis, their proprietary rights to other parties, potentially blocking our ability to pursue our program. In addition, disputes may arise under our existing or future license agreements with these institutions or with other counterparties, which may, among other things, lead to the termination or renegotiation of these agreements, or otherwise require us to incur significant financial obligations.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us, either on reasonable terms, or at all. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment, or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights on commercially reasonable terms, our ability to commercialize our products, and our business, financial condition, and prospects for growth, could suffer.

***Third-party claims alleging intellectual property infringement may prevent or delay our drug discovery and development efforts.***

Our success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including *inter partes* review, interference and reexamination proceedings before the USPTO, or oppositions and other comparable proceedings in foreign jurisdictions. The America Invents Act introduced new procedures including *inter partes* review and post grant review. The implementation of these procedures brings uncertainty to the possibility of challenges to our patents in the future and the outcome of such challenges. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing our product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our activities related to our product candidates may give rise to claims of infringement of the patent rights of others.

The pharmaceutical and biotechnology industries have produced a proliferation of patents, and it is not always clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. We cannot assure you that any of our current or future product candidates will not infringe existing or future patents. We may not be aware of patents that have already issued that a third party might assert are infringed by one of our current or future product candidates.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents of which we are currently unaware with claims to materials, compositions, formulations, methods of manufacture or methods for treatment related to our product candidates, or the use or manufacture of our product candidates. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, there may be currently pending third-party patent applications which may later result in issued patents that our product candidates, and other proprietary technologies may infringe, or which such third parties claim are infringed by the use of our technologies. Parties making claims against us for infringement or misappropriation of their intellectual property rights may seek and obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize our product candidates. Defense of these claims, regardless of their merit, could involve substantial expenses and could be a substantial diversion of management and other employee resources from our business.

If we collaborate with third parties in the development of technology in the future, our collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability. Further, collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability. In the future, we may agree to indemnify our commercial collaborators against certain intellectual property infringement claims brought by third parties.

Any claims of patent infringement asserted by third parties would be time-consuming and could:

- result in costly litigation;

- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing our product candidates until the asserted patent expires or is finally held invalid, unenforceable, or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- require us to pay damages to the party whose intellectual property rights we may be found to be infringing, which may include treble damages if we are found to have been willfully infringing such intellectual property;
- require us to pay the attorney's fees and costs of litigation to the party whose intellectual property rights we may be found to be willfully infringing; and/or
- require us to enter into royalty or license agreements, which may not be available on commercially reasonable terms, or at all.

If we are sued for patent infringement, we would need to demonstrate that our products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do either. Proving invalidity or unenforceability is difficult. For example, in the U.S., proving invalidity before federal courts requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and divert management's time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, which may not be available, defend an infringement action or challenge the validity or enforceability of the patents in court. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, if we do not obtain a license, develop or obtain non-infringing technology, fail to defend an infringement action successfully or have infringed patents declared invalid or unenforceable, we may incur substantial monetary damages, encounter significant delays in bringing our product candidates to market and be precluded from developing, manufacturing or selling our product candidates.

We do not always conduct independent reviews of pending patent applications of and patents issued to third parties. We cannot be certain that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, analysis of the scope of relevant patent claims or determination of the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third-party patent and pending application in the U.S., Europe and elsewhere that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction, because:

- some patent applications in the U.S. may be maintained in secrecy until the patents are issued;
- patent applications in the U.S. and elsewhere can be pending for many years before issuance, or unintentionally abandoned patents or applications can be revived;
- pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our product candidates or their uses;
- identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases, and the difficulty in assessing the meaning of patent claims;
- patent applications in the U.S. are typically not published until 18 months after the priority date; and

- publications in the scientific literature often lag behind actual discoveries.

Furthermore, the scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history and can involve other factors such as expert opinion. Our interpretation of the relevance or the scope of claims in a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. Further, we may incorrectly determine that our technologies or product candidates are not covered by a third party patent or may incorrectly predict whether a third party's pending patent application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the U.S. or internationally that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our products or product candidates.

Our competitors may have filed, and may in the future file, patent applications covering technology similar to ours, and others may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our product candidates or future products or impair our competitive position. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Any such patent application may have priority over one of our patent applications, which could further require us to obtain rights to issued patents covering such technologies. If another party has filed a U.S. patent application on inventions similar to ours, we may have to participate in an interference proceeding declared by the USPTO to determine priority of invention in the U.S. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful if, unbeknownst to us, the other party had independently arrived at the same or similar invention prior to our own invention, resulting in a loss of our U.S. patent position with respect to such inventions. Other countries have similar laws that permit secrecy of patent applications and may be entitled to priority over our applications in such jurisdictions.

Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on our ability to raise the funds necessary to continue our operations.

If a third party prevails in a patent infringement lawsuit against us, we may have to stop making and selling the infringing product, pay substantial damages, including treble damages and attorneys' fees if we are found to be willfully infringing a third party's patents, obtain one or more licenses from third parties, pay royalties or redesign our infringing products, which may be impossible or require substantial time and monetary expenditure.

We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize our product candidates, which could harm our business significantly. Even if we were able to obtain a license, the rights may be nonexclusive, which may give our competitors access to the same intellectual property.

***We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.***

As is common in the biotechnology and pharmaceutical industries, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates, and other proprietary technologies. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely affect our

business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

***We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court, and we may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights.***

Third parties including competitors may infringe, misappropriate or otherwise violate our patents, patents that may issue to us in the future, or the patents of our licensors that are licensed to us. To counter infringement or unauthorized use, we may need to or choose to file infringement claims, which can be expensive and time-consuming. We may not be able to prevent, alone or with our licensors, infringement, misappropriation, or other violation of our intellectual property, particularly in countries where the laws may not protect those rights as fully as in the United States, or if we require, but do not receive, the consent or cooperation of our licensors to enforce such intellectual property.

If we choose to go to court to stop another party from using the inventions claimed in our patents, that individual or company has the right to ask the court to rule that such patents are invalid, unenforceable, or should not be enforced against that third party for any number of reasons. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements for patentability, including lack of novelty, obviousness, lack of written description, indefiniteness, or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution, i.e., committed inequitable conduct. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. Similar mechanisms for challenging the validity and enforceability of a patent exist in foreign patent offices and courts and may result in the revocation, cancellation, or amendment of any foreign patents we or our licensors hold now or in the future. The outcome following legal assertions of invalidity and unenforceability is unpredictable, and prior art could render our patents or those of our licensors invalid. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference or derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to conduct our future clinical trials, continue our research programs, license necessary technology from third parties, or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace. Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions, or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our Common Shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

Our ability to enforce our patent rights depends on our ability to establish standing in a court of competent jurisdiction. Whether a patent holder or licensee of a patent has standing can be uncertain and the considerations complex. However, if a licensor is required to be joined, and they are unwilling to do so, we may be unable to proceed with an infringement action.

Our ability to enforce our patent rights depends on our ability to detect infringement. It may be difficult to detect infringers who do not advertise the components or methods that are used in connection with their products and services. Moreover, it may be difficult or impossible to obtain evidence of infringement in a competitor's or potential competitor's product or service. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded if we were to prevail may not be commercially meaningful.

***Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.***

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our issued patent or patents that may issue from patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our shareholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

***If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed. Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.***

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and/or other advisors, and inventions agreements with employees, consultants, and advisors, to protect our trade secrets and other proprietary information. In addition to contractual measures, we try to protect the confidential nature of our proprietary information using commonly accepted physical and technological security measures. Despite these efforts, we cannot provide any assurances that all such agreements have been duly executed, and these agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

In addition, such security measures may not provide adequate protection for our proprietary information, for example, in the case of misappropriation of a trade secret by an employee, consultant, customer, or third party with authorized access. Our security measures may not prevent an employee, consultant or customer from misappropriating our trade secrets and providing them to a competitor, and recourse we take against such misconduct may not provide an adequate remedy to protect our interests fully. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. Unauthorized parties may also attempt to copy or reverse engineer certain aspects of our products that we consider proprietary. Even though we use commonly accepted security measures, the criteria for protection of trade secrets can vary among different jurisdictions.

Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the U.S. are less willing or unwilling to protect trade secrets. Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. Trade secrets will over time be disseminated within the industry through independent development, the publication of journal articles, and the movement of personnel skilled in the art from company to company or academic to

industry scientific positions. Though our agreements with third parties typically restrict the ability of our advisors, employees, collaborators, licensors, suppliers, third-party contractors, and/or consultants to publish data potentially relating to our trade secrets, our agreements may contain certain limited publication rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. Because from time to time we expect to rely on third parties in the development, manufacture, and distribution of our products and provision of our services, we must, at times, share trade secrets with them. Despite employing the contractual and other security precautions described above, the need to share trade secrets increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

***If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.***

Our trademarks or trade names, once registered, may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and trade names to third parties, such as distributors. Though these license agreements may provide guidelines for how our trademarks and trade names may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, trade secrets, domain names, copyrights, or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

Moreover, any names we may propose to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties, and be acceptable to the FDA. Similar requirements exist in Europe. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

***Intellectual property discovered through government funded programs may be subject to federal regulations such as “march-in” rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers.***

As of the date of this Annual Report on Form 10-K, neither our patents nor our product candidates are subject to march-in rights. However, some of our future patents may be generated through the use of U.S. government funding, and we may acquire or license in the future intellectual property rights that have been generated through the use of U.S. government funding or grants. Pursuant to the Bayh-Dole Act of 1980, the U.S. government has certain rights in inventions developed with government funding. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (1) adequate steps have not been taken to commercialize the invention; (2) government action is necessary to meet public health or safety needs; or (3) government action is necessary to meet requirements for public use under federal regulations (also referred to as “march-in rights”). If the U.S. government exercised its march-in rights in our future intellectual property rights that are generated through the use of U.S. government funding or grants, we could be forced to license or sublicense intellectual property developed by us or that we license on terms unfavorable to us, and there can be no assurance that we would receive compensation from the U.S. government for the exercise of such rights. The U.S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

#### **Risks Related to Legal and Regulatory Compliance Matters**

***Our relationships with customers, healthcare providers, including physicians, and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.***

Healthcare providers, including physicians, and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors subject us to various federal and state fraud and abuse laws and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute, the federal civil and criminal false claims laws and the law commonly referred to as the Physician Payments Sunshine Act and regulations promulgated under such laws. These laws will impact, among other things, our clinical research, proposed sales, marketing and educational programs, and other interactions with healthcare professionals. In addition, we may be subject to patient privacy laws by both the federal government and the states in which we conduct or may conduct our business. For more information regarding the risks related to these laws and regulations please see “Business — Government Regulation — “U.S. Healthcare Fraud and Abuse Laws and Compliance Requirements.”

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Even if precautions are taken, it is possible that governmental authorities will conclude that our business practices could, despite efforts to comply, be subject to challenge under current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our



operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, reputational harm and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Prohibitions or restrictions on sales or withdrawal of future marketed products could materially affect our business in an adverse way.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

***Even if we obtain regulatory approval for PMN310, PMN442, PMN267 or any future product candidates, they will remain subject to ongoing regulatory oversight, which may result in significant additional expense.***

Even if we obtain any regulatory approval for PMN310, PMN442, PMN267 or any future product candidates, such product candidates will be subject to ongoing regulatory requirements applicable to research, development, testing, manufacturing, labeling, packaging, storage, advertising, promoting, sampling, record-keeping and submission of safety and other post-market information, among other things. Any regulatory approvals that we receive for PMN310, PMN442, PMN267 or any future product candidates may also be subject to a REMS, limitations on the approved indicated uses for which the drug may be marketed or to the conditions of approval, or requirements that we conduct potentially costly post-marketing testing and surveillance studies, including Phase 4 trials and surveillance to monitor the quality, safety and efficacy of the drug. An unsuccessful post-marketing study or failure to complete such a study could result in the withdrawal of marketing approval. We will further be required to timely report any serious and unexpected adverse events and certain quality or production problems with our products to regulatory authorities along with other periodic reports. Any new legislation addressing drug safety issues could result in delays in product development or commercialization, or increased costs to assure compliance. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

In addition, drug manufacturers are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements and adherence to commitments made in the BLA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or if a regulatory authority disagrees with the promotion, marketing or labeling of that drug, a regulatory authority may impose restrictions relative to that drug, the manufacturing facility or us, including requesting a recall or requiring withdrawal of the drug from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of a product candidate, a regulatory authority may:

- issue a Form 483, an untitled letter or warning letter asserting that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- issue a safety alert, Dear Healthcare Provider letter, press release or other communication containing warnings or safety information about the product;

- mandate corrections to promotional materials and labeling or issuance of corrective information;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending marketing application or supplement to an approved application or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the drug;
- seize or detain the drug or otherwise require the withdrawal of the drug from the market;
- refuse to permit the import or export of products or product candidates; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize a product candidate, if approved, and harm our business, financial condition, results of operations and prospects.

***Failure to comply with health and data protection laws and regulations could lead to government enforcement actions and civil or criminal penalties, private litigation or adverse publicity and could negatively affect our operating results and business.***

We are subject to or affected by federal, state and foreign data protection laws and regulations which address privacy and data security. In the U.S., numerous federal and state laws and regulations, including HIPAA, as amended by HITECH, state data breach notification laws, state health information privacy laws and federal and state consumer protection laws, including Section 5 of the Federal Trade Commission Act, which govern the collection, use, disclosure and protection of health-related and other personal information, may apply to our operations and the operations of any future collaborators. In addition, we may obtain health information from third parties, including research institutions from which we obtain clinical trial data that are subject to privacy and security requirements under HIPAA, as amended by HITECH, and other privacy and data security laws. Depending on the facts and circumstances, we could be subject to significant administrative, civil and criminal penalties if we obtain, use or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

Further, various states have implemented similar privacy laws and regulations. For example, in California the California Consumer Privacy Act of 2018, or CCPA, gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used. The CCPA also provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, as of January 1, 2023, the California Privacy Rights Act (CPRA), amended the CCPA and created additional obligations with respect to processing and storing personal information and sensitive personal information. Similar consumer privacy laws have passed or come into force in more than a dozen U.S. states. Like the CCPA, these laws grant consumers rights in relation to their personal information and impose new obligations on regulated businesses, including, in some instances, broader data security requirements. In addition, federal and state legislators and regulators have signaled their intention to further regulate health and other sensitive information, and new and strengthened requirements relating to this information could impact our business. At the state level, some states have passed or proposed laws to specifically regulate health information. For example, Washington’s My Health My Data Act, which comes into force in March 2024, requires regulated entities to obtain consent to collect health information, grants consumers certain rights, including to request deletion, and provides for robust enforcement mechanisms, including enforcement by the Washington state attorney-general and a private right of action for consumer claims. At the federal level, the FTC has used its authority over “unfair or deceptive acts or practices” to

impose stringent requirements on the collection and disclosure of sensitive categories of personal information, including health information. Moreover, the FTC's expanded interpretation of a "breach" under its Health Breach Notification Rule could impose new disclosure obligations that would apply in the event of a qualifying breach.

Foreign data protection laws may also apply to health-related and other personal information we process. For example, the collection and use of personal information (including health data) in Europe are governed by the provisions of the EU General Data Protection Regulation ("EU GDPR") as well as other national data protection legislation in force in relevant EU Member States, with respect to the European Economic Area ("EEA"), and the UK General Data Protection Regulation (the "UK GDPR," together with the EU GDPR the "GDPR") and the UK Data Protection Act 2018 with respect to the United Kingdom ("UK"). These laws impose a broad range of strict requirements on companies subject to the GDPR, such as including requirements relating to having legal bases for processing personal data relating to identifiable individuals and transferring such information outside the EEA or the UK, providing details to those individuals regarding the processing of their personal data, implementing safeguards to keep personal data secure, having data processing agreements with third parties who process personal data, providing information to individuals regarding data processing activities, responding to individuals' requests to exercise their rights in respect of their personal data, obtaining consent of the individuals to whom the personal data relates, reporting security and privacy breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments, and record-keeping. The GDPR may impose additional responsibility and liability in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with the EEA and UK data protection regimes. This may be onerous and adversely affect our business, financial condition, results of operations and prospects.

The GDPR prohibits the international transfer of personal data to countries outside of the EEA or the UK ("third countries") which are not deemed as adequate for the transfers of personal data by competent authorities, unless a derogation exists or adequate safeguards (for example, the European Commission approved Standard Contractual Clauses ("EU SCCs") and the UK International Data Transfer Agreement/Addendum ("UK IDTA")) are implemented. Where relying on the EU SCCs or UK IDTA for data transfers, we may also be required to carry out transfer impact assessments on a case-by-case basis to ensure the law in the data importer's country and the data importer can ensure sufficient guarantees for safeguarding the personal data. These international transfer restrictions will require significant effort and cost and may result in us needing to make strategic considerations around storage and transfer of personal data.

The EU Commission has adopted its adequacy decision for the EU-U.S. Data Privacy Framework ("Framework") agreed with the U.S., which entered into force on July 11, 2023. This Framework provides a further avenue to transfer European personal data to U.S. companies which self-certified with the Framework, without the need for further safeguards. However, the Framework's validity has already been challenged in European courts and the Framework could subsequently be invalidated like its predecessors Privacy Shield and Safe Harbor frameworks.

Although the UK is regarded as a third country under the EU's GDPR, the European Commission has issued an adequacy decision recognizing the UK as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EEA to the UK remain unrestricted. Likewise, the UK government has confirmed that personal data transfers from the UK to the EEA remain free flowing. The UK government has introduced a Data Protection and Digital Information Bill ("UK Bill") into the UK legislative process. The aim of the UK Bill is to reform the UK's data protection regime following Brexit. If passed, the final version of the UK Bill may have the effect of further altering the similarities between the UK and EEA data protection regime and threaten the UK adequacy decision from the European Commission.

The potential of the respective provisions and enforcement of the EU GDPR and UK GDPR further diverging in the future creates additional regulatory challenges and uncertainties for us. The lack of clarity on future UK laws and regulations and their interaction with EU laws and regulations could add legal risk, uncertainty, complexity and cost to our handling of European personal data and our privacy and data security compliance programs and could require us to implement different compliance measures for the UK and the EEA. In addition, EEA Member States have adopted national laws to implement the EU GDPR that may partially deviate from the EU GDPR and competent authorities in the EEA Member States may interpret the EU GDPR obligations slightly differently from country to country. Therefore, we do not expect to operate in a uniform legal landscape in Europe

If we are investigated by a European or UK data protection authority, we may face fines and other penalties, including bans on processing and transferring personal data. EEA and UK data protection authorities have the power to impose administrative fines for violations of the GDPR of up to a maximum of €20 (£17.5 under the UK GDPR) million or 4% of our total worldwide global turnover for the preceding fiscal year, whichever is higher, and violations of the GDPR may also lead to damages claims by data controllers and data subjects. Such penalties are in addition to any civil litigation claims by data controllers, clients, and data subjects. Compliance with U.S. and foreign data protection laws and regulations could require us to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. Failure to comply with U.S. and foreign data protection laws and regulations could result in government investigations and/or enforcement actions, fines, civil or criminal penalties, private litigation or adverse publicity and could negatively affect our operating results and business.

Moreover, clinical trial subjects about whom we or any of our potential collaborators obtain information, as well as the providers who share this information with us, may contractually limit our ability to use and disclose the information. Claims that we have violated individuals' privacy rights, failed to comply with data protection laws or breached our contractual obligations, even if we are not found liable, could be expensive and time consuming to defend and could result in adverse publicity that could materially and adversely affect our business, financial condition, results of operations and prospects.

The use of new and evolving technologies, such as artificial intelligence (AI), in our offerings may result in spending material resources and presents risks and challenges that can impact our business including by posing security and other risks to our confidential information, proprietary information and personal information, and as a result we may be exposed to reputational harm and liability.

We continue to build and integrate AI into our offerings, and this innovation presents risks and challenges that could affect its adoption, and therefore our business. The use of certain artificial intelligence technology can give rise to intellectual property risks, including compromises to proprietary intellectual property and intellectual property infringement. Additionally, we expect to see increasing government and supranational regulation related to artificial intelligence use and ethics, which may also significantly increase the burden and cost of research, development and compliance in this area. For example, the EU's Artificial Intelligence Act ("AI Act") — the world's first comprehensive AI law — is anticipated to enter into force in 2024 and, with some exceptions, become effective 24 months thereafter. This legislation imposes significant obligations on providers and deployers of high risk artificial intelligence systems, and encourages providers and deployers of artificial intelligence systems to account for EU ethical principles in their development and use of these systems. If we develop or deploy AI systems that are governed by the AI Act, we may be required to adopt higher standards of data quality, transparency, and human oversight, and adhere to specific and potentially burdensome and costly ethical, accountability, and administrative requirements. The rapid evolution of AI will require the application of significant resources to design, develop, test and maintain our products and services to help ensure that AI is implemented in accordance with applicable law and regulation and in a socially responsible manner and to minimize any real or perceived unintended harmful impacts. Our vendors may in turn incorporate AI tools into their own offerings, and the providers of these AI tools may not meet existing or rapidly evolving regulatory or industry standards, including with respect to privacy and data security. Further, bad actors around the world use increasingly sophisticated methods, including the use of AI, to engage in illegal activities involving the theft and misuse of personal information, confidential information and intellectual property. Any of these effects could damage our reputation, result in the loss of valuable property and information, cause us to breach applicable laws and regulations, and adversely impact our business.

***Even if we obtain FDA or EMA approval any of our product candidates in the U.S. or European Union, we may never obtain approval for or commercialize any of them in any other jurisdiction, which would limit our ability to realize their full market potential.***

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy.

Approval by the FDA in the U.S. or the EMA in the European Union does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our

ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. In many jurisdictions outside the U.S., a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval.

Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional nonclinical studies or clinical trials, which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

***Healthcare legislative or regulatory reform measures may have a negative impact on our business and results of operations.***

The U.S. and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system. The U.S. government, state legislatures and foreign governments also have shown significant interest in implementing cost-containment programs to limit the growth of government- paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Additional changes that may affect our business include those governing enrollment in federal healthcare programs, reimbursement changes, rules regarding prescription drug benefits under the health insurance exchanges and fraud and abuse and enforcement. Continued implementation of the ACA and the passage of additional laws and regulations may result in the expansion of new programs such as Medicare payment for performance initiatives, and may impact existing government healthcare programs, such as by improving the physician quality reporting system and feedback program. For more information regarding the risks related to recently enacted and future legislation please see “*Business — Government Regulation — Healthcare Reform Measures.*”

We cannot predict the initiatives that may be adopted in the future. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare and/or impose price controls may adversely affect:

- the demand for our product candidates, if we obtain regulatory approval;
- our ability to set a price that we believe is fair for our approved products;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare drugs and services, which could result in reduced demand for our drug candidates or additional pricing pressures. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and

bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our drugs or put pressure on our drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

***Our business activities may be subject to the Foreign Corrupt Practices Act of 1977 (“FCPA”) and similar anti-bribery and anti-corruption laws.***

Our business activities may be subject to the FCPA, U.S. domestic bribery statutes, and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we may operate, including the

U.K. Bribery Act of 2010. The FCPA generally prohibits offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to a non-U.S. government official in order to influence official action, or otherwise obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls. Our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, hospitals are owned and operated by the government, and doctors and other hospital employees would be considered foreign officials under the FCPA. There is no certainty that all of our employees, agents, contractors or those of our affiliates, will comply with all applicable laws and regulations, particularly given the high level of complexity of these laws. Violations of these laws and regulations could result in fines, criminal sanctions against us, our officers, or our employees, the closing down of our facilities, implementation of compliance programs and prohibitions on the conduct of our business. Any such violations could include prohibitions on our ability to offer our product candidates in one or more countries and could materially damage our reputation, our brand, our international expansion efforts, our ability to attract and retain employees, and our business, prospects, operating results and financial condition.

***Our employees, independent contractors, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards, FCPA and similar anti-bribery and anti-corruption laws, and requirements and insider trading, which could significantly harm our business.***

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants, commercial partners and vendors. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with health care fraud and abuse laws and regulations in the U.S. and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

***Our insurance policies are expensive and only protect us from some business risks, which will leave us exposed to significant uninsured liabilities.***

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, products liability and directors’ and officers’ insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the

commercialization of PMN310 or any other product candidate. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations.

### **Risks Related to Our Business and Industry**

*We face significant competition in an environment of rapid technological and scientific change, and there is a possibility that our competitors may achieve regulatory approval before us or develop therapies that are safer or more effective than ours.*

The development and commercialization of new drugs is highly competitive. Moreover, the AD field is characterized by strong competition and a strong emphasis on intellectual property. We may face competition with respect to any product candidates that we seek to develop or commercialize in the future from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide.

Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

If approved, PMN310 will likely compete with therapies currently approved for the treatment of patients with AD, which have primarily been developed to treat the symptoms of AD rather than the underlying cause of the disease, such as memantine and cholinesterase inhibitors. PMN310 may also compete with one or more potentially disease-modifying therapeutics that target A $\beta$  or amyloid plaques. Biogen's aducanumab (Aduhelm) was approved by the FDA in June 2021 under the Accelerated approval pathway but commercialization was discontinued in January 2024. Lecanemab (Leqembi) from Eisai and Biogen received Accelerated Approval from FDA in January 2023. Other companies known to be developing therapies with A $\beta$ /amyloid plaque-related targets include Alzheon, Inc., Alzinova AB, Chugai Pharmaceutical Co. Ltd., Cognition Therapeutics, Inc., Eisai Co., Ltd., Eli Lilly and Company, Grifols, S.A., KalGene Pharmaceuticals, Inc., Neurimmune AG, Novartis AG, Acumen Pharmaceuticals Inc., Prothena Biosciences, Inc., Roche Holding AG (including Genentech, its wholly owned subsidiary) and Wren Therapeutics, Inc. Additionally, PMN310, if approved, may also compete with other potential therapies intended to address underlying causes of AD that are being developed by several companies, including AbbVie Inc., AC Immune SA, Alektor, Inc., Anavex Life Sciences Corp., Annovis Bio, Inc., Athira Pharma, Inc., Biohaven Pharmaceuticals, Inc., Cassava Sciences, Inc., Cortexyme, Inc., Denali Therapeutics, Inc., Johnson & Johnson (including Janssen, its wholly-owned subsidiary) and Takeda Pharmaceutical Co. Ltd.

Many of our current or potential competitors, either alone or with their strategic partners, have significantly greater financial resources and expertise in research and development, manufacturing, nonclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved product candidates than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize product candidates that are safer, more effective, have fewer or less severe side effects, are more convenient, or are less expensive than any product candidates that we may develop. Furthermore, currently approved product candidates could be discovered to have application for treatment of AD, which could give such product candidates significant regulatory and market timing advantages over any of our product candidates. Our competitors also may obtain FDA, EMA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours from the FDA, which could result in our competitors establishing a strong market position before we are able to enter the market. Additionally, product candidates or technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing any product candidates we may develop against competitors.

If our competitors market product candidates that are more effective, safer or less expensive than our product candidates, if approved, or that reach the market sooner than our product candidates, we may not achieve commercial success. In

addition, the pharmaceutical industry is characterized by rapid technological change. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Technological advances or product candidates developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical.

***If we fail to attract and retain senior management and key scientific personnel, our business may be materially and adversely affected.***

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management and clinical and scientific personnel. We are highly dependent upon members of our senior management, particularly our Interim CEO, Neil Warma, as well as our senior scientists and other members of our management team. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, initiation or completion of our planned clinical trials or the commercialization of our product candidates or any future product candidates.

Competition for qualified personnel in the biopharmaceutical field is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and if we initiate commercial activities. We may not be able to attract and retain quality personnel on acceptable terms, or at all. In addition, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output.

***If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our current or future product candidates.***

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and breach of warranty. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our current or future product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- regulatory investigations, product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize our current or any future product candidates.



If we are unable to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims, the commercialization of our current or any future product candidates we develop could be inhibited or prevented. We currently carry product liability insurance covering our clinical trials. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient funds to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses. If and when we obtain approval for marketing any of our product candidates, we intend to expand our insurance coverage to include the sale of such product candidate; however, we may be unable to obtain this liability insurance on commercially reasonable terms or at all.

***We may explore strategic collaborations that may never materialize or may fail.***

We may attempt to broaden the global reach of our platform by selectively collaborating with leading therapeutic companies and other organizations. As a result, we may periodically explore a variety of possible additional strategic collaborations in an effort to gain access to additional product candidates or resources. At the current time, we cannot predict what form such a strategic collaboration might take. In the event we do form such collaborations, we intend to retain significant economic and commercial rights to our programs in key geographic areas that are core to our long-term strategy. We are likely to face significant competition in seeking appropriate strategic collaborators, and strategic collaborations can be complicated and time consuming to negotiate and document. We may not be able to negotiate strategic collaborations on acceptable terms, or at all. We are unable to predict when, if ever, we will enter into any additional strategic collaborations because of the numerous risks and uncertainties associated with establishing them.

#### **Risks Related to Ownership of Our Common Shares and Our Status as a U.S. Public Company**

***Investment in the Company's Common Shares is speculative, involves risk, and there is no guarantee of a return.***

There is no guarantee that the Common Shares will earn any positive return in the short term or long term. A holding of Common Shares is speculative and involves a high degree of risk and should be undertaken only by holders whose financial resources are sufficient to enable them to assume such risks and who have no need for immediate liquidity in their investment. A holding of Common Shares is appropriate only for holders who have the capacity to absorb a loss of some or all of their holdings.

***If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our share price and trading volume could decline.***

The trading market for our Common Shares will be influenced by the research and reports that equity research analysts publish about us and our business. As a relatively new public company, we anticipate having only limited research coverage by equity research analysts. Equity research analysts may elect not to provide research coverage of our Common Shares, and such lack of research coverage may adversely affect the market price of our Common Shares. In the event we do have equity research analyst coverage, we will not have any control over the analysts or the content and opinions included in their reports. The price of our shares could decline if one or more equity research analysts downgrade our shares or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage of our company or fails to publish reports on us regularly, demand for our shares could decrease, which in turn could cause our shares price or trading volume to decline.

***Concentration of ownership of our Common Shares among our existing executive officers, directors and principal shareholders may prevent new investors from influencing significant corporate decisions.***

Based on their shareholdings as of December 31, 2023, our directors, executive officers and beneficial owners of greater than 5% of our outstanding shares and their respective affiliates will beneficially own, in the aggregate, approximately 20.4% of our outstanding Common Shares. As a result, these persons, acting together, would be able to significantly

influence all matters requiring shareholder approval, including the election and removal of directors, any merger, consolidation, sale of all or substantially all of our assets or other significant corporate transactions.

Some of these persons or entities may have interests different than yours. For example, because many of these shareholders purchased their shares at prices substantially below the estimated public offering price and have held their shares for a longer period, they may be more interested in selling our Company to an acquirer rather than other investors, or they may want us to pursue strategies that deviate from the interests of other shareholders.

***Our constating documents permit us to issue an unlimited amount of additional Common Shares or Preferred Shares, which may prevent a third-party takeover or cause our shareholders to experience dilution in the future.***

Our constating documents authorize us to issue an unlimited number of Common Shares and an unlimited number of Preferred Shares. Our Board has the authority to cause us to issue additional Common Shares and Preferred Shares and to determine the special rights and restrictions of the shares of one or more series of our Preferred Shares, each without consent of our shareholders. The issuance of any such securities may result in a reduction of the book value or market price of our Common Shares. Given the fact that we have not achieved profitability or generated positive cash flow historically, and we operate in a capital-intensive industry with significant working capital requirements, we may be required to issue additional Common Shares or other securities that are dilutive to existing shareholders in the future in order to continue our operations. For example, on September 22, 2023, we filed a registration statement on Form S-3 (File No. 333-274658) with the SEC, which was declared effective on September 29, 2023 (Shelf Registration Statement), in relation to the registration of Common Shares, preferred shares, subscription receipts, debt securities, warrants and/or units of any combination thereof for the purposes of selling, from time to time, our Common Shares, debt securities or other equity securities in one or more offerings. On January 5, 2024, we entered into an At The Market Offering Agreement with BTIG, LLC to provide for the offering, issuance and sale of up to an aggregate amount of \$25.0 million of our Common Shares from time to time in “at-the-market” offerings under the Shelf Registration Statement and subject to the limitations thereof. Sales of Common Shares, debt securities or other equity securities by us may represent a significant percentage of our Common Shares currently outstanding. If we sell, or the market perceives that we intend to sell, substantial amounts of our Common Shares under the Shelf Registration Statement or otherwise, the market price of our Common Shares could decline significantly.

Our efforts to fund our intended business plan may result in dilution to existing shareholders. Further, any such issuances could result in a change of control or a reduction in the market price for our Common Shares. Additionally, the rights of the holders of Common Shares will be subject to, and may be adversely affected by, the rights of holders of any Preferred Shares that may be issued in the future. For example, Preferred Shares typically rank senior to Common Shares as to dividend rights, liquidation preference or both and may be convertible into Common Shares. Lastly, our ability to issue Preferred Shares could make it more difficult for a third-party to acquire a majority of our outstanding voting shares, particularly in the event we issue Preferred Shares with special voting rights, the effect of which may be to deprive our shareholders of a control premium that might otherwise be realized in connection with an acquisition of us.

***Anti-takeover provisions in our governing documents and under Canadian Law could prevent or delay transactions that shareholders may favor.***

Provisions of our governing documents and the OBCA may discourage, delay or prevent a merger or acquisition that shareholders may consider favorable, including transactions in which shareholders might otherwise receive a premium for their Common Shares, and may also frustrate or prevent any attempt by shareholders to change the direction or management. For example, these provisions:

- require a 66 <sup>2</sup>/<sub>3</sub>% majority of shareholder votes cast in favor of a resolution to effect various amendments to the Articles of Incorporation of the Company, as amended (the “**articles**”);
- require that in the event of shareholders of the Company vote via written resolution, that such resolution must be signed by all shareholders of the Company entitled to vote on that resolution;

- establish advance notice requirements for nominations for election to the Board at any annual or special meeting of shareholders of the Company; and
- Any transaction in which a third party seeks to acquire our voting securities or equity securities that would result in the acquiror holding greater than 20% of the securities of that class may be governed by Multilateral Instrument 62-104—*Take-Over Bids and Issuer Bids* (the “**Takeover Bid Rules**”) promulgated by the Canadian Securities Administrators.

***The rights of our shareholders may differ from the rights typically offered to shareholders of a U.S. corporation and these differences may make our Common Shares less attractive to investors.***

We are incorporated under the provincial laws of Ontario, Canada, and, therefore, certain of the rights of holders of our shares are governed by Canadian law, including the provisions of the OBCA, and by our articles. These rights differ in certain respects from the rights of shareholders in typical U.S. corporations and these differences may make our Common Shares less attractive to investors.

***We are an “emerging growth company” and a “smaller reporting company” and, as a result of the reduced disclosure and governance requirements applicable to emerging growth companies and smaller reporting companies, our Common Shares may be less attractive to investors.***

We are an “emerging growth company” as defined in the JOBS Act and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor’s report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- not being required to hold a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

We cannot predict if investors will find our Common Shares less attractive because we will rely on these exemptions. If some investors find our Common Shares less attractive as a result, there may be a less active trading market for our Common Shares and our share price may be more volatile. We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of the last day of the fiscal year (i) following the fifth anniversary of the filing of our Form 10 Registration Statement, (ii) in which we have total annual gross revenue of at least \$1.235 billion, or (iii) in which we are deemed to be a large accelerated filer, which means the market value of our Common Shares that are held by non-affiliates exceeds \$700 million as of the prior June 30th, and the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have elected to take advantage of the extended transition period to comply with new or revised accounting standards and to adopt certain of the reduced disclosure requirements available to emerging growth companies. As a result of the accounting standards election, we will not be subject to the same implementation timing for new or revised accounting standards as other public companies that are not emerging growth companies, which may make comparison of our financials to those of other public companies more difficult. As a result

of these elections, the information that we provide herein may be different than the information you may receive from other public companies in which you hold equity interests. In addition, it is possible that some investors will find our Common Shares less attractive as a result of these elections, which may result in a less active trading market for our Common Shares and higher volatility in our share price.

We are also a “smaller reporting company” as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies until the fiscal year following the determination that our voting and non-voting Common Shares held by non-affiliates is more than \$250 million measured on the last business day of our second fiscal quarter, or our annual revenues are more than \$100 million during the most recently completed fiscal year and our voting and non-voting Common Shares held by non-affiliates is more than \$700 million measured on the last business day of our second fiscal quarter.

***We have never paid dividends on our capital shares and we do not intend to pay dividends for the foreseeable future. Consequently, any gains from an investment in our Common Shares will likely depend on whether the price of our Common Shares increases.***

We have never declared or paid any dividends on our Common Shares and do not intend to pay any dividends in the foreseeable future. We anticipate that we will retain all of our future earnings for use in the operation of our business and for general corporate purposes. Any determination to pay dividends in the future will be at the discretion of our Board. Accordingly, investors must rely on sales of their Common Shares after price appreciation, which may never occur, as the only way to realize any future gains on their investments.

***Our internal controls over financial reporting may not be effective, which could have a material and adverse effect on our business.***

The Company is subject to reporting and other obligations under applicable Canadian and U.S. securities laws, reporting requirements and rules of any stock exchange on which the Common Shares are listed, including NI 52-109. These reporting and other obligations place significant demands on our management, administrative, operational and accounting resources. If we are unable to accomplish any such necessary objectives in a timely and effective manner, our ability to comply with our financial reporting obligations and other rules applicable to reporting issuers could be impaired. Moreover, any failure to maintain effective internal controls could cause us to fail to satisfy our reporting obligations or result in material misstatements in our financial statements, including potential significant deficiencies. If we cannot provide reliable financial reports or prevent fraud, our reputation and operating results could be materially adversely affected, which could also cause investors to lose confidence in our reported financial information, which could result in a reduction in the trading price of the Common Shares.

The Company does not expect that its disclosure controls and procedures and internal controls over financial reporting will prevent all error or fraud. A control system, no matter how well-designed and implemented, can provide only reasonable, not absolute, assurance that the control system’s objectives will be met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Due to the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues within an organization are detected. The inherent limitations include the realities that judgments in decision making can be faulty, and that breakdowns can occur because of simple errors or mistakes. Controls can also be circumvented by individual acts of certain persons, by collusion of two or more people or by management override of the controls. Due to the inherent limitations in a control system, misstatements due to error or fraud may occur and may not be detected in a timely manner or at all.

#### **General Risk Factors**

***We incur increased costs and demands upon management as a result of being a public company in the United States.***

As a public company listed in the U.S., we incur significant additional legal, accounting and other costs. These additional costs could negatively affect our financial results. In addition, changing laws, regulations and standards relating to

corporate governance and public disclosure, including regulations implemented by the SEC and Nasdaq, may increase legal and financial compliance costs and make some activities more time-consuming. These laws, regulations and standards are subject to varying interpretations and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies.

We continue to invest resources to comply with evolving laws, regulations and standards, and this investment may result in increased general and administrative expenses and a diversion of management's time and attention from revenue-generating activities to compliance activities. If notwithstanding our efforts to comply with new laws, regulations and standards, we fail to comply, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

Failure to comply with these rules might also make it more difficult for us to obtain some types of insurance, including director and officer liability insurance, and we might be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for us to attract and retain qualified persons to serve on our Board of Directors, on committees of our Board of Directors or as members of senior management.

***Adverse developments affecting the financial services industry could adversely affect our current and projected business operations and our financial condition and results of operations.***

Adverse developments that affect financial institutions, such as events involving liquidity that are rumored or actual, have in the past and may in the future lead to market-wide liquidity problems. For example, on March 10, 2023, Silicon Valley Bank was closed by the California Department of Financial Protection and Innovation, which appointed the Federal Deposit Insurance Corporation as receiver. Although we assess our banking relationships as we believe necessary or appropriate, our access to funding sources and other credit arrangements in amounts adequate to finance or capitalize our current and projected future business operations could be significantly impaired by factors that us, the financial institutions with which we have credit agreements or arrangements directly, or the financial services industry or economy in general. These factors could include, among others, events such as liquidity constraints or failures, the ability to perform obligations under various types of financial, credit or liquidity agreements or arrangements, disruptions or instability in the financial services industry or financial markets, or concerns or negative expectations about the prospects for companies in the financial services industry.

***Public health crises, such as a pandemic, epidemic or outbreak of other highly infectious or contagious diseases, could seriously harm our research, development and potential future commercialization efforts, increase our costs and expenses and have a material adverse effect on our business, financial condition and results of operations.***

Public health crises, such as a pandemic, epidemic or outbreak of other highly infectious or contagious diseases, could adversely impact our business, the business operations of third parties on whom we rely and our ongoing or planned research and development activities. Additionally, timely enrollment in our ongoing and planned clinical trials is dependent upon clinical trial sites which may be adversely affected by global health concerns. Public health crises could result in increased adverse events and deaths in our clinical trials. Some factors from public health crises that could delay or otherwise adversely affect enrollment in the clinical trials of our product candidates, as well as our business generally, include:

- the potential diversion of healthcare resources away from the conduct of clinical trials to focus on public health crises, including the attention of physicians serving as our clinical trial investigators, hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our prospective clinical trials and the need for drugs and other supplies that clinical trial sites must have on hand to conduct our clinical trials to be used to address such public health crises;
- limitations on travel that could interrupt key trial and business activities, such as clinical trial site initiations and monitoring, domestic and international travel by employees, contractors or patients to clinical trial sites,

including any government-imposed travel restrictions or quarantines that will impact the ability or willingness of patients, employees or contractors to travel to our clinical trial sites or secure visas or entry permissions, a loss of face-to-face meetings and other interactions with potential partners, any of which could delay or adversely impact the conduct or progress of our prospective clinical trials;

- interruption in global shipping affecting the transport of clinical trial materials, such as patient samples, investigational drug product and other supplies used in our prospective clinical trials;
- interruptions in operations at third-party manufacturers, which could result in delays or disruptions in the supply of our current product candidates and any future product candidates; and
- business disruptions caused by potential workplace, laboratory and office closures and an increased reliance on employees working from home, disruptions to or delays in ongoing laboratory experiments and operations, product manufacturing and supply, staffing shortages, travel limitations or mass transit disruptions, any of which could adversely impact our business operations or delay necessary interactions with local regulators, ethics committees and other important agencies and contractors.

Any of these factors, and other factors related to any such disruptions that are unforeseen, could have a material adverse effect on our business and our results of operations and financial condition. Further, uncertainty around these and related issues could lead to adverse effects on the economy of the United States and other economies, which could impact our ability to raise the necessary capital needed to develop and commercialize our product candidates.

***The elimination of monetary liability against our directors, officers, and employees under Canadian law and the existence of indemnification rights for our obligations to our directors, officers, and employees may result in substantial expenditures by us and may discourage lawsuits against our directors, officers, and employees.***

Our by-laws provide that, subject to the OBCA, we may indemnify a director or officer or a former director or officer or a corporation of which the we are or were a shareholder or creditor and their heirs and legal representatives of such person against all costs, charges, and expenses including and amount to be paid to settle an action or satisfy a judgment, reasonably incurred in respect of any civil, criminal or administrative action or proceeding to which they are made a party by reason of being or having been a director or officer of us or a director or officer of any such corporation. Each director and officer upon being elected and appointed shall be deemed to have contracted with us on the terms of this indemnity. The failure of a director or officer to comply with the provisions of the OBCA or the articles or the by-laws shall not invalidate any indemnity to which they are entitled under the by-laws.

We may also have contractual indemnification obligations under any future employment agreements with our officers or agreements entered into with our directors. The foregoing indemnification obligations could result in us incurring substantial expenditures to cover the cost of settlement or damage awards against directors and officers, which we may be unable to recoup. These provisions and the resulting costs may also discourage us from bringing a lawsuit against directors and officers for breaches of their fiduciary duties, and may similarly discourage the filing of derivative litigation by our shareholders against our directors and officers even though such actions, if successful, might otherwise benefit us and our shareholders.

***There may be difficulty in enforcing judgments and effecting service of process on directors and officers that are not citizens of the U.S.***

We are incorporated under the OBCA and some of our directors and officers reside outside of the U.S., in Canada. Consequently, it may not be possible for an investor to effect service of process within the U.S. on us or those persons. Furthermore, it may not be possible for an investor to enforce judgments obtained in U.S. courts based upon the civil liability provisions of U.S. federal securities laws or other laws of the U.S. against us or those persons. There is doubt as to the enforceability, in original actions in Canadian courts, of liabilities based upon U.S. federal securities laws and as to the enforceability in Canadian courts of judgments of U.S. courts obtained in actions based upon the civil liability provisions of the U.S. federal securities laws. Therefore, it may not be possible to enforce those actions against us and certain of our directors and officers.

***Comprehensive tax reform legislation could adversely affect our business and financial condition.***

The rules dealing with federal, state and local income taxation are constantly under review by persons involved in the legislative process and, in the case of U.S. tax laws, by the Internal Revenue Service and the U.S. Treasury Department, and in the case of Canadian tax laws, by the Canada Revenue Agency and the Department of Finance. Changes to tax laws (which changes may have retroactive application) could adversely affect us or holders of our Common Shares. For example, under Section 174 of the code, in taxable years beginning after December 31, 2021, expenses that are incurred for research and development in the U.S. are capitalized and amortized, which may have an adverse effect on our cash flow. In addition, it is unclear how these U.S. federal income tax changes will affect state and local taxation.

Additional changes to U.S. federal income tax law are currently being contemplated, and future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations. It cannot be predicted whether, when, in what form, or with what effective dates, new tax laws may be enacted, or regulations and rulings may be enacted, promulgated or issued under existing or new tax laws, which could result in an increase in our or our shareholders' tax liability or require changes in the manner in which we operate in order to minimize or mitigate any adverse effects of changes in tax law or in the interpretation thereof.

***If we are characterized as a passive foreign investment company (PFIC), U.S. Holders may be subject to adverse U.S. federal income tax consequences.***

Based on our current operations, income, assets and certain estimates and projections, including as to the relative values of our assets, including goodwill, which is based on the expected price of our Common Shares, we were not a PFIC for the 2022 taxable year and do not expect to have been a PFIC for the 2023 taxable year.

However, we must make an annual determination as to whether we are a PFIC based on the types of income we earn and the types and value of our assets from time to time, all of which are subject to change. Therefore, we cannot assure you that we will not be a PFIC for our current taxable year or any future taxable year. A non-U.S. corporation generally will be considered a PFIC for any taxable year if either (1) at least 75% of its gross income is passive income or (2) at least 50% of the value of its assets (based on an average of the quarterly values of the assets during a taxable year) is attributable to assets that produce or are held for the production of passive income. The market value of our assets may be determined in large part by the market price of the Common Shares, which is likely to fluctuate. In addition, the composition of our income and assets will be affected by how, and how quickly, we use any cash that we raise. If we were to be treated as a PFIC for any taxable year during which you hold Common Shares, certain adverse U.S. federal income tax consequences could apply to U.S. Holders.

For purposes of this discussion, a "U.S. Holder" is a holder who, for U.S. federal income tax purposes, is a beneficial owner of Common Shares, and who is: (i) an individual who is a citizen or individual resident of U.S.; (ii) a corporation, or other entity taxable as a corporation, created or organized in or under the laws of the U.S., any state therein or the District of Columbia; (iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source; or (iv) a trust if (1) a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or (2) the trust has a valid election in effect to be treated as a U.S. person under applicable U.S. Treasury Regulations.

***We are subject to the continued listing criteria of Nasdaq and our failure to satisfy these criteria may result in a delisting of our Common Shares.***

Our Common Shares are currently listed on Nasdaq. We cannot assure you that we will be able to maintain a listing of our Common Shares on any such trading venue. If we fail to satisfy any of Nasdaq's continued listing requirements, such as the corporate governance requirements or the minimum closing bid price requirement, Nasdaq may take steps to delist our Common Shares. Such a delisting would likely have a negative effect on the price of our Common Shares and would impair your ability to sell or purchase our Common Shares when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our Common Shares to become listed again, stabilize the market price or improve the liquidity of our Common Shares, prevent our

Common Shares from dropping below the required minimum bid price or prevent future non-compliance with Nasdaq listing requirements.

If Nasdaq delists our Common Shares, investors may face material adverse consequences, including, but not limited to, a lack of trading market for the Common Shares, reduced liquidity, decreased analyst coverage of the Company, and an inability for us to obtain additional financing to fund our operations.

***Our business and operations would suffer in the event of computer system failures, cyberattacks or a deficiency in our cybersecurity or a natural disaster.***

Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely, are vulnerable to damage from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyberattacks or cyber-intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization. The risk of a security incident or breach or disruption, particularly through cyberattacks or cyber intrusion, including by computer hackers, foreign governments, and cyber terrorists, has generally increased as the number, intensity, and sophistication of attempted attacks and intrusions from around the world have increased. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical trial data from completed, ongoing, or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security incident or breach was to result in a loss of or damage to our data or applications, systems, or infrastructure, or inappropriate disclosure or misuse of confidential or proprietary information, we could incur material legal claims and liability (including litigation and regulatory actions), financial costs, and damage to our reputation, and the further development of our product candidates could be delayed.

Additionally, the regulatory environment surrounding information security is increasingly demanding, with the frequent imposition of new and changing requirements. Compliance with changes in information security laws and with rapidly evolving industry standards may result in our incurring significant expense due to increased investment in technology and the development of new operational processes related to cybersecurity.

***Disruptions at the FDA, the SEC and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.***

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs or biologics to be reviewed and approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including most recently from December 22, 2018 to January 25, 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

If a prolonged government shutdown occurs, or if global health concerns prevent the FDA or other regulatory authorities from conducting business as usual or conducting inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.



***Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.***

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. Portions of our current or future clinical trials may be conducted outside of the U.S. and unfavorable economic conditions resulting in the weakening of the U.S. dollar would make those clinical trials more costly to operate. Furthermore, a severe or prolonged economic downturn, including a recession or depression resulting from potential public health crises, weather catastrophe, acts of terrorism, war (such as the military conflict between Russia and Ukraine), threats of terrorist attacks or war, political disruption or other events outside of our control could result in a variety of risks to our business, including, among other things, weakened demand for our product candidates or any future product candidates, if approved, and our ability to raise additional capital when needed on acceptable terms, if at all. Any of the foregoing could seriously harm our business, and we cannot anticipate all of the ways in which the political or economic climate and financial market conditions could seriously harm our business.

***Rising inflation rates may result in increased operating costs and reduced liquidity, and affect our ability to access credit.***

Increased inflation may result in increased operating costs (including our labor costs), reduced liquidity, and limitations on our ability to access credit or otherwise raise debt and equity capital. In addition, the United States Federal Reserve System has repeatedly raised, and may continue to raise, interest rates in response to concerns about inflation. Increases in interest rates, especially if coupled with reduced government spending and volatility in financial markets, may have the effect of further increasing economic uncertainty and heightening these risks.

**Item 1B. Unresolved Staff Comments**

None

**Item 1C. Cybersecurity**

*Risk Management and Strategy*

We recognize the importance of assessing, identifying, and managing risks to the security, confidentiality, integrity, and availability of our business systems and confidential information, including personal information and intellectual property. We have developed a cybersecurity risk management program in accordance with our risk profile and business. Leveraging the support of a third-party information technology provider, our cybersecurity risk management program includes cybersecurity awareness training for employees and periodic systems monitoring and vulnerability scanning.

We have not identified cybersecurity incidents or threats that have materially affected us or are reasonably likely to materially affect us, including our business strategy, results of operations, or financial condition. However, like other companies in our industry, we and our third-party vendors may from time to time experience threats that could affect our information or systems. For more information, please see the section entitled “Risk Factors” in this Annual Report on Form 10-K.

*Governance Related to Cybersecurity Risks*

Our Senior Director of Finance and Chief Operating Officer, with the assistance of the Company’s third-party information technology provider, are responsible for the strategic leadership and direction of the Company’s cybersecurity program.

The Board exercises oversight of risks from cybersecurity threats primarily through its Audit Committee. Our Senior Director of Finance, with input of other members of Company management and the Company’s information technology provider, periodically makes presentations to the Audit Committee on the Company’s enterprise risk management program, which may address cybersecurity risks and related cyber strategy, as applicable.

## **Item 2. Properties**

The Company does not own or lease any material properties.

## **Item 3. Legal Proceedings**

From time to time, we may become involved in litigation or other legal proceedings arising in the ordinary course of business. We are not currently a party to any litigation or legal proceedings that, in the opinion of our management, are probable to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on our business, financial condition, results of operations and prospects because of defense and settlement costs, diversion of management resources and other factors.

## **Item 4. Mine Safety Disclosures**

Not applicable.

## **PART II**

## **Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities**

### *Market Information*

Our Common Shares are listed on the Nasdaq Capital Market.

### *Shareholders*

As of March 25, 2024 there were 124 holders of record of our Common Shares.

### *Dividends*

There are no restrictions in our articles, by-laws or elsewhere which would prevent us from paying dividends. No dividends have been declared or paid on the Common Shares in the last five fiscal years, and it is not expected that dividends will be declared or paid in the immediate or foreseeable future. Consequently, to date there have been no distributions made by us.

The policy of our Board is to reinvest all available funds in operations. The Board will reassess this policy from time to time. Any decision to pay dividends on the Common Shares will be made by the Board based on the assessment of, among other factors, earnings, capital requirements and our operating and financial condition.

### *Securities Authorized for Issuance under Equity Compensation Plans*

The information required by this item will be set forth in the 2024 Proxy Statement under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance under Equity Compensation Plans" and is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

### *Ownership and Exchange Controls*

There is no limitation imposed by Canadian law or by our Constatng Documents on the right of a non-resident to hold or vote our Common Shares.

### *Recent Sales of Unregistered Securities*

The following information represents securities sold by us during the year ended December 31, 2023 which were not registered under the Securities Act. Included are new issues, securities issued in exchange for property, services or other securities and new securities resulting from the modification of outstanding securities. We sold all of the securities listed

below pursuant to the exemption from registration provided by Section 4(a)(2) of the Securities Act, or Regulation D or Regulation S promulgated thereunder.

- On August 21, 2023, we completed a PIPE Offering of 9,945,969 PIPE Common Share Units and 954,725 Pre-Funded Warrant Units to Selling Shareholders for gross proceeds of approximately \$20.5 million before deducting placement agent fees and other offering expenses.
- On October 26, 2023, we granted 69,000 Stock Options with an exercise price per Stock Option of \$1.87 to certain directors, advisors, executives and employees. No consideration was received by us for this issuance.

*Purchases of Equity Securities by the Issuer and Affiliated Purchases*

None.

*Material Canadian Federal Income Tax Considerations*

The following is, as of the date hereof, a summary of the material Canadian federal income tax considerations generally applicable under the *Income Tax Act* (Canada) and the regulations promulgated thereunder, collectively the “Tax Act”, to a purchaser who acquires as beneficial owner Common Shares under this offering, and who, for purposes of the Tax Act and at all relevant times, (i) is not, and is not deemed to be, resident in Canada for purposes of the Tax Act and any applicable income tax convention, (ii) holds the common shares as capital property, (iii) deals at arm’s length with, and is not affiliated with, the Company or the underwriters, and (iv) does not use or hold and will not be deemed to use or hold, the common shares in a business carried on in Canada, hereinafter a “Non-Resident Holder”. Special rules, which are not discussed in this summary, may apply to a Non-Resident Holder that is an “authorized foreign bank” within the meaning of the Tax Act or an insurer carrying on an insurance business in Canada and elsewhere. Any such Non-Resident Holder should consult its own tax advisor.

This summary is based upon the provisions of the Tax Act in force as of the date hereof, all specific proposals to amend the Tax Act that have been publicly announced in writing by or on behalf of the Minister of Finance (Canada) prior to the date hereof, or the “Proposed Amendments”, the Canada-U.S. Tax Treaty, or the “Treaty”, and an understanding of the current administrative policies and assessing practices of the Canada Revenue Agency, or the “CRA”, published in writing by it prior to the date hereof. This summary assumes the Proposed Amendments will be enacted in the form proposed. However, no assurance can be given that the Proposed Amendments will be enacted in their current form, or at all. This summary is not exhaustive of all possible Canadian federal income tax considerations and, except for the Proposed Amendments, does not take into account or anticipate any changes in the law or any changes in the CRA’s administrative policies or assessing practices, whether by legislative, governmental or judicial action or decision, nor does it take into account or anticipate any other federal or any provincial, territorial or foreign tax considerations, which may differ significantly from those discussed herein.

This summary is not applicable to a Non-Resident Holder who reports its “Canadian tax results” in a currency other than Canadian currency; or that has entered or enters into a “derivative forward agreement” with respect to the common shares (each as defined in the Tax Act). Any such Non-Resident Holder should consult its own tax advisor with respect to an investment in the common shares.

This summary is of a general nature only and is not intended to be, nor should it be construed to be, legal or tax advice to any prospective purchaser or holder of the common shares, and no representations with respect to the income tax consequences to any prospective purchaser or holder are made. Consequently, prospective purchasers or holders of the common shares should consult their own tax advisors with respect to their particular circumstances.

**Currency Conversion**

Generally, for purposes of the Tax Act, all amounts relating to the acquisition, holding or disposition of the common shares must be converted into Canadian dollars based on the exchange rates as determined in accordance with the Tax Act. The amounts subject to withholding tax and any capital gains or capital losses realized by a Non-Resident Holder may be affected by fluctuations in the applicable exchange rate (such as the Canadian-U.S. dollar exchange rate).

### **Dividends**

Dividends paid or credited or deemed to be paid or credited on the Common Shares to a Non-Resident Holder by the Company will be subject to Canadian withholding tax under the Tax Act at the rate of 25%, subject to any reduction under the provisions of an applicable income tax convention. For example, under the Treaty, the rate of withholding tax on dividends paid or credited or deemed to be paid or credited to a beneficially entitled Non-Resident Holder who is resident in the U.S. for purposes of the Treaty and who is fully entitled to the benefits of the Treaty is generally limited to 15% of the gross amount of the dividend. Non-Resident Holders are urged to consult their own tax advisors to determine their entitlement to relief under an applicable income tax treaty.

### **Dispositions**

A Non-Resident Holder generally will not be subject to tax under the Tax Act in respect of a capital gain realized on the disposition or deemed disposition of a Common Share, unless the Common Share constitutes “taxable Canadian property” (as defined in the Tax Act) of the Non-Resident Holder at the time of disposition and the Non-Resident Holder is not entitled to relief under an applicable income tax convention.

Generally, the Common Shares will not constitute taxable Canadian property of a Non-Resident Holder at a particular time provided the common shares are listed at that time on a “designated stock exchange,” as defined in the Tax Act (which currently includes the Nasdaq Stock Market), unless at any time during the 60-month period that ends at that time the following two conditions are satisfied concurrently: (i) (a) the Non-Resident Holder; (b) persons with whom the Non-Resident Holder did not deal at arm’s length; (c) partnerships in which the Non-Resident Holder or a person described in (b) holds a membership interest directly or indirectly through one or more partnerships; or (d) any combination of the persons and partnerships described in (a) through (c), owned 25% or more of the issued shares of any class or series of the shares of the company; and (ii) more than 50% of the fair market value of the common shares was derived directly or indirectly from one or any combination of: (a) real or immovable property situated in Canada, (b) “Canadian resource properties”, (c) “timber resource properties” (each as defined in the Tax Act), and (d) options in respect of, or interests in or for civil law rights in, such properties, whether or not such properties exist. Notwithstanding the foregoing, in certain circumstances set out in the Tax Act, the common shares could be deemed to be taxable Canadian property.

A Non-Resident Holder contemplating a disposition of Common Shares that may constitute taxable Canadian property should consult a tax advisor prior to such disposition.

### **Item 6. [Reserved]**

## Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

*All references in this management's discussion and analysis of financial condition and results of operations, or MD&A, to the "Company", "ProMIS", "we", "us", or "our" refer to ProMIS Neurosciences Inc., unless otherwise indicated or the context requires otherwise. The following MD&A is prepared as of April 1, 2024 for the years ended December 31, 2023 and 2022 and should be read in conjunction with the audited consolidated financial statements for the years ended December 31, 2023 and 2022 (collectively, the "Financial Statements"), which have been prepared by management in accordance with United States generally accepted accounting principles ("U.S. GAAP") as issued by the Financial Accounting Standards Board ("FASB"). All dollar amounts refer to United States dollars, except as stated otherwise. Unless otherwise stated herein, all share and per share numbers relating to the Company's Common Shares prior to the effectiveness of the Reverse Share Split have been adjusted to give effect to the Reverse Share Split.*

### Overview

We are applying our patented technology platform to build a portfolio of antibody therapies and therapeutic vaccines in neurodegenerative diseases and other protein-misfolding diseases, with a focus on Alzheimer's disease (AD), multiple system atrophy (MSA), and amyotrophic lateral sclerosis (ALS). We believe these diseases share a common biologic cause — misfolded versions of proteins, that otherwise perform a normal function, becoming toxic and killing neurons, resulting in disease. ProMIS' technology platform enables drug discovery through a combination of protein biology, physics and supercomputing. We believe this platform provides a potential advantage in selectively targeting the toxic misfolded proteins with therapeutics or detecting them with diagnostics.

We are developing a pipeline of antibodies aimed at selectively targeting misfolded toxic forms of proteins that drive neurodegenerative diseases without interfering with the essential functions of the same properly folded proteins. Our product candidates are PMN310, PMN267, and PMN442. Our lead product candidate is PMN310, a monoclonal antibody designed to treat AD by selectively targeting toxic, misfolded oligomers of amyloid-beta. PMN267 is our second lead product candidate targeting ALS. It has been shown in preclinical studies to selectively recognize misfolded, cytoplasmic TDP-43 aggregates without interacting with normal TDP-43. Misfolded TDP-43 is believed to play an important role in the development of ALS. In light of research suggesting that misfolded toxic a-syn is a primary driver of disease in synucleinopathies such as MSA and Parkinson's disease, our third lead product candidate, PMN442 has shown robust binding to pathogenic a-syn oligomers and seeding fibrils in preclinical studies, with negligible binding to a-syn monomers and physiologic tetramers which are required for normal neuronal function. We also have earlier stage preclinical programs and a project to refine our discovery algorithm using machine learning as highlighted in the "Other Key Projects" section below.

We were incorporated on January 23, 2004 under the Canada Business Corporations Act (CBCA). On July 13, 2023, we continued our existence from a corporation incorporated under the CBCA into the Province of Ontario under the Business Corporations Act (Ontario) (OBCA) (Continuance). The Continuance was approved by our shareholders at our 2023 Annual Meeting of Shareholders held on June 29, 2023. We have a wholly-owned U.S. subsidiary, ProMIS USA, which was incorporated in January 2016 in the State of Delaware. ProMIS USA has had no material activity and has no material financial impact on our Financial Statements. Since our inception, we have devoted substantially all of our resources to developing our platform technologies and the resultant antibody product candidates, building our intellectual property portfolio, business planning, raising capital and providing general and administrative support for these operations. We have principally financed our operations through public and private placements of Common Shares and warrants and convertible debt.

We have incurred significant operating losses since inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of our product candidates and any future product candidates. Our net losses were \$13.2 million and \$18.1 million for the years ended December 31, 2023 and 2022, respectively. As of December 31, 2023, we had an accumulated deficit of \$93.5 million. We expect to continue to incur net losses for the foreseeable future and, if able to raise additional funding, would expect our research and development expenses, general and administrative expenses and capital expenditures to increase. In particular, if we are able to raise additional funding we expect our expenses to increase as we continue our development of, and seek regulatory approvals for, our product candidates, as well as continue and initiate new clinical trials, hire additional personnel, and pay fees to outside consultants, lawyers and accountants. In addition, if we obtain marketing approval for any product candidates, we may incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. We may also incur expenses in connection with the in-licensing or acquisition of additional product candidates.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through the sale of equity, debt financings, our “at-the-market” program, or other capital sources, which may include collaborations with other companies or other strategic transactions. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as and when needed, we may have to significantly delay, reduce or eliminate the development and commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

We expect that our cash of \$12.6 million as of December 31, 2023 will not be sufficient to fund the Company’s operating expenses for at least 12 months from the date these Financial Statements were issued. Refer to additional discussion related to going concern considerations in “*Liquidity and Capital Resources*.”

## **Components of Operating Results**

### ***Revenue***

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of our products in the near future, if at all. If our product candidates are successful and result in marketing approval or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from such collaboration or license agreements.

### ***Operating Expenses***

#### ***Research and Development Expenses***

Research and development expenses consist primarily of costs incurred in connection with the development and research of our platform technologies, as well as unrelated discovery program expenses. We expense research and development costs in the periods in which they are incurred. These expenses include:

- employee-related expenses, including salaries, related benefits and share-based compensation expense, for employees engaged in research and development activities;
- external research and development expenses incurred under arrangements with third parties, such as contract research organizations (CROs), and consultants;

- the cost of acquiring, developing, and manufacturing clinical study materials; and
- costs associated with clinical and preclinical activities and regulatory operations.

We enter into consulting, research, and other agreements with commercial entities, researchers, universities, and others for the provision of goods and services. Such arrangements are generally cancelable upon reasonable notice and payment of costs incurred. Costs are considered incurred based on an evaluation of the progress to completion of specific tasks under each contract using information and data provided by the respective vendors, including our clinical sites. These costs consist of direct and indirect costs associated with our platform technologies, as well as fees paid to various entities that perform certain research on our behalf. Depending upon the timing of payments to the service providers, we recognize prepaid expenses or accrued expenses related to these costs. These accrued or prepaid expenses are based on management's estimates of the work performed under service agreements, milestones achieved, and experience with similar contracts. We monitor each of these factors and adjust estimates accordingly. See Item 1A - "Risk Factors" in this document.

Research and development activities account for a significant portion of our operating expenses. We expect our research and development expenses to increase substantially for the foreseeable future as we continue to implement our business strategy, which includes advancing our platform technologies through clinical development as well as other product candidates into clinical development, expanding our research and development efforts, including hiring additional personnel to support our research efforts, our clinical and product development efforts, and seeking regulatory approvals for our product candidates that successfully complete clinical trials.

We use our personnel and infrastructure resources across multiple research and development programs directed toward identifying and developing product candidates. Our direct research and development expenses consist primarily of external costs, including fees paid to consultants, contractors and CROs in connection with our development activities and the cost of acquiring, developing, and manufacturing clinical study materials.

#### *General and Administrative Expenses*

General and administrative expenses consist primarily of personnel costs including salary, bonus, employee-benefits and share-based compensation, costs incurred in development and protection of intellectual property, professional service fees, and other general overhead and facility costs, (including rent) depreciation and amortization. We expect our general and administrative expenses to increase substantially for the foreseeable future as we increase our administrative function to support the growth of the business and its continued research and development activities.

#### *Other Income (Expense)*

Other income (expense) consists primarily of interest expense on our 2022 Debentures, 2023 interest expense on certain deferred accounts payable and changes in the fair value of our financial instruments, the 2022 gain on extinguishment of our convertible debt and derivative liability, and interest income earned on our cash balances.

## Result of Operations

### Years Ended December 31, 2023 and 2022

The following table summarizes our results of operations for the years presented:

	Years Ended December 31,		Change
	2023	2022	
Operating expenses			
Research and development	\$ 7,883,165	\$ 16,087,168	\$ (8,204,003)
General and administrative	6,379,568	7,292,744	(913,176)
Total operating expenses	14,262,733	23,379,912	(9,117,179)
Loss from operations	(14,262,733)	(23,379,912)	(9,117,179)
Other income (expense)	1,050,251	5,317,649	4,267,398
Net loss	\$ (13,212,482)	\$ (18,062,263)	\$ (4,849,781)

### Research and Development Expenses

The following table summarizes the year-over-year changes in research and development expenses for the years presented:

	Years Ended December 31,		Change
	2023	2022	
Direct research and development expenses by program			
PMN310	\$ 4,776,411	\$ 10,508,127	\$ (5,731,716)
ALS	—	831,849	(831,849)
Platform and other programs	631,566	952,384	(320,818)
Indirect research and development expenses:			
Employee salaries and benefits	1,426,572	1,316,249	110,323
Share-based compensation	78,018	297,933	(219,915)
Consulting expense	834,765	2,064,520	(1,229,755)
Other operating costs	135,833	116,106	19,727
Total research and development expenses	\$ 7,883,165	\$ 16,087,168	\$ (8,204,003)

Research and development expenses decreased by \$8.2 million, or 51%, for the year ended December 31, 2023 compared to the year ended December 31, 2022. This decrease is primarily attributable to a \$6.9 million decrease in direct research and development expenses related to a \$5.7 million decrease in spending on our lead program, PMN310, largely attributable to 2022 expenditures of \$10.5 million on drug substance manufacturing costs and preclinical research costs in preparation of our IND filing, which was submitted in early 2023, and we initiated our Phase 1a clinical trial of PMN310 in the fourth quarter of the year ended December 31, 2023. Additionally, expenses on external research costs on ALS portfolio projects decreased by \$0.8 million and expenses on our platform technology and other projects decreased by \$0.3 million as we focused our available resources on the development and progression of PMN310. The \$1.2 million decrease in consulting expense relates to various consultants advising on the content and preparation of the IND and design of preclinical and clinical trials, much of which was completed during 2022 in preparation of the 2023 IND submission. Share-based compensation costs decreased by \$0.2 million during the year ended December 31, 2023 as compared to the year ended December 31, 2022 while salaries and benefits increased by \$0.1 million.



### **General and Administrative Expenses**

The following table summarizes the year-over-year changes in general and administrative expenses for the years presented:

	Years Ended December 31,		Change
	2023	2022	
Employee salaries and benefits	\$ 1,406,930	\$ 1,096,937	\$ 309,993
Share-based compensation	190,718	189,697	1,021
Professional and consulting fees	4,356,649	5,284,559	(927,910)
Patent expense	253,269	540,028	(286,759)
Facility-related and other	172,002	181,523	(9,521)
Total general and administrative expenses	<u>\$ 6,379,568</u>	<u>\$ 7,292,744</u>	<u>\$ (913,176)</u>

General and administrative expenses decreased by \$0.9 million, or 13%, for the year ended December 31, 2023 compared to the year ended December 31, 2022. Employee salaries and benefits and share-based compensation increased by \$0.3 million, primarily due to accrued employee termination costs of \$0.5 million. The \$0.9 million decrease in professional and consulting costs for the year ended December 31, 2023 included one-time costs of \$0.8 million related to expensing previously deferred financing costs after abandoning planned offerings while professional and consulting fees for the year ended December 31, 2022 included \$1.3 million of one-time costs related to our Nasdaq listing in July 2022. The remaining \$0.4 million decrease in professional and consulting fees was attributable to a decrease in investor relations and shareholder expenses of \$0.7 million and in recruiting expenses of \$0.2 million, offset by an increase in insurance costs of \$0.2 million and an increase in other consulting and business development of \$0.3 million. Patent fees decreased by \$0.3 million.

### **Other Income (Expense)**

Other income decreased by \$4.3 million for the year ended December 31, 2023 compared to the year ended December 31, 2022. The decrease was primarily attributable to a decrease in gain on change in fair value of financial instruments of \$3.3 million and a one-time \$1.3 million gain on extinguishment of convertible debt and derivative liability in the year ended December 31, 2022, offset by a year over year \$0.3 million increase in interest income, and a \$0.1 million reduction in interest expense.

### **Liquidity and Capital Resources**

#### **Sources of Liquidity**

We are a clinical-stage development company as we have not generated any product revenues to date and do not expect to have significant revenues until we are able to sell a product candidate after obtaining applicable regulatory approvals or we establish collaborations that provide funding, such as licensing fees, milestone payments, royalties, research funding or otherwise. Operations have been financed since inception through the sale of equity and debt securities and the conversion of common share purchase warrants and share options. Our objectives, when managing capital, are to ensure there are sufficient funds available to carry out our research, development and eventual commercialization programs. When we have excess funds, we manage our liquidity risk by investing in highly liquid corporate and government bonds with staggered maturities to provide regular cash flow for current operations. We do not hold any asset-backed commercial paper and our cash is not subject to any external restrictions. We also manage liquidity risk by frequently monitoring actual and projected cash flows. The Board reviews and approves the Company's operating and capital budgets, as well as any material transactions not in the ordinary course of business. The majority of our accounts payable and accrued liabilities have maturities of less than three months. We are dependent on our ability to generate revenues from our future products or secure additional financing in order to continue our research and development activities and meet our ongoing obligations.

In March 2021, we completed a \$7.0 million private placement of convertible unsecured debentures (the Debentures). The Debentures were initially convertible into Common Shares at the option of the holder at a conversion price of \$6.00 following the Reverse Share Split and accrued interest at 1% per annum, which is payable annually. The Debentures were amended and converted into 70,000,000 Series 1 Convertible Preferred Shares in June 2022. The Series 1 Convertible

Preferred Shares are non-voting and non-interest bearing and are convertible at a 60:1 ratio into Common Shares at the option of the holder. In December 2023, the Series 1 Convertible Preferred Shares were converted into 1,166,667 Series 2 Convertible Preferred Shares, which are convertible at a 1:1 ratio into Common Shares at the option of the holder, or upon raising a single round of equity financing in excess of \$14 million.

In October 2022, we announced the closing of a private placement for 1,383,755 Common Share units at a price of \$5.40 for gross proceeds of \$7.47 million. Each unit consisted of one of the Company's Common Shares, and one-quarter of one warrant to purchase one common share. The warrants have an exercise price of \$7.50 per whole warrant, are exercisable beginning on the calendar date following the six month anniversary of the date of issuance and will expire five years from the date when first exercisable.

In May 2023, we entered into an agreement with a vendor which gives the option to defer payment on approximately \$5.7 million of current accounts payable until March 31, 2024. The outstanding balance of invoices due to the vendor will accrue interest at an annual rate of 5.5%, which is paid monthly. We may repay the outstanding balance at any time.

In August 2023, we completed a private placement of 9,945,969 Common Shares and, in lieu of Common Shares, 954,725 pre-funded warrants, each attached to a Common Share warrant exercisable at a price of \$1.75 for gross proceeds of \$20.4 million before deducting issuance costs of \$2.7 million. Proceeds from the private placement are expected to be used to advance the clinical development of PMN310, ProMIS' lead therapeutic candidate, as well as for working capital and other general corporate expenses. 360,000 pre-funded warrants were exercised for an equivalent number of Common Shares in October 2023.

On September 22, 2023, we filed a registration statement on Form S-3 (File No. 333-274658) with the SEC, which was declared effective on September 29, 2023 (Shelf Registration Statement), in relation to the registration of Common Shares, preferred shares, subscription receipts, debt securities, warrants and/or units of any combination thereof for the purposes of selling, from time to time, our Common Shares, debt securities or other equity securities in one or more offerings. On January 5, 2024, we entered into an At The Market Offering Agreement with BTIG, LLC to provide for the offering, issuance and sale of up to an aggregate amount of \$25.0 million of our Common Shares from time to time in "at-the-market" offerings under the Shelf Registration Statement and subject to the limitations thereof.

We incurred a net loss of \$13.2 million for the year ended December 31, 2023, and reported an accumulated deficit of \$93.5 million. Management believes that these conditions raise substantial doubt as to the Company's ability to continue as a going concern within 12 months of the date the Financial Statements are issued. Additional funding will be necessary to fund future clinical activities. We will seek additional funding through public and private financings, debt financings, collaboration agreements, strategic alliances and licensing agreements. Although we have been successful in raising capital in the past, there is no assurance of success in obtaining such additional financing on terms acceptable to us, if at all, and there is no assurance that we will be able to enter into collaborations or other arrangements. If we are unable to obtain funding, it could force us to delay, reduce or eliminate research and development programs and product portfolio expansion or commercialization efforts. These potential delays, reductions and eliminations could adversely affect future business prospects, and the ability to continue operations.

### **Cash Flows**

The following table summarizes our sources and uses of cash for the periods presented:

	<b>Years Ended December 31,</b>		<b>Change</b>
	<b>2023</b>	<b>2022</b>	
Net cash used in operating activities	\$ (10,843,676)	\$ (17,033,883)	\$ 6,190,207
Net cash used in investing activities	(1,349)	(1,981)	632
Net cash provided by financing activities	17,748,800	6,494,654	11,254,146
Effect of exchange rates on cash	(181,425)	(526,899)	345,474
Net increase (decrease) in cash	<u>\$ 6,722,350</u>	<u>\$ (11,068,109)</u>	<u>\$ 17,790,459</u>

#### *Cash Flows from Operating Activities*

Cash used in operating activities was \$10.8 million for the year ended December 31, 2023, which consisted of a net loss of \$13.2 million and \$0.6 million in non-cash charges, offset by a net change of \$2.9 million in our net operating assets and liabilities. The additive non-cash activities primarily consisted of a gain on the change in fair value of financial instruments of \$0.9 million, offset by non-cash charges for share-based compensation of \$0.3 million. Changes in cash flows related to operating assets and liabilities primarily consisted of an increase of \$3.1 million of accounts payable and accrued liabilities offset by a \$0.2 million decrease in prepaid expenses and other current assets. The change in cash flows from operating assets and liabilities does not include \$0.2 million in deferred financing costs incurred in December 2023 related to the at-the-market offering program effected in January 2024.

Cash used in operating activities was \$17.0 million for the year ended December 31, 2022, which consisted of a net loss of \$18.1 million and \$4.3 million in non-cash charges, offset by a net change of \$5.4 million in our net operating assets and liabilities. The additive non-cash activities primarily consisted of a gain on the change in fair value of financial instruments of \$4.1 million and a gain of \$1.3 million on the extinguishment of the convertible debt and derivative liability, offset by non-cash charges for share-based compensation of \$0.5 million, for amortization of debt discount of \$0.2 million and foreign exchange losses of \$0.3 million. Changes in cash flows related to operating assets and liabilities primarily consisted of an increase of \$5.7 million of accounts payable and accrued liabilities offset by a \$0.3 million increase in prepaid expenses and other current assets.

#### *Cash Flows from Investing Activities*

Cash used in investing activities was nominal during the years ended December 31, 2023 and 2022.

#### *Cash Flows from Financing Activities*

Cash provided by financing activities during the year ended December 31, 2023 was \$17.7 million from the common shares, pre-funded warrants, and common share warrants sold in the August 2023 PIPE.

Cash provided by financing activities was \$6.5 million from the issuance of the October 2022 Common Share units for the year ended December 31, 2022.

#### **Critical Accounting Policies and Estimates**

Our MD&A is based on our Financial Statements, which have been prepared in accordance with U.S. GAAP and on a basis consistent with those accounting principles followed by us and disclosed in Note 2 to our audited consolidated financial statements for the year ended December 31, 2023. The preparation of these Financial Statements in conformity with U.S. GAAP requires our management to make certain judgments and estimates that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the Financial Statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgement about the carrying value of assets and liabilities that are not readily apparent from other sources. Significant estimates and judgments include, but are not limited to, accruals for research and development expenses and the valuation of warrant liabilities and embedded derivative liabilities. Accordingly, actual results may differ from these judgments and estimates under different assumptions or conditions and any such difference may be material.

We believe that the following critical accounting estimates discussed below are most important to understanding our historical and future performance, as these estimates relate to the more significant areas involving management's judgments and estimates.

#### *Accruals for Research and Development Expenses*

Substantial portions of the Company's clinical and preclinical trials and drug substance manufacturing are performed by third-party laboratories, medical centers, and other vendors. These vendors generally bill monthly for services performed, or bill based upon milestone achievement. For clinical and preclinical studies, the Company recognizes and, if necessary, accrues expenses based upon estimated percentage of work completed and the remaining contract milestones. The Company estimates the period over which such services will be performed based on the terms of the agreements as well as the level of effort to be expended in each period. Sometimes the actual timing of performance or the level of effort varies from the estimate, and if that does occur, the Company will adjust the amounts recorded accordingly.

The percentage of work completed is inherently subject to estimation uncertainty, and the Company uses third party invoices, contract terms, and support provided directly from third parties, when available, to establish the percentage of completion at each measurement date. As an example, a difference in estimated percentage of work completed compared to actual percentage of work completed of 10% for a \$1.0 million contract at the measurement date could have a \$0.1 million impact on accrued liabilities and research and development expenses. The Company had \$0.7 million of accrued research and development costs at December 31, 2023, which is from multiple contracts.

#### *Valuation of Embedded Derivatives and Accelerated Warrant Liabilities*

The Company accounts for certain financial instruments as embedded derivatives pursuant to ASC 815. These instruments include the conversion feature accounted for as derivative liability for the Debentures, which was extinguished during the year ended December 31, 2022, and certain US dollar denominated accelerated warrants, which were converted to equity measured instruments following our change in functional currency on July 1, 2023 using the fair value as of June 30, 2023. Prior to the change in functional currency, the financial instruments were recorded at fair value at issuance and adjusted to fair value at each reporting date with the difference recorded in earnings. The accelerated warrants from the 2021 August financing were initially measured and at each reporting period using a scenario-based valuation method using a Monte Carlo model. The Company determines volatility and risk-free rate mainly by reference to historical experience. The acceleration model also requires the Company to estimate the probability the warrants will meet the criteria for acceleration by estimating the timing and amount of future capital raises, which is inherently subject to uncertainty. Although the largest driver of change in value of the accelerated warrants is generally the current stock price, changes to the actual timing of capital raises could potentially materially impact the valuation.

#### **Recently Issued Accounting Pronouncements**

A description of recently issued accounting pronouncements that may potentially impact our financial position and results of operations is disclosed in Note 2 to our audited consolidated financial statements in Item 8 – “*Financial Statements and Supplementary Data*”.

#### **Item 7A. Quantitative and Qualitative Disclosures About Market Risk**

In the normal course of business, we are exposed to a number of financial risks that can affect our operating performance. These risks are credit risk, liquidity risk and market risk. Our overall risk management program and prudent business practices seek to minimize any potential adverse effects on our financial performance.

##### ***Credit Risk***

Financial instruments that potentially subject the Company to a significant concentration of credit risk consist primarily of cash and short-term investments. We manage our exposure to credit losses by placing our cash with accredited financial institutions, which at times, may exceed federally insured limits, and when we have excess funds, such funds are invested in high-quality government and corporate issuers with low credit risk. Cash held is not subject to any external restrictions. As of the year ended December 31, 2023, a hypothetical 10% relative change in interest rates would not have a material impact on our Financial Statements.

***Liquidity Risk***

Our exposure to liquidity risk is dependent on purchasing obligations and raising funds to meet commitments and sustain operations. We are a pre-revenue clinical-stage development company, and we rely on external fundraising to support our operations. We also manage liquidity risk by continuously monitoring actual and projected cash flows. Our Board reviews and approves the Company's operating budget, as well as any material transaction.

***Foreign Currency Exchange Risk***

We are exposed to foreign exchange risk on our non-U.S. dollar denominated cash and non-U.S. dollar denominated liabilities. We do not believe that foreign exchange impacts had a material effect on our business, financial condition or results of operations during the years ended December 31, 2023 or 2022.

***Inflation Risk***

Inflation generally affects us by increasing our cost of labor, outside consultants and CROs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2023 or 2022.

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**Item 8. Financial Statements and Supplementary Data**

**PROMIS NEUROSCIENCES INC.**

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## REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and Board of Directors of ProMIS Neurosciences Inc. and Subsidiary

### Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of ProMIS Neurosciences Inc. and Subsidiary (the “Company”) as of December 31, 2023 and 2022, and the related consolidated statements of operations and comprehensive loss, changes in shareholders’ equity (deficit), and cash flows for each of the two years in the period ended December 31, 2023, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2023 and 2022, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2023, in conformity with accounting principles generally accepted in the United States of America.

### Going Concern Uncertainty

The accompanying consolidated financial statements have been prepared assuming that ProMIS Neurosciences Inc and Subsidiary will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, the Company has an accumulated deficit and has suffered net losses and negative cash flows from operations and has an accumulated deficit as of December 31, 2023. These factors raise substantial doubt about the Company’s ability to continue as a going concern. Management’s plans in regard to these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

### Basis for Opinion

These consolidated financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (“PCAOB”) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company’s internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Baker Tilly US, LLP

We have served as the Company’s auditor since 2021.

Tewksbury, Massachusetts  
April 1, 2024



PROMIS NEUROSCIENCES INC.

Consolidated Balance Sheets

(expressed in US dollars, except share amounts)

	December 31,	
	2023	2022
<b>Assets</b>		
Current assets:		
Cash	\$ 12,598,146	\$ 5,875,796
Short-term investments	32,358	31,009
Prepaid expenses and other current assets	988,641	996,682
Total current assets	13,619,145	6,903,487
Property and equipment, net	—	321
Intangible assets, net	—	20,838
Total assets	<u>\$ 13,619,145</u>	<u>\$ 6,924,646</u>
<b>Liabilities and Shareholders' Equity (Deficit)</b>		
Current liabilities:		
Accounts payable	\$ 7,843,136	\$ 2,975,398
Accrued liabilities	1,506,526	3,437,646
Total current liabilities	9,349,662	6,413,044
Share-based compensation liability	422,002	—
Warrant liability	94,185	1,859,374
Total liabilities	<u>9,865,849</u>	<u>8,272,418</u>
Commitments and contingencies (Note 12)		
Shareholders' equity (deficit):		
Series 1 Convertible Preferred Shares, no par value, 70,000,000 shares authorized, 0 and 70,000,000 shares issued and outstanding as of December 31, 2023 and December 31, 2022, respectively	—	—
Series 2 Convertible Preferred Shares, no par value, unlimited shares authorized, 1,166,667 and 0 shares issued and outstanding as of December 31, 2023 and December 31, 2022, respectively	—	—
Common shares, no par value, unlimited shares authorized, 18,885,254 and 8,579,284 shares issued and outstanding as of December 31, 2023 and December 31, 2022, respectively	—	—
Additional paid-in capital	97,590,426	79,101,061
Accumulated other comprehensive loss	(371,184)	(195,369)
Accumulated deficit	(93,465,946)	(80,253,464)
Total shareholders' equity (deficit)	<u>3,753,296</u>	<u>(1,347,772)</u>
Total liabilities and shareholders' equity (deficit)	<u>\$ 13,619,145</u>	<u>\$ 6,924,646</u>

The accompanying notes are an integral part of these consolidated financial statements.

PROMIS NEUROSCIENCES INC.

Consolidated Statements of Operations and Comprehensive Loss

(expressed in US dollars, except share amounts)

	Years Ended December 31,	
	2023	2022
Operating expenses:		
Research and development	\$ 7,883,165	\$ 16,087,168
General and administrative	6,379,568	7,292,744
Total operating expenses	<u>14,262,733</u>	<u>23,379,912</u>
Loss from operations	(14,262,733)	(23,379,912)
Other income (expense):		
Change in fair value of financial instruments	866,738	4,176,767
Other interest expense	(201,390)	—
Interest expense on convertible debt	—	(282,064)
Gain on extinguishment of convertible debt and derivative liability	—	1,307,421
Other income	384,903	115,525
Total other income (expense), net	<u>1,050,251</u>	<u>5,317,649</u>
Net loss	<u>(13,212,482)</u>	<u>(18,062,263)</u>
Other comprehensive loss		
Foreign currency translation adjustment	—	(7,450)
Comprehensive loss	<u>\$ (13,212,482)</u>	<u>\$ (18,069,713)</u>
Net loss per share, basic and diluted	\$ (1.07)	\$ (2.41)
Weighted-average shares outstanding of common shares, basic and diluted	<u>12,292,707</u>	<u>7,502,609</u>

The accompanying notes are an integral part of these consolidated financial statements.

PROMIS NEUROSCIENCES INC.

Consolidated Statements of Shareholders' Equity (Deficit)

(expressed in US dollars, except share amounts)

	Series 1 Preferred Shares		Series 2 Preferred Shares		Common Shares		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total
	Shares	Amount	Shares	Amount	Shares	Amount				
Balance, January 1, 2022	—	—	—	—	7,195,529	—	68,039,178	(187,919)	(62,191,201)	5,660,058
Share-based compensation	—	—	—	—	—	—	487,630	—	—	487,630
Conversion of convertible debt and derivative liability to Series 1 Convertible Preferred Shares	70,000,000	—	—	—	—	—	5,600,000	—	—	5,600,000
Issuance of Common Shares, net of issuance costs of \$977,624	—	—	—	—	1,383,755	—	4,974,253	—	—	4,974,253
Foreign currency translation	—	—	—	—	—	—	—	(7,450)	—	(7,450)
Net loss	—	—	—	—	—	—	—	—	(18,062,263)	(18,062,263)
Balance, December 31, 2022	70,000,000	—	—	—	8,579,284	—	79,101,061	(195,369)	(80,253,464)	(1,347,772)
Share-based compensation	—	—	—	—	—	—	271,542	—	—	271,542
Proceeds from the issuance of common stock, pre-funded warrants and accompanying common warrants in August 2023 PIPE, net of issuance costs of \$2,738,558	—	—	—	—	9,945,969	—	17,745,200	—	—	17,745,200
Exercise of pre-funded warrants	—	—	—	—	360,001	—	3,600	—	—	3,600
Reclassification of USD denominated warrants from warrant liability to additional paid-in capital due to change in functional currency	—	—	—	—	—	—	1,287,400	—	—	1,287,400
Reclassification of CAD denominated warrants from additional paid-in capital to warrant liability due to change in functional currency	—	—	—	—	—	—	(396,375)	—	—	(396,375)
Reclassification of CAD equity-classified stock options to share-based compensation liability due to change in functional currency	—	—	—	—	—	—	(1,435,912)	—	—	(1,435,912)
Re-measurement of liability-classified CAD stock options as of December 31, 2023	—	—	—	—	—	—	1,013,910	—	—	1,013,910
Exchange of Series 1 Convertible Preferred Shares for Series 2 Convertible Preferred Shares	(70,000,000)	—	1,166,667	—	—	—	—	—	—	—
Foreign currency translation	—	—	—	—	—	—	—	(175,815)	—	(175,815)
Net loss	—	—	—	—	—	—	—	—	(13,212,482)	(13,212,482)
Balance, December 31, 2023	—	\$ —	1,166,667	\$ —	18,885,254	\$ —	\$ 97,590,426	\$ (371,184)	\$ (93,465,946)	\$ 3,753,296

The accompanying notes are an integral part of these consolidated financial statements.

**PROMIS NEUROSCIENCES INC.**  
**Consolidated Statements of Cash Flows**  
(expressed in US dollars)

	<b>Years Ended December 31,</b>	
	<b>2023</b>	<b>2022</b>
<b>Cash flows from operating activities</b>		
Net loss	\$ (13,212,482)	\$ (18,062,263)
Adjustments to reconcile net loss to net cash used in operating activities:		
Share-based compensation	271,542	487,630
Foreign currency exchange (gain) loss	(1,817)	305,407
Change in fair value of derivative liability	—	(2,550,877)
Change in fair value of warrant liability	(866,738)	(1,561,987)
Depreciation of property and equipment	321	6,144
Amortization of debt discount and issuance costs	—	241,854
Amortization of intangible assets	20,838	5,072
Gain on extinguishment of convertible debt and derivative liability	—	(1,307,421)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(187,321)	(318,747)
Accounts payable	4,963,218	2,675,693
Accrued liabilities	(1,831,237)	3,045,612
Net cash used in operating activities	<u>(10,843,676)</u>	<u>(17,033,883)</u>
<b>Cash flows from investing activities</b>		
Purchase of short-term investments	(32,358)	(31,009)
Maturity of short-term investment	31,009	31,009
Purchase of property and equipment	—	(1,981)
Net cash used in investing activities	<u>(1,349)</u>	<u>(1,981)</u>
<b>Cash flows from financing activities</b>		
Proceeds from issuance of Common Shares from October 2022 PIPE, net of issuance costs	—	4,974,253
Proceeds from issuance of warrants from October 2022 PIPE	—	1,520,401
Proceeds from issuance of common shares, pre-funded warrants and accompanying common warrants from August 2023 PIPE, net of issuance costs	17,745,200	—
Proceeds from exercise of pre-funded warrants	3,600	—
Net cash provided by financing activities	<u>17,748,800</u>	<u>6,494,654</u>
Effect of exchange rates on cash	(181,425)	(526,899)
Net decrease in cash	6,722,350	(11,068,109)
Cash at beginning of year	5,875,796	16,943,905
Cash at end of year	<u>\$ 12,598,146</u>	<u>\$ 5,875,796</u>
<b>Noncash financing activities</b>		
Conversion of convertible debt and derivative liability to Series 1 Convertible Preferred Shares	\$ —	\$ 5,600,000
Deferred share issuance costs related to January 2024 ATM Offering included in accounts payable and accrued liabilities as of December 31, 2023	\$ 195,362	\$ —
Fair value of noncash compensation warrants issued to placement agents in the October 2022 and August 2023 PIPEs	\$ 466,658	\$ 317,000
Reclassification of historical CAD denominated warrants from equity to liability	\$ (396,375)	\$ —
Reclassification of historical USD warrants from liability to equity	\$ 1,287,400	\$ —
Decrease in share-based compensation liability on CAD denominated share options reducing additional paid-in-capital	\$ 681,308	\$ —
<b>Supplemental disclosure of cash flow information</b>		
Cash paid for interest on convertible debt	\$ —	\$ 87,069
Cash paid for other interest	\$ 201,390	\$ —

The accompanying notes are an integral part of these consolidated financial statements.

**PROMIS NEUROSCIENCES INC.**

**Notes to Consolidated Financial Statements**

(expressed in US dollars, except share and per share amounts)

**1. DESCRIPTION OF BUSINESS**

**Business Description**

ProMIS Neurosciences Inc. (the “**Company**” or “**ProMIS**”) is applying its patented technology platform to build a portfolio of antibody therapies, therapeutic vaccines, and other antibody-based therapies in neurodegenerative diseases and other protein-misfolding diseases, with a focus on Alzheimer’s disease (AD), multiple system atrophy (MSA), and amyotrophic lateral sclerosis (ALS). The Company believes these diseases share a common biologic cause — misfolded versions of proteins, that otherwise perform a normal function, becoming toxic and killing neurons, resulting in disease. ProMIS’ technology platform enables drug discovery through a combination of protein biology, physics and supercomputing. ProMIS believes this platform provides a potential advantage in selectively targeting the toxic misfolded proteins with therapeutics or detecting them with diagnostics.

The Company is developing a pipeline of antibodies aimed at selectively targeting misfolded toxic forms of proteins that drive neurodegenerative diseases without interfering with the essential functions of the same properly folded proteins. The Company’s product candidates are PMN310, PMN267 and PMN442. The lead product candidate is PMN310, a monoclonal antibody designed to treat AD by selectively targeting toxic, misfolded oligomers of amyloid-beta. PMN267 is our second lead product candidate targeting ALS. It has been shown in preclinical studies to selectively recognize misfolded, cytoplasmic TDP 43 aggregates without interacting with normal TDP 43. Misfolded TDP 43 is believed to play an important role in the development of ALS. In light of research suggesting that misfolded toxic a-syn is a primary driver of disease in synucleinopathies such as MSA and Parkinson’s disease, our third lead product candidate, PMN442, has shown robust binding to pathogenic a-syn oligomers and seeding fibrils in preclinical studies, with negligible binding to a-syn monomers and physiologic tetramers which are required for normal neuronal function.

The Company was incorporated on January 23, 2004 under the Canada Business Corporations Act (“**CBCA**”). On July 13, 2023, the Company continued its existence from a corporation incorporated under the CBCA into the Province of Ontario under the Business Corporations Act (Ontario) (“**OBCA**”) (“**Continuance**”). The Continuance was approved by the Company’s shareholders at the Company’s 2023 Annual Meeting of Shareholders held on June 29, 2023. The Company is located at 1920 Yonge Street, Toronto, Ontario. The Company’s Common Shares are traded on the Nasdaq Capital Market (“**Nasdaq**”) under the symbol PMN. The Company has a wholly-owned U.S. subsidiary, ProMIS Neurosciences (US) Inc. (“**ProMIS USA**”), which was incorporated in January 2016 in the State of Delaware. As of December 31, 2023, ProMIS USA has had no material activity and has no material financial impact on the Company’s consolidated financial statements.

The success of the Company is dependent on obtaining the necessary regulatory approvals of its product candidates, marketing its products, if approved, and achieving profitable operations. The continuation of the research and development activities and the commercialization of its products, if approved, are dependent on the Company’s ability to successfully complete these activities and to obtain additional financing through a combination of financing activities and operations. It is not possible to predict either the outcome of future research and development or commercialization programs, the Company’s ability to fund these programs, or the Company’s ability to continue as a going concern.

## **Liquidity Risk**

The accompanying consolidated financial statements were prepared on a going concern basis, which assumes that the Company will continue its operations for the foreseeable future and will be able to realize its assets and discharge its liabilities in the normal course of business. To date, the Company has not generated revenues from its activities. The Company had a net loss of \$13,212,482 for the year ended December 31, 2023 and an accumulated deficit of \$93,465,946 as of December 31, 2023 and negative cash flows from operations. Management believes these conditions raise substantial doubt about the Company's ability to continue as a going concern within the next twelve months from the date these consolidated financial statements are issued. The Company will require additional funding to conduct future clinical activities. The Company will seek additional funding through public and private financings, debt financings, collaboration agreements, strategic alliances and licensing agreements. Although the Company has been successful in raising capital in the past, there is no assurance of success in obtaining such additional financing on terms acceptable to us, if at all, and there is no assurance that the Company will be able to enter into collaborations or other arrangements. If the Company is unable to obtain funding, it could force delays, reduce or eliminate research and development programs, product portfolio expansion or commercialization efforts, which could adversely affect future business prospects, and the ability to continue operations.

The Company expects to incur net losses for at least the next several years as the Company advances its product candidates. The Company is actively pursuing additional financing to further develop certain of the Company's scientific initiatives, but there is no assurance these initiatives will be successful, timely or sufficient.

## **2. BASIS OF PRESENTATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES**

### **Basis of Presentation**

The accompanying consolidated financial statements have been prepared in conformity with generally accepted accounting principles in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and as amended by Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

On June 21, 2022, the directors of the Company authorized a reverse share split of the issued and outstanding Common Shares in a ratio of 60:1, effective June 28, 2022 (the "**Reverse Share Split**"). All information included in these consolidated financial statements has been adjusted, on a retrospective basis, to reflect the Reverse Share Split, unless otherwise stated.

### **Principles of Consolidation**

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary. All intercompany balances and transactions have been eliminated in consolidation.

### **Use of Estimates**

The preparation of consolidated financial statements in conformity with GAAP requires management to make certain estimates, judgements and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. Significant estimates and assumptions made in the accompanying consolidated financial statements include, but are not limited to, the accrual for research and development expenses, the valuation of warrant liabilities and embedded derivative liabilities. Actual results could differ from those estimates, and such differences could be material to the consolidated financial statements.

### **Segment Information**

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker (“**CODM**”), or decision-making group, in making decisions on how to allocate resources and assess performance. The Company has one operating segment and its Chief Executive Officer serves as the CODM. Substantially all of the Company’s assets are located in Canada.

### **Foreign and Functional Currency**

The Company determines its functional currency as the currency of the primary economic environment in which the Company operates. To determine the primary economic environment, the Company considers salient economic factors, including cash flow indicators, expense indicators and financing indicators. Functional currency is a matter of fact, not a policy election and the Company will only reevaluate its functional currency if there is a significant change in facts and circumstances.

Prior to July 1, 2023, the Company’s functional currency was the Canadian dollar (“**C\$**”). Translation gains and losses from the application of the United States dollar (“**US\$**”) as the reporting currency during the period that the Canadian dollar was the functional currency were included as part of cumulative foreign currency translation adjustment, which is reported as a component of stockholders’ equity (deficit) as accumulated other comprehensive loss.

Following the Company’s voluntary delisting from the Toronto Stock Exchange in July 2023, the Company determined there was a significant change in its facts and circumstances, and completed a reassessment of its functional currency. The Company determined that, as of July 1, 2023, the Company’s functional currency had changed from the C\$ to the US\$. The Company analysis included various factors, including: the Company’s cash flows and expenses denominated primarily in US\$, the primary market for the Company’s Common Shares trading in US\$ and a majority ownership by U.S. shareholders from financings denominated in US\$. The change in functional currency was accounted for prospectively from July 1, 2023 and consolidated financial statements prior to and including the period ended June 30, 2023 were not restated for the change in functional currency.

For periods commencing July 1, 2023, monetary assets and liabilities denominated in foreign currencies are translated into US\$ using exchange rates in effect at the end of the reporting period. Opening balances related to non-monetary assets and liabilities are based on prior period translated amounts, and non-monetary assets acquired, and non-monetary liabilities incurred after July 1, 2023 are translated at the approximate exchange rate prevailing at the date of the transaction. Revenue and expense transactions are translated at the approximate exchange rate in effect at the time of the transaction. Foreign exchange gains and losses are included in the consolidated statement of operations and comprehensive loss within operating expenses.

### **Cash and Cash Equivalents**

The Company considers all highly liquid investments with an original maturity of three months or less at the date of purchase to be cash equivalents. As of December 31, 2023 and 2022, the Company did not have any material cash equivalents.

### **Short-term Investments**

Short-term investments consist of guaranteed certificates of deposit with a maturity greater than 90 days and up to one year at the time of purchase. Accordingly, all short-term investments are classified as current assets in the accompanying consolidated balance sheets. The short-term investment is being held as collateral for the Company’s credit cards.

### **Concentration of Credit Risk**

Financial instruments that potentially subject the Company to a significant concentration of credit risk consist of cash and short-term investments. Cash is deposited in checking and money market accounts at accredited financial institutions, which at times, may exceed federally insured limits. The short-term investment is deposited in a guaranteed certificate of deposit with an accredited financial institution that guarantees 100% of the original amount invested. Management believes that these financial institutions are financially sound, and, accordingly, minimal credit risk exists with respect to these high-quality financial institutions. As of December 31, 2023, the Company has not experienced any losses on its cash or short-term investments as a result of credit risk.

### **Fair Value Measurements**

FASB ASC 820, *Fair Value Measurements and Disclosures*, (“ASC 820”) defines fair value as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, as established by ASC 820, of which the first two are considered observable and the last is considered unobservable:

- Level 1 – Observable inputs, such as unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.
- Level 2 – Inputs (other than Level 1 quoted prices) are either directly or indirectly observable inputs for similar assets or liabilities. These include quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities.
- Level 3 – Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement.

The Company’s warrant liabilities and share-based compensation liability were classified as Level 3 financial instruments for the years ended December 31, 2023 and 2022.

The carrying amounts of prepaid and other current assets, short-term investments, accounts payable, and accrued expenses are generally considered to be representative of their fair value based on the short-term nature of these financial instruments.

### **Impairment of Long-lived Assets**

The Company evaluates its long-lived assets, which consist of property and equipment and definite-lived intangible assets, for impairment whenever events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to the estimated future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the asset exceeds the fair value of the asset. No material impairments have been identified as of each of December 31, 2023 and 2022.



### **Property and Equipment**

Property and equipment, net are stated at cost less accumulated depreciation. Depreciation expense is recognized using the straight-line method over the estimated useful life of each asset. Laboratory and equipment are depreciated over two to five years. Computer equipment is depreciated over two to three years. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accompanying consolidated balance sheets and any resulting gain or loss is included in loss from operations in the accompanying consolidated statements of operations and comprehensive loss. Expenditures for repairs and maintenance are expensed as incurred. The Company did not have any material property and equipment as of December 31, 2023.

### **Intangible Assets**

Definite-lived intangible assets are stated at cost less accumulated amortization and any accumulated impairment losses. An intangible asset's carrying amount is assessed for impairment whenever there is an indication that the asset may be impaired. The Company's definite-lived intangible assets consist of acquired rights and patents. Intangible assets are amortized on a straight-line basis over the lesser of the life of the intangible asset or its estimated useful life, which is 15 years. The Company did not have any material intangible assets as of December 31, 2023.

### **Derivative Liability**

The Company evaluates its convertible debt, warrants or other contracts to determine if those contracts or embedded components of those contracts qualify as derivatives to be separately accounted for in accordance with FASB ASC Topic 815, *Derivatives and Hedging* and Topic 480, *Distinguishing Liabilities from Equity*. The result of this accounting treatment is that the fair value of the embedded derivative, if required to be bifurcated, is marked-to-market at each balance sheet date and recorded as a liability. The change in fair value is recorded in the accompanying consolidated statements of operations and comprehensive loss as a component of other income or expense. Upon conversion or exercise of a derivative instrument, the instrument is marked to fair value at the conversion date and then that fair value is reclassified to equity. The Company did not have any bifurcated derivative liabilities as of December 31, 2023.

### **Collaboration Arrangements**

The Company may enter into collaboration arrangements with pharmaceutical and biotechnology partners. The Company analyzes its collaboration arrangements to assess whether they are within the scope of FASB ASC 808, *Collaborative Arrangements*, ("**ASC 808**"), to determine whether such arrangements involve joint operating activities performed by the parties that are both active participants in the activities and exposed to significant risks and rewards dependent on the commercial success of such activities. This assessment is performed throughout the life of the arrangement based on changes in responsibilities of all parties in the arrangement. ASC 808 does not provide guidance on the recognition of consideration exchanged or accounting for the obligations that may arise between parties. The Company concluded that ASC Topic 730, *Research and Development*, should be applied by analogy to payments between parties during the development activities of its collaboration arrangements.

### **General and Administrative Expenses**

General and administrative expenses consist primarily of personnel costs including salary, bonus, employee-benefits and share-based compensation, costs incurred in development and protection of intellectual property, professional service fees, and other general overhead and facility costs, including rent, depreciation and amortization, which relate to the Company's general and administrative functions.

### **Research and Development Expenses**

Research and development expenses consist primarily of costs incurred in connection with the development and research of the Company's platform technology, as well as discovery program expenses. The Company expenses research and development costs as incurred. These expenses include:

- employee-related expenses, including salaries, related benefits and share-based compensation expense, for employees engaged in research and development functions;
- external research and development expenses incurred under arrangements with third parties, such as contract research organizations ("CROs"), and consultants;
- the cost of acquiring, developing, and manufacturing clinical study materials; and
- Costs associated with preclinical and clinical activities and regulatory operations.

### **Prepaid and Accrued Research and Development Expenses**

Substantial portions of the Company's pre-clinical development, manufacturing and clinical trials are performed by third-party laboratories, medical centers, CROs and other vendors. These vendors generally bill monthly for services performed, or bill based upon milestone achievement. For preclinical and clinical studies, the Company accrues expenses based upon estimated percentage of work completed and the remaining contract milestones. At times, the Company is obligated to make upfront payments upon execution of research and development agreements. Upfront payments, including nonrefundable amounts, for goods or services that will be used or rendered for future research and development activities are capitalized as prepaid expenses until such goods are delivered or the related services are performed. The Company estimates the period over which such services will be performed based on the terms of the agreements as well as the level of effort to be expended in each period. Sometimes the actual timing of performance or the level of effort varies from the estimate, and if that does occur, the Company will adjust the amounts recorded accordingly.

### **Patent Costs**

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure. Amounts incurred are classified as general and administrative expenses in the accompanying consolidated statements of operations and comprehensive loss.

### **Warrants**

The Company issues warrants on its common shares in connection with financings as well as for compensation of intermediaries and advisors. The Company accounts for warrants as either equity instruments or as liabilities depending on the specific terms of the warrant agreements in accordance with FASB ASC Topic 815, *Derivatives and Hedging* and Topic 480, *Distinguishing Liabilities from Equity*. When classified as equity, warrants are recorded within additional paid-in-capital at the time of issuance and are not subsequently remeasured. Warrants identified as meeting the definition of a liability are recognized as a liability and treated in accordance with the derivative liability accounting policy described above. The Company also issues pre-funded warrants, warrants exercisable for \$0.01, which follow the same accounting policy as the common share warrants.

### **Debt Issuance Costs**

Debt issuance costs are specifically identifiable costs associated with issuance of a new debt instrument. Debt issuance costs are reported on the consolidated balance sheet as a direct deduction from the face amount of the related debt. Debt issuance costs are amortized to interest expense using the effective interest method over the term of the related debt.

### Share-based Compensation

Share-based compensation expense related to share awards granted to employees, directors and non-employees is recognized based on the grant-date estimated fair values of the awards using the Black-Scholes option pricing model (“**Black-Scholes**”). The value is recognized as expense ratably over the requisite service period, which is generally the vesting term of the award. The Company adjusts the expense for actual forfeitures as they occur. Share based compensation expense is classified in the accompanying consolidated statements of operations and comprehensive loss based on the function to which the related services are provided.

Black Scholes requires a number of assumptions, of which the most significant are expected volatility, expected option term (the time from the grant date until the options are exercised or expire) and risk-free rate. Expected volatility is determined using the historical volatility for the Company. The risk-free interest rate is based on the yield of Canadian government bonds with a remaining term equal to the expected life of the option for C\$ options and based on the yield of U.S. government treasury bonds for US\$ options. Expected dividend yield is zero because the Company has never paid cash dividends on common shares and the Company does not expect to pay cash dividends in the foreseeable future.

Awards of options that provide for an exercise price that is not denominated in: (a) the currency of a market in which a substantial portion of the Company's equity securities trades in, (b) the currency in which the employee's pay is denominated, or (c) the Company's functional currency, are required to be classified as liabilities. The change in the Company's functional currency, effective July 1, 2023, resulted in the reclassification of outstanding stock options that were previously denominated in C\$ from equity-classified to liability-classified options (see Note 8), which are accounted for as a share option modification in accordance with FASB's ASC 718 – *Compensation – Stock Compensation* (“**ASC 718**”). Under ASC 718, when an award is reclassified from equity to liability, if at the reclassification date the original vesting conditions are expected to be satisfied, then the minimum amount of compensation cost to be recognized is based on the grant date fair value of the original award. Fair value changes below this minimum amount are recorded in additional paid-in capital. For each reporting period after the modification date, the stock option liability is adjusted so that it equals the portion of the requisite service provided multiplied by the modified award's fair value at the end of the reporting period. Increases in the fair value of the liability in excess of the minimum grant date compensation cost described above are recognized as share-based compensation in operating expenses in the consolidated statement of operations and comprehensive loss.

### Share Issuance Costs

Common share issuance costs are incremental costs directly associated with an offering of securities. These costs typically include fees paid to bankers or underwriters, attorneys, accountants, as well as printers and other third parties. Prior to the effective date of an offering of equity securities, specific incremental costs directly attributable to a proposed or actual offering of securities may be deferred and charged against the gross proceeds of the offering. The Company capitalizes these deferred financing costs as prepaid expenses and other current assets in the accompanying consolidated balance sheets until the completion of the offering, unless the offering is abandoned, at which time the deferred financing costs will be recognized in the consolidated statements of operations and comprehensive loss. During the year ended December 31, 2023, the Company recognized general and administrative expenses of \$0.8 million related to abandoned offerings and had deferred financing costs of \$0.2 million related to the Company's at-the-market offering in prepaid expenses and other current assets on the consolidated balance sheet as of December 31, 2023.

## Income Taxes

The Company is a taxable entity under the Income Tax Act (Canada). Deferred income tax assets and liabilities are determined based on differences between the financial statement carrying amounts and the respective income tax bases of assets and liabilities, measured using substantively enacted income tax rates and laws that are expected to be in effect when the differences are expected to reverse. Deferred tax assets are recognized to the extent it is more likely than not that taxable income will be available against which the deferred tax asset can be utilized. Deferred tax assets are reduced by a valuation allowance if it is more likely than not that some portion or all of the deferred tax assets will not be realized.

The Company follows the provisions of ASC 740-10, *Uncertainty in Income Taxes* (“ASC 740-10”). The Company has not recognized a liability as a result of the implementation of ASC 740-10. A reconciliation of the beginning and ending amount of unrecognized tax benefits has not been provided since there is no unrecognized benefit since the date of adoption. The Company has not recognized interest expense or penalties as a result of the implementation of ASC 740-10. If there were an unrecognized tax benefit, the Company would recognize interest accrued related to unrecognized tax benefits in interest expense and penalties in operating expenses.

## Basic and Diluted Net Loss Per Share

Basic net loss per common share is computed by dividing net loss by the weighted-average number of common shares outstanding during each period. Diluted net loss per share of common shares includes the effect, if any, from the potential exercise or conversion of securities, such as convertible debt, share options and warrants, which would result in the issuance of incremental shares of common shares. For diluted net loss per share, the weighted-average number of common shares is the same for basic net loss per share due to the fact that when a net loss exists, dilutive securities are not included in the calculation as the impact is anti-dilutive. For all periods presented, basic and diluted net loss per share are the same, as any additional share equivalents would be anti-dilutive. As the Company has reported a net loss for all periods presented, diluted net loss per common share is the same as basic net loss per common share. Both basic and diluted net loss per share calculations include financial instruments that allow for the purchase of common shares issuable for little to no consideration, including pre-funded warrants.

## Emerging Growth Company Status

The Company is an Emerging Growth Company, as defined in Section 2(a) of the Securities Act of 1933, as modified by the Jumpstart Our Business Startups Act of 2012 (“JOBS Act”). Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act, until such time as those standards apply to private companies. The Company has elected to use this extended transition period for complying with new or revised accounting standards that have different effective dates for public and private companies until the earlier of the date that it (i) is no longer an emerging growth company or (ii) affirmatively and irrevocably opts out of the extended transition period provided in the JOBS Act. As a result, these consolidated financial statements may not be comparable to companies that comply with the new or revised accounting pronouncements as of public company effective dates.

## Recently Issued Accounting Pronouncements

In August 2020, the FASB issued ASU No. 2020-06, *Debt—Debt with Conversion and Other Options* (“Subtopic 470-20”) and *Derivatives and Hedging Contracts in Entity’s Own Equity* (“Subtopic 815-40”): *Accounting for Convertible Instruments and Contracts in an Entity’s Own Equity*. ASU 2020-06 will simplify the accounting for convertible instruments by reducing the number of accounting models for convertible debt instruments and convertible preferred shares. Limiting the accounting models results in fewer embedded conversion features being separately recognized from the host contract as compared with current GAAP. Convertible instruments that continue to be subject to separation models are (i) those with embedded conversion features that are not clearly and closely related to the host contract, that meet the definition of a derivative, and that do not qualify for a scope exception from derivative accounting and (ii) convertible debt instruments issued with substantial premiums for

which the premiums are recorded as additional paid-in capital. ASU 2020-06 also amends the guidance for the derivatives scope exception for contracts in an entity's own equity to reduce form-over-substance-based accounting conclusions. ASU 2020-06 will be effective for the Company for fiscal years beginning after December 15, 2023. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020, including interim periods within those fiscal years. The Company does not expect adopting ASU 2020-06 will have a material impact on the Company's consolidated financial statements and related disclosures as it does not have any outstanding debt as of December 31, 2023.

In June 2016, and in later clarifying amendments, the FASB issued ASU No. 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. The pronouncement changes the impairment model for most financial assets and requires the use of an "expected loss" model for instruments measured at amortized cost. Under this model, entities are required to estimate the lifetime expected credit loss on such instruments and record an allowance to offset the amortized cost basis of the financial asset, resulting in a net presentation of the amount expected to be collected on the financial asset. ASU 2016-13 is effective for the Company for fiscal years beginning after December 15, 2022, with early adoption permitted. The Company adopted this standard effective January 1, 2023 with no material impact on the Company's consolidated financial statements.

In 2023, the FASB issued ASU 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* ("ASU 2023-07"), which requires public entities to disclose significant segment expenses and other segment items. ASU 2023-07 also requires public entities to provide in interim periods all disclosures about a reportable segment's profit or loss and assets that are currently required annually. ASU 2023-07 becomes effective for the annual period starting on January 1, 2024, and for the interim periods starting on January 1, 2025. The Company is in the process of analyzing the impact that the adoption of ASU 2023-07 will have on its consolidated financial statements.

In 2023, the FASB issued ASU 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09"), which requires public entities to disclose in their rate reconciliation table additional categories of information about federal, state and foreign income taxes and to provide more details about the reconciling items in some categories if items meet a quantitative threshold. ASU 2023-09 becomes effective for the annual period starting on January 1, 2025. The Company is in the process of analyzing the impact that the adoption of ASU 2023-09 will have on its income tax disclosures.

### 3. FAIR VALUE MEASUREMENTS

The following are the major categories of assets measured at fair value on a recurring basis as of December 31, 2023 and 2022:

	As of December 31, 2023			Total
	Level 1	Level 2	Level 3	
<b>Assets:</b>				
Short-term investments	\$ 32,358	\$ —	\$ —	\$ 32,358
Total assets measured at fair value	<u>\$ 32,358</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 32,358</u>
<b>Liabilities:</b>				
Share-based compensation liability	\$ —	\$ —	\$ 422,002	\$ 422,002
Warrant liability	\$ —	\$ —	\$ 94,185	\$ 94,185
Total liabilities measured at fair value	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 516,187</u>	<u>\$ 516,187</u>

	As of December 31, 2022			Total
	Level 1	Level 2	Level 3	
<b>Assets:</b>				
Short-term investments	\$ 31,009	\$ —	\$ —	\$ 31,009
Total assets measured at fair value	<u>\$ 31,009</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 31,009</u>
<b>Liabilities:</b>				
Share-based compensation liability	\$ —	\$ —	\$ —	\$ —
Warrant liability	\$ —	\$ —	\$ 1,859,374	\$ 1,859,374
Total liabilities measured at fair value	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 1,859,374</u>	<u>\$ 1,859,374</u>

No transfers between levels have occurred in either reporting period presented.

### 4. PREPAID EXPENSES AND OTHER CURRENT ASSETS

Prepaid expenses and other current assets consist of the following:

	December 31,	
	2023	2022
Upfront research payments	\$ 146,851	\$ 346,015
Goods and services tax receivable	20,485	71,626
Accrued interest receivable	58,152	—
Insurance	482,297	471,088
Dues and subscriptions	12,529	7,926
Consultants	21,535	56,797
License fee	30,472	25,700
Deposits	14,161	12,907
Deferred financing costs	195,632	—
Miscellaneous	6,527	4,623
Total prepaid expenses and other current assets	<u>\$ 988,641</u>	<u>\$ 996,682</u>

## 5. ACCOUNTS PAYABLE AND ACCRUED LIABILITIES

Accrued liabilities consist of the following:

	December 31,	
	2023	2022
Legal	\$ 66,254	\$ —
Deferred financing costs	99,883	—
Accounting	101,528	73,970
Research and development	691,908	3,185,346
Severance	518,704	—
Other	28,249	178,330
Accrued liabilities	<u>\$ 1,506,526</u>	<u>\$ 3,437,646</u>

In May 2023, the Company entered into an agreement with a vendor which gives the option to defer payment on approximately \$5.4 million of current accounts payable and accrued liabilities until March 31, 2024. The outstanding balance of invoices due to the vendor will accrue interest at an annual rate of 5.5%, which is paid monthly. The Company may repay the outstanding balance at any time. As of December 31, 2023, the amount outstanding under the agreement recorded in accounts payable was \$5.7 million. As of December 31, 2022, the Company amounts outstanding to the vendor were \$1.3 million and \$2.7 million in accounts payable and accrued liabilities, respectively.

## 6. CONVERTIBLE DEBT

In March 2021, the Company completed a \$7.0 million private placement of convertible debentures (the “Debentures”). The Company allocated \$3,567,442 of proceeds to the Debenture. The Company incurred \$48,220 of issuance costs in connection with the private placement of which \$24,575 was allocated to the Debentures and amortized over the life of the Debenture. The Debentures were convertible into Common Shares at the option of the holder at any time and from time to time at a conversion price of \$6.00 following the Reverse Share Split and accrued interest at 1% per annum, which was payable annually. At the Company’s election, accrued interest was payable in in cash or Common Shares (such number of shares determined by dividing the interest due by the 5-day VWAP of the Common Shares). The Debentures were originally scheduled to mature on March 22, 2026. The Company recognized \$0 and \$241,854 of interest expense relating to the amortization of the debt discount related to the derivative liability and issuance costs allocated to the Debentures during the years December 31, 2023 and 2022, respectively.

The conversion feature was recognized as a derivative liability recorded as a discount to the Debenture, adjusted to fair value each reporting period and recorded in the consolidated statements of operations and comprehensive loss during the year ended December 31, 2021.

In June 2022, the Company amended the conversion feature of the Debentures (the “**Amended and Restated Debentures**”). Previously, the Debentures were convertible into Common Shares at the option of the holder at any time and from time to time at a conversion price of \$6.00 following the Reverse Share Split. Following the amendment, the Amended and Restated Debentures became convertible into Series 1 Convertible Preferred Shares at the option of the holder at any time and from time to time at a conversion price of \$6.00 following the Reverse Share Split. No other terms of the Debentures were amended. The modification of the Debentures was determined to be non-substantial.

In June 2022, the Company received notices of conversion from the holders of the Company’s Amended and Restated Debentures, requesting conversions in the aggregate of \$7.0 million, representing the entirety of the outstanding balance thereof. In satisfaction of the notices of conversion, the Company issued 70,000,000 Series 1 Convertible Preferred Shares, described further in Note 7, to the Amended and Restated Debenture holders in

accordance with the terms of the Amended and Restated Debentures and made cash payments to settle accrued interest of \$17,069.

The Company recognized the redemption as an extinguishment of the outstanding debt and the related derivative, which required a remeasurement of the derivative liability as of June 19, 2022, the date of conversion. The derivative liability at June 19, 2022 was valued at \$2,741,058 using a scenario-based valuation method under the Monte Carlo simulation model, volatility of 87%, a risk-free interest rate of 2.94% and a selected debt yield of 27.2%. Following the remeasurement of the derivative liability the Company recognized a total gain on the change in fair value of the derivative liability of \$2,643,123 during the year ended December 31, 2022. The extinguishment of the convertible notes was accounted for as follows:

	<b>June 19, 2022</b>
Carrying value of convertible debt net of issuance costs and debt discount	\$ 4,166,363
Derivative liability remeasured as of June 19, 2022	2,741,058
<b>Total liabilities extinguished on conversion</b>	<b>6,907,421</b>
Fair value of Series 1 Convertible Preferred Shares recorded to additional paid-in-capital	5,600,000
<b>Gain on extinguishment of convertible debt and derivative liability</b>	<b>\$ 1,307,421</b>

The fair value of Series 1 Convertible Preferred Shares recorded to additional paid-in-capital was calculated using the observable market price of Common Shares as the basis for determining fair value. The fair value of Common Shares was \$0.08 per share on the conversion date. Legal fees resulting from the debt modification were expensed as incurred.

The summary of activity for derivative liability for the year ended December 31, 2022 consists of the following:

	<b>December 31, 2022</b>
Balance at December 31, 2021	\$ 5,379,878
Change in fair value of the derivative liability	(2,643,123)
Foreign exchange loss	4,303
Gain on extinguishment of the derivative liability	(2,741,058)
<b>Balance at December 31, 2022</b>	<b>\$ —</b>

There was no debt or related derivative liability during the year ended December 31, 2023.

## 7. EQUITY

The Company has authorized an unlimited number of both Common and Preferred shares. As of December 31, 2023 and 2022, the Company had 18,885,254 and 8,579,284 issued and outstanding Common Shares, 0 and 70,000,000 issued and outstanding Series 1 Convertible Preferred Shares, and 1,166,667 and 0 issued and outstanding Series 2 Convertible Preferred Shares, respectively. All share classes have no par value.



Common Shares reserved for future issuance consists of the following:

	<u>December 31,</u>	
	<u>2023</u>	<u>2022</u>
Warrants	13,595,987	1,873,622
Series 1 Convertible Preferred Shares	—	1,166,667
Series 2 Convertible Preferred Shares	1,166,667	—
Options issued and outstanding under stock option plan	898,262	1,043,025
Deferred Share Units	1,061	1,061
Common Shares available for grant under stock option plan	471,843	396,080
<b>Total Common Shares reserved for future issuance</b>	<b><u>16,133,820</u></b>	<b><u>4,480,455</u></b>

#### Common Shares

The preferences, privileges, and rights of the Common Shares are as follows:

##### *Voting*

Subject to any special voting rights or restrictions, holders of common shares entitled to vote shall have one vote per share.

##### *Dividends*

The Company's board of directors may from time to time declare and authorize payment of dividends, if any, as they may deem advisable and need not give notice of such declaration to any shareholder. Subject to the rights of common shareholders, if any, holding shares with specific rights as to dividends, all dividends on common shares shall be declared and paid according to the number of such shares held and paid in Canadian dollars.

##### *Liquidation Rights*

In the event of the liquidation, dissolution or winding-up of the Company or any other distribution of the Company's assets for the purpose of winding up the Company's affairs, after the payment of dividends declared but unpaid, the holders of Common Shares shall be entitled *pari passu* to receive any remaining property of the Company.

#### Series 1 Convertible Preferred Shares

In June 2022, the directors of the Company authorized the issuance of 70,000,000 Series 1 Convertible Preferred Shares ("Series 1 Shares") with the following preferences, privileges and rights:

##### *Dividends*

If the Company declares, pays or sets aside any dividends on shares of any other class or series of capital stock the holders of the Series 1 Shares shall receive a dividend on each outstanding share of Series 1 Shares in an amount equal to that dividend per share of the Series 1 Shares as would equal the product of the dividend payable as if all shares of such series had been converted into Common Shares.

### *Liquidation*

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, the holders of the Series 1 Shares shall be entitled to be paid out of the assets of the Company available for distribution to the shareholders an amount per share equal to \$6.00, plus any dividends declared but not paid. If, upon any such liquidation event, the assets available for distribution to the shareholders are insufficient to pay the holders of the Series 1 Shares, the holders of the Series 1 Shares shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

### *Voting*

The Series 1 Shares do not confer any voting rights or privileges.

### *Redemption*

The Series 1 Shares are not subject to mandatory redemption or other redemption provisions for which the events resulting in redemption are not within the Company's control.

### *Optional Conversion*

Series 1 Shares are convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and non-assessable Common Shares as is determined by dividing \$0.10 by the applicable conversion price in effect at the time of conversion. The Conversion Price was initially equal to \$0.10 and, following the Reverse Share Split on June 28, 2022, is equal to \$6.00, such that 60 Preferred Shares are convertible into 1 Common Share.

### *Mandatory Conversion*

All outstanding Series 1 Shares shall automatically convert into Common Shares, at the effective conversion rate upon the closing of one or more sales of equity securities resulting in at least \$30 million of cumulative gross proceeds to the Company. As of the exchange date for the Series 2 Convertible Preferred Shares, described below, the remaining conversion threshold was approximately \$2.0M, which was subsequently raised to \$14M as described below.

### Series 2 Convertible Preferred Shares

In November 2023, the directors of the Company authorized the issuance of an unlimited number of Series 2 Convertible Preferred Shares ("**Series 2 Shares**"). In December 2023, the Company entered into an agreement with the Series 1 Shareholders to exchange all 70,000,000 outstanding Series 1 Shares for 1,166,667 Series 2 Shares (an equivalent number of as-converted Common Shares) in exchange for the Series 1 Shareholders waiving their rights under a financing limitation side letter entered into amongst the Company and the Series 1 Shareholders during the August 2023 PIPE. Following the Series 2 exchange, the Company was no longer subject to any financing limitations.

The Series 2 Shares carry the same rights and privileges as the Series 1 Shares, except the mandatory conversion threshold was increased as described below. The Company treated the exchange for Series 2 Shares as a modification of the Series 1 Shares and determined there was no material difference in fair value between the Series 2 Shares and the Series 1 Shares, and as such no deemed dividend was recognized in the consolidated financial statements as a result of the exchange.

The Series 2 Shares have the following preferences, privileges and rights:

#### *Dividends*

If the Company declares, pays or sets aside any dividends on shares of any other class or series of capital stock the holders of the Series 2 Shares shall receive a dividend on each outstanding share of Series 2 Shares in an amount equal to that dividend per share of the Preferred Share as would equal the product of the dividend payable as if all shares of such series had been converted into Common Shares.

#### *Liquidation*

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company, the holders of the Series 2 Shares shall be entitled to be paid out of the assets of the Company available for distribution to the shareholders an amount per share equal to \$6.00, plus any dividends declared but not paid. If, upon any such liquidation event, the assets available for distribution to the shareholders are insufficient to pay the holders of the Series 2 Shares, the holders of the Series 2 Shares shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

#### *Voting*

The Series 2 Shares do not confer any voting rights or privileges.

#### *Redemption*

The Series 2 Shares are not subject to mandatory redemption or other redemption provisions for which the events resulting in redemption are not within the Company's control.

#### *Optional Conversion*

Series 2 Shares are convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, at ratio of 1 Series 2 Share into 1 Common Share.

#### *Mandatory Conversion*

All outstanding Series 2 Shares shall automatically convert into Common Shares, at the effective conversion rate upon the closing of one singular financing, including a financing with multiple tranches in which any subsequent tranches are closed within 18 months of the initial closing, which financing results in at least single sale, executable in one or more tranches, of equity securities resulting in at least \$14.0 million of cumulative gross proceeds to the Company.

#### *Equity Transactions*

In August 2021, the Company announced the closing of a public offering of 2,096,357 Common Share units at a price of \$9.60 per unit for gross proceeds of \$20,125,000. The Company incurred \$2,109,657 of cash issuance costs in conjunction with the public offering. Each Common Share unit consisted of one Common Share and one-quarter Common Share warrant ("**2021 accelerated warrants**"). Each whole warrant entitles the holder thereof to purchase one Common Share at an exercise price of \$12.60 per share at any time for five years. The warrants contain an acceleration clause allowing the Company to accelerate the expiry date of the warrants to 30 days following a time period during which the common share VWAP exceeds a trading price of C\$37.80 for ten consecutive trading days.

The Common Share warrants were accounted for as a warrant liability since the exercise price is in US\$ while the Company's functional currency in 2021 was C\$. As of December 31, 2022, the fair value of the 2021 accelerated warrants was calculated using the Monte Carlo model with the following parameters: risk free interest rate of 4.14%; annual volatility of 87.5%; and expected life of 3.65 years. The balance at December 31, 2022 was approximately \$931,000.

In October 2022, the Company announced the closing of a private offering of 1,383,755 Common Share units at a price of \$5.40 per unit for gross proceeds of \$7,472,278. The Company incurred \$1,227,357 of cash issuance costs in conjunction with the public offering. Each Common Share unit consisted of one Common Share and one-quarter Common Share warrant ("**2022 warrants**"). Each whole warrant entitles the holder thereof to purchase one Common Share at an exercise price of \$7.50 per share at any time for a period of five years beginning six months from the issuance date.

The Company determined the allocation of the \$5.40 Unit issue price to the Common Shares and the one-quarter Common Share purchase warrants based on the relative fair values of the warrants, with the residual charged to equity. The Common Shares were allocated gross proceeds of \$5,951,877 and share issue costs of \$977,624. The Common Share warrants are accounted for as a warrant liability since the exercise price is in US\$ while the Company's functional currency is C\$. The initial balance was calculated using the assumptions below resulting an allocation of gross proceeds of \$1,520,401. The Company determined it was appropriate to adjust the warrant amounts to fair value as of each reporting period using Black-Scholes option pricing model. The Common Shares issued were allocated a price of \$4.30 per share and the quarter Common Share purchase warrants were allocated a price of \$1.10. Assumptions used to determine the value of the Common Share warrants were: a weighted average risk-free interest rate of 4.10%; annual volatility of 94.0%; and expected life of 5.0 years. The issuance costs allocated to the warrants based on the relative fair values of the warrants, amounted to \$249,733 and were charged to general and administrative expense in the consolidated statements of operations and comprehensive loss.

As of December 31, 2022, the fair value of the 2022 warrants was calculated using the Black Scholes model with the following parameters: risk free interest rate of 4.00%; annual volatility of 86.0%; and expected life of 4.8 years. The balance at December 31, 2022 was approximately \$928,500.

Following the change in functional currency effective July 1, 2023, the Company reassessed the classification of its historical US\$ and C\$ denominated warrants in accordance with the Company's accounting policy for warrants. As a result of the reassessment, the Company determined that 870,026 US\$ warrants to purchase Common Shares, originally issued in financing transactions in 2021 and 2022, previously classified as warrant liabilities met the criteria under ASC 815-40 for permanent equity classification. The fair value of US\$ warrants of \$1,287,400, calculated using a Black Scholes calculation as of June 30, 2023, was reclassified from warrant liability to additional paid-in-capital in the accompanying consolidated financial statements. The fair value of the US\$ warrants represented the entirety of the Company's warrant liability as of June 30, 2023. The US\$ warrants will not be re-measured prospectively.

As result of the reassessment the Company determined that 687,591 C\$ warrants, originally issued in financing transactions between 2018 and 2020, which were previously classified in permanent equity no longer met the criteria for equity classification. The C\$ warrants were remeasured as of July 1, 2023. The C\$ warrants have exercise prices between C\$12.00 and C\$28.80 and expire between January 2024 and November 2025. The Company measured the fair value of the C\$ warrants on July 1, 2023 using a Black Scholes calculation and the resulting fair value of \$396,375 was recorded as a reclassification from additional paid-in-capital to warrant liability. The C\$ warrant liability was subsequently re-measured at December 31, 2023 to a fair value of \$94,185, with the change in fair value of \$302,190 reported in other income in the accompanying consolidated statement of operations and comprehensive loss.

The weighted-average values of the significant assumptions used in the Black Scholes valuation of the C\$ warrants as of July 1, 2023 included historical volatility of 84.6%, a risk-free rate of 4.54%, exercise price of C\$12.80 and an expected term of 2.3 years. The weighted-average values of the significant assumptions used in

the Black Scholes valuation of the C\$ warrants as of December 31, 2023 included volatility of 131.5%, a risk-free rate of 3.88%, exercise price of C\$10.80 and an expected term of 1.7 years.

A summary of warrant liability activity for the years ended December 31, 2023 and 2022 is as follows:

	<b>December 31, 2023</b>
Balance at December 31, 2022	\$ 1,859,374
Change in fair value of US\$ warrant liability	(564,548)
Foreign exchange loss	(7,426)
Fair value of US\$ warrant liability as of June 30, 2023	1,287,400
Fair value of previously liability-classified US\$ warrants reclassified to additional paid-in-capital as of July 1, 2023	(1,287,400)
Fair value of previously equity-classified C\$ warrants reclassified to warrant liability as of July 1, 2023	396,375
Change in fair value of C\$ warrant liability	(302,190)
Balance at December 31, 2023	<u>\$ 94,185</u>
	<b>December 31, 2022</b>
Balance at December 31, 2021	\$ 1,871,687
October 2022 PIPE warrant liability at issuance	1,520,401
Change in fair value of the warrant liability	(1,533,644)
Foreign exchange loss	930
Balance at December 31, 2022	<u>\$ 1,859,374</u>

Related to the sale of the units in October 2022, the Company paid certain intermediaries \$597,780 and issued 69,188 compensation warrants. The compensation warrants are exercisable at any time for five years beginning six months from the issuance date at an exercise price of \$6.10 and do not have an acceleration clause. The compensation warrants have been issued as consideration for services provided by the intermediaries. The Company used Black Scholes to determine the fair value of the compensation warrants at the issuance date, which were recorded as equity instruments. The fair value of \$317,000 has a net zero impact to additional paid-in capital. Significant assumptions used in Black Scholes included risk free interest rate of 4.10%; historical volatility of 94.0%; and a 5.0 year expiry.

In August 2023, through a private placement (“**August 2023 PIPE**”), the Company issued 9,945,969 Common Shares, and, in lieu of Common Shares, Pre-Funded Warrants to purchase an aggregate of 954,725 Common Shares, and, in each case, accompanying Common Warrants to purchase an aggregate of up to 10,900,604 additional Common Shares at a unit price of \$1.88 per Common Share and accompanying Common Warrant (or \$1.87 per Pre-Funded Warrant and accompanying Common Warrant). The private placement resulted in aggregate gross proceeds of \$20,483,758 before \$2,738,558 of issuance costs. The Common Warrants are exercisable for five years commencing six months after the issuance date at a price of \$1.75.

The Company determined the Pre-Funded Warrants and Common Warrants both met the permanent equity criteria classification. The Pre-Funded Warrants and Common Warrants are classified as a component of permanent equity because they are freestanding financial instruments that are legally detachable and separately exercisable from the Common Shares with which they were issued, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, and permit the holders to receive a fixed number of common shares upon exercise. In addition, the Pre-Funded Warrants and Common Warrants do not provide any guarantee of value or return. The Company used a Black Scholes calculation to determine the fair value of the Common Warrants at issuance and allocated a share of the net proceeds based on the relative fair value of the Common Warrants. Net proceeds allocated to the Common Warrants were \$7,972,736, with the remaining net

proceeds of \$9,772,464 allocated to the Common Shares. The aggregate net proceeds of the transaction are recorded in additional paid-in-capital.

The Company also issued 327,020 compensation warrants to purchase Common Shares as compensation to a placement agent as part of the August 2023 PIPE. The compensation warrants have an exercise price of \$1.75 and expire in February 2029. The Company used a Black Scholes calculation to determine the fair value of the compensation warrants at the issuance date. The fair value of \$466,658 of issuance costs are recorded in additional-paid-in capital, which results in a net zero impact to additional paid-in-capital and issuance costs. Significant assumptions used in the Black Scholes calculation included risk free interest rate of 4.36%; historical volatility of 107.3%; and a 5.5-year expiry.

## 8. WARRANTS

As of December 31, 2023, outstanding Common Share warrants and exercise prices denominated in C\$ unless otherwise noted, related to unit offerings are as follows:

Exercise Price \$	Number of Warrants	Expiry date
28.80	139,659	January 2024
18.00	68,334	June 2024
18.00	150,818	November 2024
18.00	49,167	December 2024
12.00	279,613	November 2025
USD 12.60	524,088	August 2026
USD 9.60	146,744	August 2026
USD 7.50	345,938	April 2028
USD 6.10	69,188	April 2028
USD 0.01	594,724	None
USD 1.75	11,227,714	February 2029
	<u>13,595,987</u>	

In April 2023, 100,073 warrants with an exercise price of C\$28.80 expired without being exercised. 360,000 pre-funded warrants were exercised for an equivalent number of common shares for net proceeds of \$3,600 during the year ended December 31, 2023.

## 9. SHARE-BASED COMPENSATION

### 2015 Stock Option Plan

The Company maintains the 2015 Stock Option Plan (“**2015 Option Plan**”), originally referred to as the 2007 Option Plan. In June 2015, the 2015 Option Plan was amended from a fixed option plan to a rolling share option plan pursuant to which the Company is authorized to grant options of up to 20% of its issued and outstanding Common Shares. Share options granted vest at various rates and have a term not exceeding ten years. As of December 31, 2023 and 2022, the Company had 471,843 and 396,080 options, respectively, available for grant under the 2015 Option Plan.

### Canadian Dollar Share Options

Share options under the 2015 Option Plan are granted in either US\$ or C\$. Upon the change in the Company’s functional currency, effective July 1, 2023, C\$ share options previously classified as equity were reclassified as liabilities. On July 1, 2023, these options had a fair value of \$1,768,515, which was recorded as share-based compensation liability, of which \$1,435,912 was reclassified from additional paid-in-capital and the remainder of \$332,602 was recorded as additional share-based compensation expense. The C\$ options were re-measured as of December 31, 2023 and had a fair value of \$442,002, resulting in a decrease in fair value of \$1,013,910 during

the year ended December 31, 2023, of which \$332,602 was reduced from share-based compensation expense in the Company's consolidated statement of operations and comprehensive loss, with the remaining reduction of \$681,308 applied to additional paid-in-capital.

The following table summarizes the activity of the C\$ share options under the 2015 Option Plan for the years ended December 31, 2023 and 2022. All amounts are denominated in Canadian dollars, except year and share amounts:

	Number of Share Options	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value
Outstanding as of January 1, 2022	738,037	\$ 8.40	5.1	\$ 2,231,293
Granted	360,000	7.54		
Forfeited	(55,012)	15.98		
Outstanding as of December 31, 2022	1,043,025	\$ 5.60	6.1	\$ 1,183,860
Granted	—	—		
Forfeited	(143,230)	7.10		
Expired	(1,533)	15.76		
Outstanding as of December 31, 2023	898,262	7.58	6.5	—
Vested and exercisable as of December 31, 2023	792,965	\$ 7.46	6.5	—

The aggregate intrinsic value of options outstanding, exercisable, and vested and exercisable is calculated as the difference between the exercise price of the underlying options, and the fair value of the Company's Common Shares. There were no C\$ share options granted during the year ended December 31, 2023.

The following table summarizes the weighted average of significant assumptions used to calculate the fair value of C\$ share options outstanding and exercisable as of July 1, 2023 and December 31, 2023:

	Period Ended	
	December 31, 2023	July 1, 2023
Weighted average fair value of C\$ Options	C\$ 1.30	C\$ 2.54
Expected volatility	116.3 %	83.3 %
Risk-free interest rate	4.04 %	4.30 %
Expected dividend yield	— %	— %
Expected term (years)	6.5	6.8

Expected volatility is based on historical volatility of the Company's Common Shares over the expected life of the option, as the Company's options are not readily tradable.

#### US Dollar Share Options

The Company began making share option grants denominated in US\$ following the Company's change in functional currency in July 2023. During the year ended December 31, 2023, the Company granted 69,000 share options with a grant date fair value of \$105,790 and there were no options exercised or forfeited.

The fair value of the US\$ share options granted was estimated using Black Scholes with the following assumptions:

	<u>Year Ended December 31,</u>	
	<u>2023</u>	
Weighted average fair value of US\$ Options	\$	1.53
Expected volatility		101.9 %
Risk-free interest rate		4.77 %
Expected dividend yield		— %
Expected term (years)		6.1

#### **DSU Plan**

The Company has a Deferred Share Unit plan (“**DSU Plan**”) for senior officers. Under the DSU Plan, rights to the Company’s Common Shares may be awarded on a deferred payment basis up to a maximum of 16,666 common share units. Each common share unit will fully vest upon cessation of employment with the Company and then can be redeemed for one common share of the Company by the unitholder. The Company has 1,061 units outstanding as of December 31, 2023.

#### **Share-based Payment Expense**

The following table summarizes total share-based compensation for both the C\$ and US\$ share options included in the Company’s accompanying consolidated statements of operations and comprehensive loss:

	<u>Year Ended December 31,</u>	
	<u>2023</u>	<u>2022</u>
Research and development	\$ 80,825	\$ 297,933
General and administrative	190,717	189,697
Total share-based compensation	<u>\$ 271,542</u>	<u>\$ 487,630</u>

Total share-based compensation expense for C\$ and US\$ denominated share options was \$266,701 and \$4,841, respectively, for the year ended December 31, 2023. As of December 31, 2023, there was \$100,948 of unrecognized share-based compensation related to US\$ options outstanding, which is expected to be recognized over a weighted-average remaining service period of 3.8 years.

## **10. INCOME TAXES**

As of December 31, 2023 and 2022, the net deferred tax assets have not been recognized in the accompanying consolidated financial statements. A valuation allowance is recognized to reduce the deferred tax asset as it is more likely than not that a tax benefit will not be realized.



The following are the significant components of the Company's deferred taxes as of December 31:

	2023	2022
Non-capital losses carried forward	\$ 21,151,000	\$ 17,614,000
Research and development expenditures	3,246,000	3,346,000
Investment tax credits	2,088,000	2,152,000
Tax value of technology rights and property and equipment in excess of accounting basis	221,000	250,000
Share issue costs	1,019,000	656,000
Total deferred income tax assets	27,725,000	24,018,000
Valuation allowance	(27,725,000)	(24,018,000)
Net deferred income tax assets	<u>\$ —</u>	<u>\$ —</u>

As of December 31, 2023, the Company has available research and development expenditure credits for income tax purposes of approximately \$12,248,000, which may be carried forward without expiration to reduce future taxable income.

As of December 31, 2023, the Company has non-capital income tax loss carry-forwards of approximately \$79,816,000 available to reduce future income for income tax purposes. The income tax loss carry-forwards have expiry dates between the years 2026 and 2043.

As of December 31, 2023, the Company has approximately \$2,088,000 of non-refundable investment tax credits available to offset future income taxes. The non-refundable investment tax credits have expiry dates between 2025 and 2035.

A reconciliation of the combined federal and provincial statutory income tax rate applied to the net loss for the year to the income tax recovery as of December 31 is as follows:

	2023	2022
Basic combined Canadian statutory income tax rate	26.5 %	26.5 %
Income tax recovery based on statutory rate	\$ (3,559,000)	\$ (4,887,000)
Permanent differences	(157,000)	(1,164,000)
Share issue costs recorded, net of equity	(731,000)	(271,000)
Unrecognized benefit of current year tax losses	4,447,000	6,322,000
	<u>\$ —</u>	<u>\$ —</u>

The Company does not expect a significant change in the amount of unrecognized tax benefits over the next 12 months. However, any adjustments arising from certain ongoing examinations by tax authorities could alter the timing or amount of taxable income or deductions and these adjustments could differ from the amount accrued. The Company's federal and provincial income tax returns files for all years remain subject to examination by the taxation authorities.

## 11. RELATED PARTY TRANSACTIONS

### UBC Collaborative Research Agreement

In April 2016, the Company entered into a collaborative research agreement ("CRA") with the University of British Columbia ("UBC") and the Vancouver Coastal Health Authority in the amount of C\$787,500, with the Company's Chief Scientific Officer, as principal investigator at the UBC. In January 2022, the UBC CRA was amended to extend the project for an additional three years, and funding was increased to an aggregate total of C\$5,030,000. This amendment, along with the November 2021 amendment extends the project for an additional three years, effective January 1, 2022. During the years ended December 31, 2023 and 2022, the Company made cash payments of \$588,136 and \$461,516, respectively, and incurred costs of \$592,810 and \$557,665,

respectively, which are included in research and development expenses in the accompanying consolidated statements of operations and comprehensive loss.

#### Title 19 Promis

The Company entered into the following transactions with a related party that holds an equity interest in the Company during the years ended December 31 2023 and 2022:

- In March 2021, the Company issued a convertible unsecured debenture to Title 19 Promis in the principal amount of \$3,000,000, convertible into Common Shares at the option of the holder at a conversion price of \$6.00 (the “**Title 19 Debenture**”). The Title 19 Debenture was later amended to provide that it was convertible into Series 1 Preferred Shares at the option of the holder at a conversion price of \$6.00. In June 2022, Title 19 Promis elected to convert the Title 19 Debenture and was issued 30,000,000 Series 1 Convertible Preferred Shares. In December 2023, Title 19 Promis entered into an agreement with Company to exchange all of its Series 1 Convertible Preferred Shares into 500,000 Series 2 Convertible Preferred Shares, which are convertible into an aggregate of 500,000 Common Shares.
- In October 2022, in a private offering, Title 19 Promis acquired 106,391 Common Shares and a warrant to purchase 26,597 Common Shares for an aggregate purchase price of \$574,511.
- In August 2023, in a private offering, Title 19 Promis acquired 797,872 Common Shares and a warrant to purchase 797,827 Common Shares for an aggregate purchase price of \$1,500,000.

#### Crocker Mountain LLC

The Company entered into the following transactions with a related party that holds an equity interest in the Company during the years ended December 31 2023 and 2022:

- In March 2021, the Company issued a convertible unsecured debenture to Crocker Mountain in the principal amount of \$900,000, convertible into Common Shares at the option of the holder at a conversion price of \$6.00 (the “**Crocker Mountain Debenture**”). The Crocker Mountain Debenture was later amended to provide that it was convertible into Series 1 Convertible Preferred Shares. In December 2023, Crocker Mountain entered into an agreement with Company to exchange all of its Series 1 Convertible Preferred Shares into 150,000 Series 2 Convertible Preferred Shares, which are convertible into an aggregate of 150,000 Common Shares.
- In March 2021, the Company issued a convertible unsecured debenture to the Jeremy M. Sclar 2012 Irrevocable Family Trust, an affiliate of Crocker Mountain (the “**Trust**”), in the principal amount of \$900,000, convertible into Common Shares at the option of the holder at a conversion price of \$6.00 (the “**Trust Debenture**”). The Trust Debenture was later amended to provide that it was convertible into Series 1 Convertible Preferred Shares. In December 2023, the Trust entered into an agreement with Company to exchange all of its Series 1 Convertible Preferred Shares into 150,000 Series 2 Convertible Preferred Shares, which are convertible into an aggregate of 150,000 Common Shares.
- In October 2022, in a private offering, the Trust acquired 104,869 Common Shares and a warrant to purchase 26,217 Common Shares for an aggregate purchase price of \$566,292.
- In August 2023, in a private offering, the Trust acquired 664,894 Common Shares and a warrant to purchase 664,894 Common Shares for an aggregate purchase price of \$1,250,001.
- In August 2023, in a private offering, Crocker Mountain acquired 664,893 Common Shares and a warrant to purchase 664,893 Common Shares for an aggregate purchase price of \$1,249,999.

## 12. COMMITMENTS AND CONTINGENCIES

### Research, Development and License Agreements

The Company enters into research, development and license agreements with various parties in the ordinary course of business where the Company receives research services and rights to proprietary technologies. The agreements require compensation to be paid by the Company, typically, by a combination of the following:

- fees comprising amounts due initially on entering into the agreements and additional amounts due either on specified timelines or defined services to be provided;
- milestone payments that are dependent on products developed under the agreements proceeding toward specified plans of clinical trials and commercial development; and
- royalty payments calculated as a percentage of net sales, commencing on commercial sale of any product candidates developed from the technologies.

Milestone and royalty related amounts that may come due under various agreements are dependent on, among other factors, preclinical safety and efficacy, clinical trials, regulatory approvals and, ultimately, the successful development and commercial launch of a new drug, the outcomes and timings of which are uncertain. Amounts due per the various agreements for milestone payments will accrue once the occurrence of a milestone is likely. Amounts due as royalty payments will accrue as commercial revenues from the product are earned. Through December 31, 2023, no events have occurred that require accrual of any milestone or royalty related amounts.

#### *UBC and the Vancouver Coastal Health Authority Agreement*

In April 2016, the Company entered into a three-year, CRA with the UBC and the Vancouver Coastal Health Authority. The agreement was amended various times through November 2021. Refer to Note 11 Related Party Transactions.

#### *UBC Agreement*

In February 2009, the Company entered into an agreement with UBC to further the development and commercialization of certain technology developed, in part, by the Company's Chief Scientific Officer. The agreement was amended and restated in October 2015. Under the amended and restated agreement, the Company is committed to make royalty payments based on revenue earned from the licensed technology. An annual license fee is payable over the term of the agreement. The agreement remains effective unless terminated under the provisions of the agreement. The Company made annual license payments of C\$25,000 during each of the years ended December 31, 2023 and 2022. Through December 31, 2023 no accruals for royalty payments have been made.

### Indemnification

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend an indemnified party for losses suffered or incurred by the indemnified party. Some of the provisions will limit losses to those arising from third party actions. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amount of future payments the Company could be required to make under these provisions is not determinable. The Company has never incurred material costs to defend lawsuits or settle claims related to these indemnification provisions. The Company has also entered into indemnification agreements with its directors and officers that may require the Company to indemnify its directors and officers

against liabilities that may arise by reason of their status or service as directors or officers. The Company currently has directors' and officers' insurance.

### 13. NET LOSS PER SHARE

Basic net earnings per share applicable to common shareholders is calculated by dividing net earnings applicable to common shareholders by the weighted average shares outstanding during the period, without consideration for common share equivalents. Diluted net earnings per share applicable to common shareholders is calculated by adjusting the weighted average shares outstanding for the dilutive effect of common share equivalents outstanding for the period, determined using the treasury-stock method and the if-converted method. For purposes of the calculation of dilutive net loss per share applicable to common shareholders, share options, and warrants are considered to be common share equivalents but are excluded from the calculation of diluted net loss per share applicable to common shareholders, as their effect would be anti-dilutive; therefore, basic and diluted net loss per share applicable to common shareholders were the same for all periods presented.

As of December 31, 2023, 594,725 Pre-Funded Warrants to purchase common shares for little to no consideration, issued in connection with the August 2023 private placement (see Note 7), were included in the basic and diluted net loss per share calculation. The following table sets forth the computation of basic and diluted net loss per share attributable to common shareholders:

	<u>Years Ended December 31,</u>	
	<u>2023</u>	<u>2022</u>
<b>Numerator:</b>		
Net loss attributable to common shareholders	\$ 13,212,482	\$ 18,062,263
<b>Denominator:</b>		
Weighted-average shares outstanding used in computing net loss per share attributable to common shareholders, basic and diluted	12,292,707	7,502,609
Net loss per share attributable to common shareholders, basic and diluted	\$ (1.07)	\$ (2.41)

The following outstanding potentially dilutive common shares equivalents were excluded from the computation of diluted net loss per share for the periods presented because including them would have been antidilutive:

	<u>December 31,</u>	
	<u>2023</u>	<u>2022</u>
Options issued and outstanding under stock option plan	967,262	1,043,025
Warrants	13,001,262	1,873,622
Series 1 Convertible Preferred Shares	—	1,166,667
Series 2 Convertible Preferred Shares	1,166,667	—
Deferred Share Units	1,061	1,061
Total	<u>15,136,252</u>	<u>4,084,375</u>

### 14. SUBSEQUENT EVENTS

In January 2024, the Company entered into an At The Market Offering Agreement to initiate an at-the-market offering program under which the Company may offer and sell, from time to time at its sole discretion, its common shares, having an aggregate offering price of up to \$25.0 million. As of the date that these financial statements were issued, the Company had sold 75,862 common shares for gross proceeds of approximately \$194,000.

## **Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure**

None.

### **Item 9A. Controls and Procedures**

#### ***Evaluation of Disclosure Controls and Procedures***

The Company maintains “disclosure controls and procedures,” as defined in Rule 13a-15(e) and Rule 15d-15(e) under the Exchange Act that are designed to ensure that information required to be disclosed in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to our management, including our principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure.

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) as of December 31, 2023. Based on the evaluation of our disclosure controls and procedures, our management concluded that, as of December 31, 2023, our disclosure controls and procedures were effective to provide reasonable assurance that the information required to be disclosed by us in this Annual Report on Form 10-K was (a) reported within the time periods specified by SEC rules and regulations, and (b) communicated to our management, including our Chief Executive Officer and Chief Financial Officer, to allow timely decisions regarding any required disclosure.

#### ***Management’s Annual Report on Internal Control Over Financial Reporting***

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is a process designed to provide reasonable assurance of the reliability of financial reporting and of the preparation of financial statements for external reporting purposes, in accordance with U.S. generally accepted accounting principles.

Internal control over financial reporting includes policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect transactions and disposition of assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with U.S. generally accepted accounting principles, and that receipts and expenditures are being made only in accordance with the authorization of its management and directors; and (3) provide reasonable assurance regarding the prevention or timely detection of unauthorized acquisition, use, or disposition of our assets that could have a material effect on its financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of the effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies and procedures included in such controls may deteriorate.

Our management has assessed the effectiveness of our internal control over financial reporting as of December 31, 2023. In making this assessment, management used the criteria established by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control - Integrated Framework (2013). These criteria are in the areas of control environment, risk assessment, control activities, information and communication, and monitoring. Management’s assessment included extensive documentation, evaluating and testing the design and operating effectiveness of its internal controls over financial reporting.

Based on management’s processes and assessment, as described above, management has concluded that, as of December 31, 2023, our internal control over financial reporting was effective.

#### ***Attestation Report of the Registered Public Accounting Firm***

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for “emerging growth companies.”

#### ***Changes in Internal Control Over Financial Reporting***

There have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Securities Exchange Act of 1934, as amended, that occurred during the three months ended December 31, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

#### ***Inherent Limitations on Effectiveness of Internal Controls***

In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable, not absolute, assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs. Our management, including our Chief Executive Officer and Chief Financial Officer, believes that our disclosure controls and procedures and internal control over financial reporting are designed to provide reasonable assurance of achieving their objectives and are effective at the reasonable assurance level. However, our management does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all fraud.

#### **Item 9B. Other Information**

During the three months ended December 31, 2023, none of our directors or officers (as defined in Rule 16a-1(f) of the Exchange Act) adopted, terminated or modified a Rule 10b5-1 trading arrangement or non-Rule 10b5-1 trading arrangement (as such terms are defined in Item 408 of Regulation S-K).

#### **Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections**

Not applicable.

### **PART III**

#### **Item 10. Directors, Executive Officers, and Corporate Governance**

The information required by this item will be contained in our 2024 Proxy Statement, to be filed with the SEC not later than 120 days after the end of our fiscal year ended December 31, 2023 and is incorporated in this report by reference.

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees, including our principal executive officer and principal financial officer. The Code of Business Conduct and Ethics is posted on our website at <https://www.promisneurosciences.com/investors/corporate-governance/governance-documents>.

We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of this Code of Business Conduct and Ethics by posting such information on our website, at the address and location specified above and, to the extent required by the listing standards of Nasdaq, by filing a Current Report on Form 8-K with the SEC, disclosing such information. .

#### **Item 11. Executive Compensation**

The information required by this item will be contained in our 2024 Proxy Statement, to be filed with the SEC not later than 120 days after the end of our fiscal year ended December 31, 2023 and is incorporated in this report by reference.

**Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters**

The information required by this item will be contained in our 2024 Proxy Statement, to be filed with the SEC not later than 120 days after the end of our fiscal year ended December 31, 2023 and is incorporated in this report by reference.

**Item 13. Certain Relationships and Related Transactions, and Director Independence**

The information required by this item will be contained in our 2024 Proxy Statement, to be filed with the SEC not later than 120 days after the end of our fiscal year ended December 31, 2023 and is incorporated in this report by reference.

**Item 14. Principal Accountant’s Fees and Services**

The information required by this item will be contained in our 2024 Proxy Statement, to be filed with the SEC not later than 120 days after the end of our fiscal year ended December 31, 2023 and is incorporated in this report by reference.

Our independent public accounting firm is Baker Tilly US, LLP, Tewksbury, Massachusetts, PCAOB Auditor ID 23.

**Part IV**

**Item 15. Exhibits and Financial Statement Schedules**

(a) The following documents are filed as part of this Annual Report on Form 10-K:

(1) Financial Statements:

Report of Independent Registered Public Accounting Firm  
Consolidated Balance Sheets as of December 31, 2023 and December 31, 2022  
Consolidated Statements of Operations and Comprehensive Loss for the Fiscal Years Ended December 31, 2023, December 31, 2022  
Consolidated Statements of Shareholders’ Equity (Deficit) for the Fiscal Years Ended December 31, 2023 and December 31, 2022  
Consolidated Statements of Cash Flows for the Fiscal Years Ended December 31, 2023, and December 31, 2022  
Notes to Consolidated Financial Statements

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(3) Exhibits. The exhibits required by Item 601 of Regulation S-K and Item 15(b) of this Annual Report on Form 10-K are listed in the Exhibit Index immediately preceding the signature page of this Annual Report on Form 10-K. The exhibits listed in the Exhibit Index are incorporated by reference herein.

**Item 16. Form 10-K Summary**

Not applicable

## EXHIBIT INDEX

Exhibit Number	Description
3.1	Articles. (incorporated herein by reference to Exhibit 3.1 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
3.1.1	Certificate of Amendment to the Articles dated July 8, 2015. (incorporated herein by reference to Exhibit 3.1.1 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
3.1.2	Certificate of Amendment to the Articles dated June 17, 2022. (incorporated herein by reference to Exhibit 3.1.2 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
3.1.3	Certificate of Amendment to the Articles dated June 21, 2022. (incorporated herein by reference to Exhibit 3.1.3 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
3.1.4	Articles of Continuance. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on July 14, 2023).
3.1.5	Certificate of Amendment to the Articles dated December 4, 2023. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on December 8, 2023).
3.2	Amended and Restated By-law No. 1. (incorporated herein by reference to Exhibit 3.2 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
3.2.1	By-law 2. (incorporated herein by reference to Exhibit 3.2.1 to ProMIS' 10 Registration Statement filed June 22, 2022, as amended).
3.2.2	Amended and Restated By-law No. 1. (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on July 14, 2023).
3.2.3	Amended and Restated By-law No. 2. (incorporated by reference to Exhibit 3.3 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on July 14, 2023).
4.1	Form of Amended and Restated Unsecured Convertible Debenture dated June 17, 2022. (incorporated herein by reference to Exhibit 4.1 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
4.2	Form of PIPE Warrant. (incorporated herein by reference to Exhibit 4.2 to ProMIS' Current Report on Form 8-K filed October 17, 2022).
4.3	Form of Placement Agent Warrant. (incorporated herein by reference to Exhibit 4.3 to ProMIS' Current Report on Form 8-K filed October 17, 2022).
4.4	Description of the Registrant's Securities (incorporated herein by reference to Exhibit 4.4 to ProMIS' Annual Report on Form 10-K filed March 8, 2023).
4.5	Form of Warrant. (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on August 22, 2023).
4.6	Form of Pre-Funded Warrant. (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on August 22, 2023).
10.1+	Joint Venture Agreement dated July 7, 2020 by and between ProMIS Neurosciences Inc. and BC Neuroimmunology Lab Inc. (incorporated herein by reference to Exhibit 10.1 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
10.2+	Joint Venture Agreement dated July 8, 2020 by and between ProMIS Neurosciences Inc. and BC Neuroimmunology Lab Inc. (incorporated herein by reference to Exhibit 10.2 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
10.3+	Collaborative Research Agreement by and between The University of British Columbia and Provincial Health Services Authority (on behalf of Children's & Women's Health Centre of British Columbia Branch, a public hospital) and ProMIS Neurosciences Inc. effective April 1, 2016. (incorporated herein by reference to Exhibit 10.3 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
10.3.1+	Amendment No. 1 dated February 13, 2017 to the Collaborative Research Agreement by and between The University of British Columbia and Provincial Health Services Authority (on behalf of Children's & Women's Health Centre of British Columbia Branch, a public hospital) and ProMIS Neurosciences Inc. (incorporated herein by reference to Exhibit 10.3.1 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
10.3.2+	Amendment No. 2 dated July 5, 2018 to the Collaborative Research Agreement by and between The University of British Columbia and Provincial Health Services Authority (on behalf of Children's & Women's Health Centre of British Columbia Branch, a public hospital) and ProMIS Neurosciences Inc. (incorporated herein by reference to Exhibit 10.3.2 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).



- 10.3.3+ Amendment No. 3 dated February 13, 2019 to the Collaborative Research Agreement by and between The University of British Columbia and Provincial Health Services Authority (on behalf of Children's & Women's Health Centre of British Columbia Branch, a public hospital) and ProMIS Neurosciences Inc. (incorporated herein by reference to Exhibit 10.3.3 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.3.4+ Amendment No. 4 dated September 9, 2019 to the Collaborative Research Agreement by and between The University of British Columbia and Provincial Health Services Authority (on behalf of Children's & Women's Health Centre of British Columbia Branch, a public hospital) and ProMIS Neurosciences Inc. (incorporated herein by reference to Exhibit 10.3.4 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.3.5+ Amendment No. 5 dated January 11, 2022 to the Collaborative Research Agreement by and between the University of British Columbia and Provincial Health Services Authority (on behalf of Children's & Women's Health Centre of British Columbia Branch, a public hospital) and ProMIS Neurosciences Inc.
- 10.3.6+ Memo dated November 24, 2021 confirming increase of ProMIS Neurosciences Inc. SRA with the University of British Columbia.
- 10.4+ Amended and Restated License Agreement dated October 6, 2015 by and between The University of British Columbia and ProMIS Neurosciences Inc. (incorporated herein by reference to Exhibit 10.4 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.5+ License Agreement dated August 3, 2006 by and between Amorfix Life Sciences Ltd. and an Affiliate of Biogen Idec Inc. (incorporated herein by reference to Exhibit 10.5 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.6+ Exclusive License Agreement dated July 14, 2010 by and between Amorfix Life Sciences Ltd. and Biogen Idec MA Inc. (incorporated herein by reference to Exhibit 10.6 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.7+ License Agreement dated April 4, 2006 by and between University Health Network and Amorfix Life Sciences Inc. (incorporated herein by reference to Exhibit 10.7 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.7.1 Amendment dated July 13, 2006 to the License Agreement dated April 4, 2006 by and between University Health Network and Amorfix Life Sciences Inc. (incorporated herein by reference to Exhibit 10.7.1 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.7.2+ Amendment No. 2 dated July 11, 2007 to the License Agreement dated April 4, 2006 by and between University Health Network and Amorfix Life Sciences Ltd. (incorporated herein by reference to Exhibit 10.7.2 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.7.3+ Amendment No. 3 dated November 4, 2013 to the License Agreement dated April 4, 2006 by and between University Health Network and Amorfix Life Sciences Ltd. (incorporated herein by reference to Exhibit 10.7.3 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.8†+ Consulting Agreement dated April 1, 2021 by and between Elliot Paul Goldstein, MD and ProMIS Neurosciences Inc. (incorporated herein by reference to Exhibit 10.8 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.8.1†+ Consulting Agreement dated October 1, 2021 by and between Elliot Goldstein, MD and ProMIS Neurosciences Inc. (incorporated herein by reference to Exhibit 10.8.1 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.9†+ Advisory Consulting Agreement dated May 26, 2021 by and between ProMIS Neurosciences Inc. and David Wishart. (incorporated herein by reference to Exhibit 10.9 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.10†+ Consulting and Advisory Agreement dated March 1, 2005 by and between Amorfix Life Sciences Ltd. and Neil Cashman. (incorporated herein by reference to Exhibit 10.10 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.11†+ Consulting Agreement dated June 29, 2015 by and between Amorfix Life Sciences Ltd. and Virtua, LLC. (incorporated herein by reference to Exhibit 10.11 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.12†+ Consulting Agreement dated October 17, 2016 by and between ProMIS Neurosciences Inc. and Danforth Advisors, LLC. (incorporated herein by reference to Exhibit 10.12 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.12.1†+ Amendment No. 1 dated March 27, 2017 to Consulting Agreement dated October 17, 2016 by and between ProMIS Neurosciences Inc. and Danforth Advisors, LLC. (incorporated herein by reference to Exhibit 10.12.1 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.12.2† Amendment No. 2 dated December 12, 2017 to Consulting Agreement dated October 17, 2016 by and between ProMIS Neurosciences Inc. and Danforth Advisors, LLC. (incorporated herein by reference to Exhibit 10.12.2 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).

- 10.12.3† Amendment No. 3 dated August 28, 2018 to Consulting Agreement dated October 17, 2016 by and between ProMIS Neurosciences Inc. and Danforth Advisors, LLC. (incorporated herein by reference to Exhibit 10.12.3 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.12.4†+ Amendment No. 4 dated March 27, 2017 to Consulting Agreement dated October 17, 2016 by and between ProMIS Neurosciences Inc. and Danforth Advisors, LLC. (incorporated herein by reference to Exhibit 10.12.4 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.13 Form of Finder's Warrant Certificate dated April 30, 2018. (incorporated herein by reference to Exhibit 10.13 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.14 Form of Non-US Warrant Certificate dated April 30, 2018. (incorporated herein by reference to Exhibit 10.14 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.15 Form of Employee Stock Option Commitment. (incorporated herein by reference to Exhibit 10.15 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.16+ Form of Unit Subscription Agreement for Non-U.S. Subscribers dated February 25, 2020. (incorporated herein by reference to Exhibit 10.16 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.17+ Form of Unit Subscription Agreement for Non-U.S. Subscribers dated June 17, 2019. (incorporated herein by reference to Exhibit 10.17 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.18+ Form of Unit Subscription Agreement for U.S. Subscribers dated November 27, 2018. (incorporated herein by reference to Exhibit 10.18 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.19+ Form of Unit Subscription Agreement for U.S. Subscribers dated October 21, 2019. (incorporated herein by reference to Exhibit 10.19 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.20+ Form of Unit Subscription Agreement for U.S. Subscribers dated April 13, 2018. (incorporated herein by reference to Exhibit 10.20 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.21+ Form of Unit Subscription Agreement for Non-U.S. Subscribers dated April 13, 2018. (incorporated herein by reference to Exhibit 10.21 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.22+ Form of Unit Subscription Agreement for Non-U.S. Subscribers dated November 27, 2018. (incorporated herein by reference to Exhibit 10.22 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.23+ Form of Unit Subscription Agreement for Non-U.S. Subscribers dated October 21, 2019. (incorporated herein by reference to Exhibit 10.23 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.24+ Form of Finder's Warrant Certificate dated November 2020. (incorporated herein by reference to Exhibit 10.24 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.25+ Form of Non-U.S. Finder's Warrant Certificate dated January 2019. (incorporated herein by reference to Exhibit 10.25 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.26+ Form of Non-U.S. Warrant Certificate dated January 2019. (incorporated herein by reference to Exhibit 10.26 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.27+ Form of Non-U.S. Warrant Certificate dated June 2019. (incorporated herein by reference to Exhibit 10.27 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.28+ Form of U.S. Warrant Certificate dated January 2019. (incorporated herein by reference to Exhibit 10.28 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.29+ Form of U.S. Warrant Certificate dated November 2020. (incorporated herein by reference to Exhibit 10.29 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.30 Form of Special Warrant Certificate dated November 4, 2020. (incorporated herein by reference to Exhibit 10.30 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.31 Form of U.S. Special Warrant Certificate dated November 4, 2020. (incorporated herein by reference to Exhibit 10.31 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.32+ Form of Warrant Certificate dated November 2020. (incorporated herein by reference to Exhibit 10.32 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.33+ Technology License Agreement dated February 1, 2006 by and between Dr. Neil Roy Cashman and Amorfix Life Sciences Ltd. (incorporated herein by reference to Exhibit 10.33 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.34+ Service Agreement dated September 1, 2020 by and between The University of Saskatchewan and ProMIS Neurosciences Inc. (incorporated herein by reference to Exhibit 10.34 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.35+ Assignment Agreement dated February 18, 2005 by and between Neil R. Cashman and Marty Lehto and the Governing Council of the University of Toronto and Amorfix Life Sciences Ltd. (incorporated herein by reference to Exhibit 10.35 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.35.1 Amendment Agreement dated April 1, 2005 to the Assignment Agreement dated February 18, 2005 by and between Neil R. Cashman and Marty Lehto and the Governing Council of the University of Toronto and Amorfix Life Sciences Ltd. (incorporated herein by reference to Exhibit 10.35.1 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).

- 10.36†+ Executive Employment Agreement of Eugene Williams dated December 31, 2021. (incorporated herein by reference to Exhibit 10.36 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.37†+ Executive Employment Agreement of Gavin Malenfant dated December 31, 2021. (incorporated herein by reference to Exhibit 10.37 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.38† ProMIS Neurosciences Inc. 2015 Stock Option Plan.
- 10.39† Amorfix Life Sciences Ltd. Deferred Share Unit Plan for Canadian Senior Officers. (incorporated herein by reference to Exhibit 10.39 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.40 Form of Non-U.S. Finder's Warrant Certificate dated November 2019. (incorporated herein by reference to Exhibit 10.40 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.41 Form of Non-U.S. Warrant Certificate dated November 2019. (incorporated herein by reference to Exhibit 10.41 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.42 Form of U.S. Warrant Certificate dated November 2019. (incorporated herein by reference to Exhibit 10.42 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.43 Form of Non-U.S. Warrant Certificate dated November 2020. (incorporated herein by reference to Exhibit 10.43 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.44 Form of Broker Warrant dated August 2021. (incorporated herein by reference to Exhibit 10.44 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.45 Form of Non-U.S. Warrant Certificate dated August 2021. (incorporated herein by reference to Exhibit 10.45 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.46 Form of U.S. Warrant Certificate dated August 2021. (incorporated herein by reference to Exhibit 10.46 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.47†+ Consulting Agreement dated April 1, 2022 by and between ProMIS Neurosciences Inc. and Larry Altstiel. (incorporated herein by reference to Exhibit 10.47 to ProMIS' Form 10 Registration Statement filed June 22, 2022, as amended).
- 10.48 Strategic Services Agreement, dated September 12, 2022, by and between ProMIS Neurosciences Inc. and Eugene Williams, effective September 19, 2022. (incorporated herein by reference to Exhibit 10.48 to ProMIS' Current Report on Form 8-K filed September 13, 2022).
- 10.49 Executive Employment Agreement of Gail Farfel dated September 12, 2022, effective September 19, 2022. (incorporated herein by reference to Exhibit 10.49 to ProMIS' Current Report on Form 8-K filed September 13, 2022).
- 10.50+ Unit Purchase Agreement by and between ProMIS Neurosciences Inc. and various investors (incorporated herein by reference to Exhibit 10.50 to ProMIS' Registration Statement on Form S-1 filed on November 1, 2022, as amended).
- 10.51 Registration Rights Agreement by and between ProMIS Neurosciences Inc. and various investors (incorporated herein by reference to Exhibit 10.51 to ProMIS' Registration Statement on Form S-1 filed on November 1, 2022, as amended).
- 10.52 Executive Employment Agreement of Neil Cashman dated January 21, 2022, effective February 1, 2022 (incorporated herein by reference to Exhibit 10.52 to ProMIS' Registration Statement on Form S-1 filed on November 1, 2022, as amended).
- 10.53 Amended and Restated Placement Agent Agreement, dated September 22, 2022, by and between ProMIS Neurosciences Inc. and Ceros Financial Services, Inc. (incorporated herein by reference to Exhibit 1.1 to ProMIS' Current Report on Form 8-K filed October 17, 2022).
- 10.54 Amendment No. 1 to Amended and Restated Placement Agent Agreement, dated October 5, 2022 by and between ProMIS Neurosciences Inc. and Ceros Financial Services, Inc. (incorporated herein by reference to Exhibit 1.2 to ProMIS' Current Report on Form 8-K filed October 17, 2022).
- 10.55 Form of Unit Purchase Agreement. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on August 22, 2023).
- 10.56 Form of Registration Rights Agreement. (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on August 22, 2023).
- 10.57 Share Exchange Agreement between the Company and holders of Series 1 Preferred Shares dated December 4, 2023. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on December 8, 2023).
- 10.58 Employment Agreement between ProMIS Neurosciences Inc. and Mr. Neil Warma, dated as of December 30, 2023. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on January 3, 2024).
- 10.59 At The Market Offering Agreement, January 5, 2024, by and between ProMIS Neurosciences, Inc. and BTIG, LLC. (incorporated by reference to Exhibit 1.1 to the Registrant's Current Report on Form 8-K, filed with the Securities and Exchange Commission on January 5, 2024).

16.1	Letter from PricewaterhouseCoopers LLP dated July 28, 2022 to the Securities and Exchange Commission regarding change in certifying accountant. (incorporated herein by reference to Exhibit 16.1 to ProMIS' Current Report on Form 8-K filed July 29, 2022).
21.1*	List of Subsidiaries of the Registrant
23.1*	Consent of Baker Tilly US, LLP, independent registered public accounting firm
31.1*	Certification of Chief Executive Officer Pursuant to Rule 13a-15(e) or Rule 15d-15(e)
31.2*	Certification of Chief Financial Officer Pursuant to Rule 13a-15(e) or Rule 15d-15(e)
32*	Certification of Chief Executive Officer and Chief Financial Officer of Periodic Report Pursuant to 18 U.S.C. Section 1350
97.1*	ProMIS Neurosciences Inc. Clawback Policy.
101.INS*	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document
101.SCH*	Inline XBRL Taxonomy Extension Schema Document
101.CAL*	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB*	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104*	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101*).

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† Management Contract or compensatory plan or arrangement.

+ Portions of this exhibit (indicated by asterisks) have been omitted pursuant to Item 601(b)(10) of Regulation S-K.

\* Filed herewith.



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## PROMIS NEUROSCIENCES INC. CORPORATE AND OTHER INFORMATION

### Board Of Directors

#### Eugene Williams

*Chairman of the Board of Directors and former Chief Executive Officer; Co-founder, of Virtua, LLC, a private biotechnology consulting firm*

#### Neil Warma

*Interim Chief Executive Officer and Director; Former President and CEO of Genexine, Inc.; Executive Chairman of Ridgeline Therapeutics; Director of TGM Biosciences*

#### Neil Cashman

*Chief Scientific Officer and Director; Professor, University of British Columbia; Canada Research Chair in Neurodegeneration and Protein Misfolding Diseases; Director, ALS Clinic Vancouver General*

#### Madge “Maggie” Shafmaster

*Director; Independent consultant*

#### William Wyman

*Director; Management consultant; Director of Allston Trading, a trading firm; Founder of Oliver Wyman, a management consulting firm*

#### Patrick Kirwin

*Director; Barrister & Solicitor; Founding partner of Kirwin LLP, Lawyers & Trademark Agents*

#### Josh Mandel-Brehm

*Director; President and Chief Executive Officer, CAMP4 Therapeutics Corporation; Entrepreneur Partner, Polaris Partners; Founder, Vico Therapeutics*

### Executive Officers

#### Neil Warma

*Interim Chief Executive Officer and Director; Former President and CEO of Genexine, Inc.; Executive Chairman of Ridgeline Therapeutics; Director of TGM Biosciences*

#### Daniel Geffken

*Chief Financial Officer; Co-founder of Danforth Advisors LLC and chief financial officer of various companies and on the board of directors of Windtree Therapeutics*

#### Neil Cashman

*Chief Scientific Officer and Director; Professor, University of British Columbia; Canada Research Chair in Neurodegeneration and Protein Misfolding Diseases; Director, ALS Clinic Vancouver General*

#### Gavin Malenfant

*Chief Operating Officer*

#### Larry Altstiel

*Chief Medical Officer*

#### Johanne Kaplan

*Chief Development Officer*

### Board Committees

*Audit Committee*

*Compensation Committee*

*Corporate Governance and Nominating Committee*

### Annual Meeting

The 2024 Annual Meeting Stockholders will be held online, on the day and time as set forth in the notice of the meeting, proxy statement and form of proxy that will be mailed to stockholders in advance of the meeting.

#### Investor Relations

[annemarie.fields@sternir.com](mailto:annemarie.fields@sternir.com)

#### Visit us on the Web

<https://www.promisneurosciences.com>

### Form 10-K Report

The Company's Annual Report on Form 10-K for the year ended December 31, 2023, as filed with the Securities and Exchange Commission, is printed as part of this Annual Report. Additional copies are available without charge upon written request to:

Attention: Investor Relations  
ProMIS Neurosciences Inc.  
Suite 200, 1920 Yonge Street  
Toronto, Ontario, Canada M4S 3E2

### Stock Exchange

ProMIS Neurosciences Inc.'s common shares are listed on Nasdaq Global Select Market under the trading symbol “PMN.”

#### Transfer Agent

Computershare Trust Company of Canada  
510 Burrard Street, 3rd Floor  
Vancouver, British Columbia V6C 3B9  
<https://www.computershare.com>