Risk Factors Comparison 2025-03-31 to 2024-04-01 Form: 10-K

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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~~ **approved** . ● We have concentrated a portion of our research and development efforts on the treatment of ~~AD~~ **Alzheimer' s Disease** , 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. ● **Clinical and** ~~Nonclinical~~ **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 ●..... 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~~ 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** . 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 **. ● 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** . 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~~ **able to obtain** , ~~with such laws~~ **or if there are delays in obtaining, required regulatory approvals** , we ~~could face substantial penalties~~ **will not be able to commercialize future product candidates, and our ability to generate revenue be materially impaired** . ● 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 ● **We are currently not in compliance with Nasdaq' s continued listing requirements. If we are unable to regain compliance with Nasdaq' s listing requirements, our Common Shares could be delisted, which could affect the market price of our Common Shares and liquidity and reduce our ability to raise capital. ●** 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~~ **are** 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. 4CAUTIONARY NOTE REGARDING FORWARD- LOOKING STATEMENTSThis 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 **; ● our efforts to maintain our listing on Nasdaq** ; ● 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; 5 ● 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. 6PART IItem 1. BusinessOverviewProMIS 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, FTLD, 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 TechnologyProMIS' 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 ProMISTM target epitope identification technology from the University of British Columbia (UBC) to predict novel DSEs on the molecular surface of misfolded proteins. ProMISTM 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 ProMISTM, 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 PipelineWe 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. ~~71~~ **7Arrows denote the stage of each program1** The ~~Company~~ **company** ~~may consider~~ **plans to investigate** additional synucleinopathies, including **PD:** Parkinson' s disease and **dementia with** Lewy **bodies** ~~Body dementia. * Arrows denote the stage of each programAdditional Development Programs 2 Initial~~ **2Initial** indication ~~* Arrows denote the stage of each programProMIS~~ **AD: Alzheimer' s disease, ALS: Amyotrophic lateral sclerosis, MSA: Multiple system atrophy, HD: Huntington' s disease, FTLD: Frontotemporal lobar degeneration, PSP: Progressive supranuclear palsy, CBD: Corticobasal degenerationProMIS** ' Objectives for ~~2024The~~ **2025The** Company plans to pursue the following key objectives for ~~2024~~ **2025** : ● ~~Complete the Phase 1a~~ **Advancing Clinical Development: Drive patient enrollment and** clinical **progress** ~~study with PMN310~~ in ~~Healthy Volunteers ● Prepare for~~ the **PRECISE- AD** Phase 1b **trial for** ~~clinical study with PMN310 in~~ Alzheimer' s ~~patients~~ **disease, maintaining rigorous execution and data integrity.** ● ~~Conduct further preclinical studies~~ **Strategic Growth and Corporate Visibility: Expand corporate awareness through targeted investor and industry engagement while actively evaluating partnership and business development opportunities to enhance the company' s pipeline. ● Operational Readiness for Future Success: Strengthen organizational infrastructure and capabilities** to support ~~pipeline candidates8PRODUCT~~ **potential clinical milestones and position the company for long- term growth. PRODUCT** CANDIDATESDevelopment of a Therapy for the Treatment of Alzheimer' s Disease (AD) AD OverviewAD, 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~~ **8During** ~~2023~~ **2024** , it was estimated there were 6. ~~7~~ **9** million Americans 65 and older living with AD, and that number is projected to rise to 12. 7 million by 2050 (www. alz. org, Alzheimer' s disease Facts and Figures ~~2023~~ **2024**). 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~~ **Three** mAbs (Aduhelm, Leqembi **, Kisunla**) were approved in 2021 ~~and - 2022~~ **2024 which creates a third category of marketed AD treatments, and the first to be considered disease modifying. Aduhelm was approved in 2021** under the U. S. Food and Drug Administration' s (~~the~~ FDA) Accelerated Approval pathway **but** ~~, which creates a third category of marketed AD treatments, and the first to be considered disease modifying. Commercialization~~ **commercialization** ~~of Aduhelm~~ was discontinued in January 2024 **. Leqembi and Kisunla received traditional approval in 2023 and 2024, respectively** . 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 Aβ in the pathogenesis of AD. Published genetic studies support a direct link between increased levels of Aβ and disease susceptibility. Research suggests that genetic mutations in the Aβ 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 Aβ and Aβ 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 Aβ deposits and often develop AD ~~9at~~ **at** a premature age (Podlisny et al, 1987). Aβ 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 Aβ deposit, while the APOE2 allele, which has been linked to a decreased risk, is associated with decreased Aβ 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 Aβ (Jonsson et al, 2012). In a preclinical study, it was reported that intracerebral injection of Aβ- containing brain extracts from human AD patients into susceptible mice induced cerebral amyloidosis and associated pathology. Depletion of Aβ from the extracts reversed this activity, supporting a link between Aβ and disease induction (Meyer- Luehmann et al, 2006). While the presence of Aβ 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 Aβ 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 Aβ 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~~ **9severity** and levels of soluble Aβ in the central nervous system was reported by Lue et al (Lue et al, 1999), and the direct neurotoxicity of soluble Aβ 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 Aβ, but not soluble monomers or plaque, was shown to induce synaptic damage and cognitive dysfunction (Cleary et al, 2005; Hong et al, 2016). Figure 1Synaptotoxicity of Ab oligomers on hippocampal neurons in vitro (Lacor et al, 2007, J Neuroscience) The mechanism by which soluble oligomeric Aβ 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 Aβ that adopt a β- sheet- rich conformation transmissible to native Aβ in a template- like manner. The self- propagation of these prion- like oligomers follows the stereotypical progression of AD, with initial involvement of the enthorhinal cortex followed by spreading to the hippocampus and neocortex as described by Khan et al (Khan et al, 2014). The prion- like spread of Aβ 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 " Aβ 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 Aβ oligomers therefore represents an attractive strategy to inhibit progression of the neurodegenerative Aβ- Tau cascade (Choi et al, 2015; Khan et al, 2014). ~~10PMN310ProMIS --~~ **PMN310ProMIS** ' lead therapeutic program is PMN310, a mAb designed to treat AD by selectively targeting the toxic misfolded form of Aβ. Based on the understanding of Aβ biology described above, PMN310 was designed to be more selective for the toxic oligomer of amyloid than other anti- Aβ 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 **treatment** ~~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 Aβ 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 AβO 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 Aβ have produced more promising results, including aducanumab ~~and~~ **(Aduhelm),** lecanemab

(Leqembi) and donanemab (Kisunla) , which ~~have both~~ received ~~Accelerated Approval~~ **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 Aβ 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~~ **10provide** an improved product profile with enhanced efficacy. ~~In July 2022, we presented results~~ **Results** ~~at the Alzheimers' Association International Conference~~ of our analysis of the binding response of Aβ- directed antibodies (aducanumab, lecanemab, donanemab, crenezumab, solanezumab **) were presented at the Alzheimers' s Association International Conference in July 2022 and published in 2024 (Kaplan et al, 2024, https: / / www. biorxiv. org / content / 10. 1101 / 2024. 04. 20. 590412v2**). All antibodies showed some binding signal to toxic AβO 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 Aβ- 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 AβO but not Aβ monomers or plaque. The use of AbO- restricted epitopes as the immunogen to generate antibodies is drastically different from the conventional immunization methods used by others. Immunization with Ab peptide or synthetic aggregates used by others to generate Ab- 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 AbO conformational epitopes displayed selectivity for Aβ oligomers vs monomers or plaque, and inhibited AβO 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 AβO and little or no binding to Aβ 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 AbO species suggesting that PMN310 can recognize an AβO epitope shared across AD brains. In vitro, PMN310 inhibited AβO propagation in a thioflavin- T (ThT) based assay measuring the formation of Aβ 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 AβO 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 AβO were co- delivered (mAb: AβO 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 AβO- induced neurotoxicity. Treatment groups consisted of day 0 ICV injection of vehicle alone, AβO alone, vehicle with PMN310 or AβO 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) ~~11and~~ -- **and** inflammation (TNF- α) markers were measured by ELISA in hippocampal homogenates from individual mice. AβO- 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 AβO was associated with inflammation and synaptic damage in the hippocampus, a region important in the development of memory. Hippocampal homogenates from AβO- treated mice displayed an increase in levels of TNF- α and decreases in PSD- 95 and SNAP25. Partial protection from these changes was observed in mice co- injected with synthetic AβO and PMN310. ~~Figure~~ **11Figure** 2Fig. 2. Administration of PMN310 to mice prevented the loss of short- term memory formation caused by toxic AβO. * $p < 0.05$ vs Vehicle, # $p < 0.05$ vs AβO. 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 Aβ 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 AβO 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). 12Figure 3Fig. 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 AβO may result in greater neutralization of this disease- causing species (no target distraction) compared with Aβ 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. **This premise is supported by preclinical toxicology studies in which weekly dosing of a murine IgG2a version of PMN310 in plaque- bearing knock- in APPSAA mice at 800 mg / kg for 26 weeks did not cause brain hemorrhages (ARIA- H) upon microscopic examination using Perls' Prussian Blue staining to detect the presence of hemosiderin (Kaplan et al, 2024, https: / / www. biorxiv. org / content / 10. 1101 / 2024. 04. 20. 590412v2).** The Company has conducted a ~~GLP~~ toxicology study **following Good Laboratory Practice (GLP) guidelines** in cynomolgus monkeys. PMN310 was administered as a 30- minute **intravenous (** 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 PlanThe Company successfully manufactured PMN310 clinical supply under cGMP conditions and received clearance on its **Investigational New Drug (** 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~~ **13volunteers** testing single intravenous doses of PMN310 escalating from 2. 5 to 40 mg / kg in 2- fold increments **(NCT06105528)** ~~, and potentially up to 60 mg / kg in adults~~. Each dosing cohort ~~consists~~ **consisted** of 6 drug-treated and 2 placebo- treated subjects. **Topline data on the first four cohorts were released in July 2024 and** ~~Results~~ **results** ~~of~~ **from all cohorts were presented at** the ~~Phase 1a trial~~ **Clinical Trials on Alzheimer' s Disease Alzheimer Congress in October 2024. PMN310 was** ~~will~~ **well - tolerated and there were no adverse events that precluded dose escalation. PMN310 crossed the blood brain barrier in a dose dependent manner with kinetics suggesting that monthly dosing can** provide **levels of PMN310 adequate for target engagement. The results informed** ~~a safety and tolerability assessment across a wide dose range and enable~~ dose selection for ~~a~~ **the** Phase 1b, multiple ~~13ascending~~ -- **ascending** dose (MAD) study in **patients with mild cognitive impairment due to** AD ~~patients. Assessment of PMN310 levels in CSF will also be leveraged to determine well- tolerated dose (s) that achieve concentrations required for~~ - **or** ~~target engagement~~ **early AD** . **Initiation** ~~Phase 1a data are expected in mid- 2024. Pending review by the FDA~~ of the ~~trial design, the planned~~ Phase 1b **PRECISE-** ~~MAD~~ - **AD** trial ~~will consist of two phases~~ **(NCT06750432) commenced in December 2024 and was announced in early January 2025** . ~~The first phase~~ **PRECISE- AD** is a **randomized,** ~~6- month~~ double- blind, placebo- controlled ~~monthly~~ **, MAD study of PMN310 to evaluate safety, tolerability, pharmacokinetics (PK), pharmacodynamics, and preliminary efficacy of multiple** intravenous ~~dosing~~ **infusions** of PMN310 in ~~the 5~~ **patients with early Alzheimer' s disease. The study will also evaluate key biomarkers and clinical measures of efficacy to gather data on PMN310' s therapeutic potential. The PRECISE** - **AD study plans to enroll** ~~40 mg / kg range with~~ approximately **100 subjects across 22 active sites in the United States. Eligible** ~~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 **dosed** ~~informed by results from the Phase 1a SAD study. The second phase is a 6- month~~ **monthly** ~~open label extension (OLE) phase~~ at **one of the** ~~the three~~ ~~same~~ dose levels **or placebo over 12 months with assessment of safety, tolerability, PK, and pharmacodynamic blood- and brain- based markers of treatment effect at baseline and every three months. Frequent MRI scans throughout the study will be conducted to monitor for emergence of ARIA** . 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 **is** ~~will be~~ powered to provide 95 % confidence for detection of ARIA. ~~Plasma and CSF~~ **The study has been designed with a sample size intended to provide sufficient power to provide meaningful insight into effects of PMN310 on** biomarkers **and clinical outcomes. PRECISE** ~~which have been reported to reflect treatment effects in the timeframe of the planned study (p~~ - **AD** ~~tau, GFAP, neurogranin, etc)~~ will be **the first study to examine the** ~~measured as early indicators of potential efficacy. Cognition endpoints will also be measured and could potentially reveal trends for a treatment effect~~ **effects** . ~~Subject to feedback from the FDA and securing the necessary capital, initiation~~ of ~~the Phase 1b trial is expected in 2H' 24~~ **a monoclonal antibody directed solely against AβO on biomarkers associated with AD pathology and clinical outcomes** . Development of a Therapy for the Treatment of Amyotrophic Lateral SclerosisALS OverviewAmyotrophic 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 FTLD, 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. ~~PMN267Using~~ **14PMN267Using** 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 FTLD 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). ~~14Figure~~ -- **Figure** 4Fig. 4. High affinity mAbs. In **Surface Plasmon Resonance (** 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 5Fig. 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~~ **15mAb** (green) shows co- localization with TDP- 43 aggregates with no staining of endogenous, normal TDP- 43 in the nucleus (nuclei stained blue). ~~15Figure~~ -- **Figure** 6Fig. 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 7Fig. 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). 16Figure 8Fig. 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 (dNLS) 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 FTLD individuals. Systemic IP delivery of PMN267 was tested in a transgenic mouse model of ALS / FTLD. In this model, doxycycline- regulated expression of human ΔNLS- TDP- 43 is under control of the neurofilament heavy chain promoter such that progression of disease is driven by intracellular expression of aggregating ΔNLS- 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 17humanized 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 OverviewMultiple 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. PMN442Multiple 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 918Fig. 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 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 10Fig. 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 11Fig. 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 SEM of two (A) or four (B) independent studies. 19In 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 12Fig. 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 SEM of 6 replicate cultures. BDNF was used as a positive control. # $p = 0.0004$ vs. CTL, * $p < 0.002$ vs. a- synO, * * $p < 0.003$ vs. a- synO. Figure 13Fig. 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 SEM of 6 replicate cultures. * $p < 0.02$ vs PFF. 20DEVELOPMENT PROGRAMSExpansion to Include Other Neurodegenerative and

Misfolded Protein DiseasesThe ProMIS discovery platform is being applied to other toxic misfolded proteins that drive disease including tau in AD, FTLD, 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 **and alpha- synuclein** discovery ~~program~~ **programs** to generate ~~a~~ vaccine ~~candidate~~ **candidates** that potentially could be used for prophylactic treatment of Alzheimer' s disease **and synucleinopathies, respectively** . 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 diseaseTauPropagation of misfolded, pathogenic aggregates of tau has also been implicated in the progression of AD and other tauopathies such as PSP, CBD, CTE, and FTLD- 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 1421Fig. 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 15Fig. 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. SchizophreniaDISC1 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. 22Amyotrophic Lateral SclerosisRACK1RACK1 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 AβO 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 AβO epitope of PMN310) in a vaccine configuration showed robust induction of antibodies selective for AβO with no binding to monomers or plaque. There was also no induction of a potentially deleterious T cell response as observed previously with other Ab vaccines. ProMIS performed studies to optimize adjuvant formulation and dosing regimen as well as to explore multivalent vaccine configurations containing additional AbO- restricted epitopes identified by the ProMIS discovery platform. Results from these studies ~~have been submitted for presentation~~ **showed that maximal reactivity with toxic oligomers from AD brain was achieved with immune IgG against conformational epitope 301 alone and that there was no advantage of including additional epitopes in the vaccine. These data were presented** at the 2024 Alzheimer' s Association International Conference. In previous studies reported in the literature, a first- generation vaccine consisting of aggregated human Aβ 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 Aβ vaccine gave rise to a pro- inflammatory Th1- type response against the same Aβ epitopes in the brain). The Company believes it can ~~avoid~~ **23avoid** this issue with a vaccine candidate consisting of its AβO B cell epitopes (no Aβ 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 ~~23to~~ **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 AβO 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' AβO 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 AβO 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 AβO 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 AβO- restricted conformational B cell epitopes conjugated to KLH for T cell help may successfully induce a protective antibody response against AβO without eliciting a potentially inflammatory Aβ- directed Th response. Characterization of immune sera from the mice also showed the desired antibody binding profile: selective binding to AβO compared to Aβ monomers as determined by SPR, and no binding to plaque in brain sections from AD patients as determined by IHC. 24Figure 16Fig. 16. Illustration of vaccine conceptFigure 17Fig. 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 **a lead candidate vaccine to** ~~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~~ **this** amyloid vaccine into preclinical development. 25Alpha- 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~~ **accepted** for presentation at the ~~2024 meeting of~~ **International Conference on Alzheimer' s and Parkinson' s Diseases and related neurological disorders (AD / PD) and at** the American Academy of Neurology (AAN) **conference** . ProMIS' Technology Platform and Intellectual Property PortfolioThe 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 AβOs, not the monomeric or plaque forms of Aβ. ProMIS has generated a portfolio of over 20 peptide antigens that have led to selective antibodies against toxic misfolded forms of Aβ for AD, a- syn for MSA and PD, tau for AD, FTLD, 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) PortfolioThe ProMIS IP program consists of a three- layered strategy. The first layer of protection comprises two computational algorithms, ProMISTM 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~~ **26epitopes** have been submitted and comprise the second layer of IP protection. Finally, the third layer of protection consists ~~26of~~ **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 PatentsLicense 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~~ **2024** , the Company has paid a total of C $ ~~225~~ **250** , 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 PatentsThe 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 Aβ ~~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 **- TDP- 43**), a patent family related to antisense molecules and biologics directed at RACK1 relevant in ALS and Huntington' s (ALS disease family **- RACK1**), **a PCT patent application related to ubiquitin ligase fusions directed to misfolded SOD1 targets relevant in ALS and related diseases (ALS disease family –**

SOD1) ~~and~~ **27and** a patent family related to immunogens and antibodies directed to a- ~~syn~~ **synuclein** targets relevant in PD, MSA, LBD and related diseases (PD family). ~~27The~~ -- **The** AD family includes patent families related to three Aβ epitope targets. The first Aβ epitope target patent family ~~,~~ includes several patent subfamilies and includes specifically ~~one~~ **three** issued and one allowed U. S. ~~patent~~ **patents**, four pending U. S. applications, ~~seven~~ **nineteen** issued or allowed foreign patents and ~~15~~ **eight** 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 country** and absent any disclaimers or extensions available. The second Aβ epitope target patent family includes ~~one~~ **two** issued U. S. ~~patent~~ **patents** ~~and one pending U. S. application~~, two issued foreign patents and five foreign pending **/ reinstatable** applications. Issued patents from this family are expected to expire in November 2036, absent any disclaimers or extensions available. The third Aβ epitope target patent family includes ~~one~~ **two** issued ~~and one allowed U. S. patent~~ **patents**, ~~one~~ **three** issued ~~and one allowed~~ foreign ~~patent~~ **patents** and ~~five~~ **four** foreign pending **/ reinstatable** 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 Aβ epitope target antibodies and an issued U. S. patent directed to combinations of the three Aβ 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 Aβ 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 **- TDP- 43** 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~~ **Patents that issue** from this family ~~are~~ **would be** expected to expire in December 2039 and April 2041, respectively, absent any disclaimers or extensions available. The ALS disease family **- SOD1** includes a patent family related to a SOD1 epitope target. The patent family includes a PCT application. ~~Issued patents~~ **Patents that issue** from this PCT application ~~are~~ **would be** 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~~ **Patents that issue** 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~~ **allowed U. S. patent, one soon to be filed** 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 PatentsWe 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~~ **March** ~~2024~~ **2026** and December 2026, absent any disclaimers or further extensions available. We also own ~~three~~ **a** U. S. ~~patents~~ **patent** related to SOD- 1 immunogens and / or antibodies **which is** ~~. Issued patents from this family are~~ expected to expire **March** ~~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 **and July 2034**, 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 **and to the timely payment of maintenance fees**. 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. ~~28In 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~~ **28For** 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 OverviewMarketsProMIS 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, FTLD, 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 MilestonesMarketing 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 RegulationsGovernment 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 CertificationAll 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 ProductsIn 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 ~~29regulations~~ **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~~ **29sanctions**. 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 DevelopmentProMIS' 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 ~~30and~~ **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~~ **30humans**, 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 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. ~~31Progress~~ -- **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~~ **31sponsor** 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 ApprovalAssuming 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. ~~32After~~ -- **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~~ **32preclinical** 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 ExclusivityUnder 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 ProgramsThe 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. ~~33A~~ **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~~ **33be** 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 ExclusivityUnder 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 ~~34granted~~ -- **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~~ **34the** 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 **for all formulations, dosage forms, and indications of the active moiety** 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 **, provided that at the time pediatric exclusivity is granted there is not less than nine months of term remaining** . Post- approval RequirementsDrugs 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~~ **35Once** 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 ~~35risks~~ -- **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 **. From time to time, legislation is drafted, introduced, passed in Congress and signed into law that could significantly change the statutory provisions governing the approval, manufacturing, and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations, guidance, and policies are often revised or reinterpreted by the agency in ways that may significantly affect the manner in which pharmaceutical products are regulated and marketed** . Companion DiagnosticsThe 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~~ **36other** 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~~ **a companion diagnostic may** 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 ExclusivityDepending 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, ~~36commonly~~ -- **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 ExclusivityCertain 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~~ **37A** 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 ~~37a~~ **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 RequirementsWe 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~~ **38laws** 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, ~~38including~~ **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~~ **39disgorgement** , 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, ~~39could~~ **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 RegulationThe 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 ReimbursementPrecision 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~~ **40countries** 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 ~~40product~~ -- **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 MeasuresThe 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 **(a requirement that was later replaced by the Part D Manufacturer Discount Program under the Inflation Reduction Act of 2022)** ; 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 **and subsequent legislation** , among other things, **resulted** ~~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~~ . ● **The** ~~On January 2, 2013, the~~ American Taxpayer Relief Act **of 2012** ~~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 41FDA 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~~ **included** 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~~ **41on** 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 **will have** 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~~ **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. **42Impact of a new U. S. administration on FDA and NIH policies: Changes in U. S. government administration and potential reforms to the FDA and NIH may adversely affect the regulatory environment and our business operations. The regulatory landscape for biotechnology and pharmaceutical companies is heavily influenced by policies set by the U. S. government, including the Food and Drug Administration (FDA) and the National Institutes of Health (NIH). With a new presidential administration taking office, there is a heightened risk of regulatory uncertainty, policy shifts, and potential reform efforts that could impact drug development, clinical trial oversight, and funding for biomedical research. Proposed changes to FDA approval processes, accelerated pathways, or regulatory requirements could result in delays, increased costs, or additional hurdles in advancing our clinical programs, including the PRECISE- AD Phase 1b trial in Alzheimer' s disease. Additionally, modifications to NIH funding priorities or grant allocations could impact broader research collaborations and the availability of scientific resources that support our programs. If the new administration enacts policies that slow down clinical trial approvals, alter market access dynamics, or introduce new compliance burdens, our ability to efficiently develop and commercialize our therapies could be adversely affected. We continue to monitor regulatory developments and engage with industry stakeholders to navigate potential challenges; however, there can be no assurance that future policy changes will not materially and negatively impact our business, financial condition, or results of operations.** Regulation Outside of the United StatesIn 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 ~~42approval --~~ **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 StrategiesProMIS 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~~ **43Generate** Product RevenuesRevenues, 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 AgreementsIn 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 RequirementsWhere 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. CompetitionHuman Healthcare Products CompetitionProMIS 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 ~~43to~~ **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~~ **from** 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 Aβ 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~~ **Bioge** ~~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 **lecanemab (Leqembi) and** ~~gantenerumab were announced in November 2022, while results from Phase 3 trials of~~ Lilly' s donanemab ~~were announced~~ **(Kisunla) received traditional approval** in ~~May~~ 2023 **and 2024, respectively** . 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 Aβ / 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, Alector, Inc., Anavex Life Sciences Corp., Annovis Bio, Inc., Athira Pharma, Inc., Biohaven Pharmaceuticals, Inc., Cassava Sciences, Inc., ~~Cortexyme~~ **44Cortexyme** , 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 ProtectionProMIS 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 **and RACK1** for ALS, toxic oligomers of Aβ 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 **disease- specific epitopes (** 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. ~~44Human~~ -- **Human** Capital ManagementProMIS seeks to hire

qualified scientists and key employees as needed. As of December 31, ~~2023~~ **2024** , the Company employed ~~six~~ **seven** 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 StructureProMIS 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~~ **45number** is (416) 847- 6898 and our website address is 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 InformationWe 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 ~~45SEC~~ -- **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 **. Investors and others should note that we announce material information to our investors using our investor relations website (https: / / www. promisneurosciences. com / investors), SEC filings, press releases, public conference calls and webcasts. We use these channels as well as social media, including LinkedIn and our Twitter (@ ProMISInc), to communicate with the public about our company, our business, our product candidates and other matters. It is possible that the information we post on social media could be deemed to be material information. Therefore, we encourage investors, the media, and others interested in our company to review the information we post on the social media channels listed on our investor relations website. Information that is contained in and can be accessed through our website or our social media posts are not incorporated into, and does not form a part of, this Annual Report on Form 10- K** . Item 1A. Risk FactorsInvestors 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~~ **46Risks** Related to the Development of Our Product CandidatesOur product candidates are still in the early stages of development and there is significant uncertainty that any such products will ~~actually~~ **ever** be ~~developed~~ **approved** . 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. ~~46If~~ **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~~ **47The** 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; ~~47~~ ● 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; **48** ● 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 AβO, or AβOs, to treat

AD. Our approach is based on research on AβOs, globular assemblies of the Aβ peptide that are distinct from other forms of amyloid. AβOs 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 AβOs. 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 ~~48approved --~~ **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~~ **49Nonclinical** 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 ~~49ability --~~ **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~~ **not** completed ~~a~~ **any pivotal** clinical trial or submitted a BLA. We are early in our development efforts for PMN310 and **we have only completed one Phase 1a clinical trial. We** 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~~ **50In** 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; ~~50~~ ● 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; **51** ● 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; ~~51~~ ● 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; **52** ● 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; ~~52~~ ● 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~~ **53Our** 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. ~~53We~~ **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~~ **54approval** . 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. **The FDA, EMA, and other comparable regulatory authorities have substantial discretion in the approval process and determining when or whether regulatory approval will be granted for any product candidate that we develop and may decide that our data are insufficient for approval or require additional preclinical, clinical, or other data. The U. S. Supreme Court' s July 2024 decision to overturn prior established case law giving deference to regulatory agencies' interpretations of ambiguous statutory language has introduced uncertainty regarding the extent to which FDA' s regulations, policies and decisions may become subject to increasing legal challenges, delays, and / or changes.** 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~~ **three** 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 **lecanemab (** Leqembi **) and Lilly' s donanemab** (~~lecabemab~~ **Kisunla**) ~~, also a mAb administered via infusion,~~ received ~~Accelerated~~ **traditional** ~~Approval~~ **approval in** ~~on January 6,~~ 2023 **and 2024, respectively** . We cannot be certain that our approach will lead to the development of approvable or marketable products. With the exception of ~~Aduhelm and~~ Leqembi **and Kisunla** , the only **available FDA- approved** 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~~ **(discontinued),** Leqembi **and Kisunla** 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 ~~54regulatory~~ -- **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~~ **55We** 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 ~~eGCP~~ **GCP** , 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. ~~55Further~~ -- **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~~ **56with** 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 **59Risks Related** to Our Financial Position and Capital NeedsWe 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 ~~operating losses of $ 16.8 million and~~ working capital of approximately $ ~~17~~ **4** . ~~0~~ **3** million as of December 31, ~~2024~~ **2023** .Management believes its **working capital position** ~~recurring losses from operations raise~~ **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, ~~2024~~ **2023** ,we had a deficit of $ ~~90~~ **93** . ~~7~~ **5** million.The cumulative deficit incurred from when we changed our name and focus in July 2015,through December 31, ~~2024~~ **2023** was $ ~~60~~ **63** . ~~4~~ **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 ~~57next --~~ **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~~ **60numerous** 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.** product candidates. Risks Related to the Commercialization of Our Product CandidatesSuccessful 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. ~~56There --~~ **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~~ **58product** 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; ~~57~~ ● 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~~ **59We** 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; ~~58~~ ● safe, effective and medically necessary; ● appropriate for the specific patient; ● cost- effective; and ● neither experimental nor investigational. ~~Even~~ **60Even** 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. 59Risks Related to Our Financial Position and..... develop and market additional product candidates. Risks Related to Our Dependence on Third PartiesWe 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~~ **61Should** 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 ~~61resources~~ **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~~ **62us** 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 ~~62closed~~ **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~~ **63no** 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; ~~63~~ ● 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; **64** ● 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 ~~64combinations~~ **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~~ **65Risks** Related to Our Intellectual PropertyIf 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; ~~65~~ ● 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; **66** ● 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 byU. 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; ~~66~~ ● 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~~ **or67** ● 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 ~~67business --~~ **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~~ **68Our** 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 Action 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; ~~68~~ ● 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~~ **69Obtaining** 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 ~~69change~~ **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~~ **70we** 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. ~~70We~~ **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~~ **71necessary** 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 ~~71technology~~ **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~~ **72to** 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; ~~72~~ ● 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; **73** ● 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~~ ~~73~~ -- **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~~ **74consider** 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 ~~74business~~ - **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~~ **75We** 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. ~~75Our~~ -- **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~~ **76a** 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 ~~76industry~~ -- **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~~ **77relating** 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. ~~77Intellectual~~ **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~~ **78government** 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 MattersOur 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 ~~78operations~~ **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~~ **79sanctions**, 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. **If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize future product candidates, and our ability to generate revenue will be materially impaired. In addition, we could be adversely affected by several significant administrative law cases decided by the U. S. Supreme Court in 2024. In Loper Bright Enterprises v. Raimondo, for example, the court overruled Chevron U. S. A., Inc. v. Natural Resources Defense Council, Inc., which for 40 years required federal courts to defer to permissible agency interpretations of statutes that are silent or ambiguous on a particular topic. The U. S. Supreme Court stripped federal agencies of this presumptive deference and held that courts must exercise their independent judgment when deciding whether an agency such as the FDA acted within its statutory authority under the Administrative Procedure Act (APA). Additionally, in Corner Post, Inc. v. Board of Governors of the Federal Reserve System, the court held that actions to challenge a federal regulation under the APA can be initiated within six years of the date of injury to the plaintiff, rather than the date the rule is finalized. The decision appears to give prospective plaintiffs a personal statute of limitations to challenge longstanding agency regulations. Another decision, Securities and Exchange Commission v. Jarkesy, overturned regulatory agencies' ability to impose civil penalties in administrative proceedings. These decisions could introduce additional uncertainty into the regulatory process and may result in additional legal challenges to actions taken by federal regulatory agencies, including the FDA and CMS, that we rely on. In addition to potential changes to regulations as a result of legal challenges, these decisions may result in increased regulatory uncertainty and delays and other impacts, any of which could adversely impact our business and operations. Further, our ability to develop and market new drug products may be impacted by litigation challenging the FDA' s approval of another company' s drug product. In April 2023, the U. S. District Court for the Northern District of Texas invalidated the approval by the FDA of mifepristone, a drug product which was originally approved in 2000 and whose distribution is governed by various measures adopted under a REMS. The Court of Appeals for the Fifth Circuit declined to order the removal of mifepristone from the market but did hold that plaintiffs were likely to prevail in their claim that changes allowing for expanded access of mifepristone, which the FDA authorized in 2016 and 2021, were arbitrary and capricious. In June 2024, the Supreme Court reversed that decision after unanimously finding that the plaintiffs (anti- abortion doctors and organizations) did not have standing to bring this legal action against the FDA. On October 11, 2024, the Attorneys General of three states (Missouri, Idaho and Kansas) filed an amended complaint in the district court in Texas challenging FDA' s actions. On January 16, 2025, the district court agreed to allow these states to file an amended complaint and continue to pursue this challenge. Depending on the outcome of this litigation, our ability to develop new drug product candidates and to maintain approval of existing drug products could be delayed, undermined or subject to protracted litigation. Finally, with the change in presidential administrations in 2025, there is substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA and other regulatory agencies with jurisdiction over our product candidates. The impending uncertainty could present new challenges or potential opportunities as we navigate the clinical development and approval process for our product candidates. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of that product candidate and could materially adversely impact our business and prospects.** ~~Even~~ **80Even** 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; ~~79~~ ● 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~~ **81Any** 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~~ **similarly comprehensive** privacy laws and regulations. For example, ~~in California~~ the California Consumer Privacy Act ~~of 2018~~, or CCPA, **as amended by the California Privacy Rights Act** gives California residents **certain** expanded rights **including** 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 **and limit sharing of sensitive personal information** . The CCPA ~~also~~ provides for civil penalties ~~for violations~~, as well as a private right of action for **certain** data breaches **which may** ~~that is expected to~~ increase ~~data breach~~ **the risk of** 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 **numerous other U. S. states with several** more **expected to pass in the coming years** ~~than a dozen U. S. states~~. Like the CCPA, these laws grant consumers rights in relation to their personal information and impose new **privacy and data security** obligations on regulated businesses, ~~including,~~ **which may vary** in ~~some instances~~ **their scope and application but unlike the CCPA** , ~~broader~~ **which also applies to personal information collected in the business- to- business and human resources contexts, to** ~~data~~ **date** ~~security requirements~~ **, the other state privacy laws are generally limited to personal information collected from consumers** . 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~~ **Actrequires** 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 ~~80impose~~ -- **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. **Regulators and legislators in the U. S. are increasingly scrutinizing and restricting certain personal data transfers and transactions involving ~~Foreign~~ foreign countries. For example, Executive Order 14117 of February 28, 2024, Preventing Access to Americans' Bulk Sensitive Personal Data and United States Government- Related Data by Countries of Concern as implemented by Department of Justice regulations issued in December 2024, prohibits data brokerage transactions involving certain sensitive personal data categories, including health data, genetic data, and biospecimens, to countries of concern, including China. The regulations also restrict certain investment agreements, employment agreements and vendor agreements involving such data and countries of concern, absent specified cybersecurity controls. Actual or alleged violations of these regulations may be punishable by criminal and / or civil sanctions, and may result in exclusion from participation in federal and state programsForeign** 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~~ **82EU** Member States, with respect to the European Economic Area (" EEA "), and the ~~UK~~ **U. K.** General Data Protection Regulation (the" ~~UK~~ **U. K.** GDPR," together with the EU GDPR the" GDPR") and the ~~UK~~ **U. K.** Data Protection Act 2018 with respect to the United Kingdom (" ~~UK~~ **U. K.** "). 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~~ **U. K.** , 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~~ **U. K.** 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~~ **U. K.** (" 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~~ **U. K.** International Data Transfer Agreement / Addendum (" ~~UK~~ **U. K.** IDTA")) are implemented. Where relying on the EU SCCs or ~~UK~~ **U. K.** 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~~ **U. K.** is regarded as a third country under the EU' s GDPR, the European Commission has issued an adequacy decision recognizing the ~~UK~~ **U. K.** as providing adequate protection under the EU GDPR and, therefore, transfers of personal data originating in the EEA to the ~~UK~~ **U. K.** remain unrestricted. Likewise, the ~~UK~~ **U. K.** government has confirmed that personal data transfers from the ~~UK~~ **U. K.** to the EEA remain free flowing. The ~~UK~~ **U. K.** government has introduced a Data ~~Protection~~ **(Use** and ~~Digital Information~~ **Access)** Bill (" ~~UK~~ **U. K.** Bill") into the ~~UK~~ **U. K.** legislative process. The aim of the ~~UK~~ **U. K.** Bill is to reform the ~~UK~~ **U. K.** ' s data protection regime following Brexit. If passed, the final version of the ~~UK~~ **U. K.** Bill may have the effect of further altering the similarities between the ~~UK~~ **U. K.** and EEA data protection regime and threaten the ~~UK~~ **U. K.** adequacy decision from the European Commission. The potential of the respective provisions and enforcement of the EU GDPR and ~~UK~~ **U. K.** GDPR further diverging in the future creates additional regulatory challenges and uncertainties for us. The lack of clarity on future ~~UK~~ **U. K.** 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~~ **U. K.** 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 ~~81If~~ **If** we are investigated by a European or ~~UK~~ **U. K.** data protection authority, we may face fines and other penalties, including bans on processing and transferring personal data. EEA and ~~UK~~ **U. K.** 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~~ **U. K.** 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~~ **83exercises** , 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 ") **has now** ~~— the world' s first comprehensive AI law — is anticipated to enter~~ **entered** into force ~~in 2024 and~~ **. This sweeping legislation** , with ~~some exceptions~~ **broad extraterritorial reach** , ~~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 **. Likewise, in the U. S., several states, including Colorado and California, passed laws that will take effect in 2026, to regulate various uses of artificial intelligence, including to make consequential decisions. In addition, various federal regulators have issued guidance and focused enforcement efforts on the use of AI in regulated sectors. The U. S. Food and Drug Administration, for example, issued guidance on the use of artificial intelligence in medical devices, requiring detailed risk management and review processes to obtain approvals. If we develop or use AI systems governed by these laws or regulations, we will need to meet higher standards of data quality, transparency, monitoring and human oversight, and we would need to adhere to specific and potentially burdensome and costly ethical, accountability, and administrative requirements, with the potential for significant enforcement or litigation in the event of any perceived non- compliance** . 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~~ **84Approval** 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 ~~82ability~~ - - **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~~ **85product** 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 ~~83bulk~~ -- **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 theU. 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~~ **86we** 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 ~~84commercialization~~ -- **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. Significant political, trade, regulatory developments, and other circumstances beyond our control, could have a material adverse effect on our financial condition or results of operations. We may in the future operate beyond the United States and, if approved, we may sell our products in countries throughout the world. Significant political, trade, or regulatory developments in the jurisdictions in which we may sell our products, such as those stemming from the change in U. S. federal administration, are difficult to predict and may have a material adverse effect on us. Similarly, changes in U. S. federal policy that affect the geopolitical landscape could give rise to circumstances outside our control that could have negative impacts on our business operations. For example, on February 1, 2025, the U. S. imposed a 25 % tariff on imports from Canada and Mexico, which were subsequently suspended for a period of one**

month, and a 10 % additional tariff on imports from China. Historically, tariffs have led to increased trade and political tensions. In response to tariffs, other countries have implemented retaliatory tariffs on U. S. goods. Political tensions as a result of trade policies could reduce trade volume, investment, technological exchange and other economic activities between major international economies, resulting in a material adverse effect on global economic conditions and the stability of global financial markets. Any changes in political, trade, regulatory, and economic conditions, including U. S. trade policies, could have a material adverse effect on our financial condition or results of operations. Risks Related to Our Business and IndustryWe 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 Aβ 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 ~~Aeeelerated~~ **traditional** ~~Approval~~ **approval** from FDA in ~~January~~ 2023 **, and donanemab (Kisunla) from Lilly received approval in 2024** . Other companies known to be developing therapies with Aβ / 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, Alector, 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~~ **87the** 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 ~~85addition --~~ **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; **88** ● 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. ~~86If~~ **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~~ **89Risks** Related to Ownership of Our Common Shares and Our Status as a U. S. Public ~~CompanyInvestment~~ **CompanyWe are currently not in compliance with Nasdaq' s continued listing requirements. If we are unable to regain compliance with Nasdaq' s listing requirements, our Common Shares could be delisted, which could affect the market price of our Common Shares and liquidity and reduce our ability to raise capital. 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. On July 2, 2024, we received written notice from Nasdaq stating that we were not in compliance with Nasdaq Listing Rule 5550 (b) (2) because we had not maintained a minimum Market Value of Listed Securities of at least $ 35 million for the preceding 30 consecutive business days. We subsequently regained compliance as of July 29, 2024. On January 3, 2025, we received a letter from Nasdaq notifying us that we were no longer in compliance with the $ 1. 00 minimum bid price requirement (the " Bid Price Rule ") for continued listing on Nasdaq under Nasdaq Listing Rule 5550 (a) (2). Although Nasdaq has granted us 180 calendar days, or until July 2, 2025, to regain compliance with the Bid Price Rule, there can be no assurance that we will regain such compliance and Nasdaq could make a determination to delist our Common Shares. If we are not deemed in compliance with the Bid Price Rule before the expiration of the 180- day compliance period, we may be afforded an additional 180- day compliance period. If necessary to regain compliance with Nasdaq listing standards, we may, subject to approval of our board of directors and stockholders, implement a reverse stock split. However, there can be no assurance that a reverse stock split, or any other alternatives we may consider to regain compliance with the minimum bid price requirement, would be approved or would result in a sustained higher stock price that would allow us to meet the Nasdaq stock price listing requirements, and such reverse stock split may limit our ability to conduct subsequent measures to meet Nasdaq listing criteria in accordance with the new Nasdaq rules. 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. While a listing on an over- the- counter exchange could maintain some degree of a market in our Common Shares, we could face substantial material adverse consequences, including, but not limited to, the following: limited availability for market quotations for our Common Shares; reduced liquidity with respect to and decreased trading prices of our Common Shares; a determination that shares of our Common Shares are " penny stock " under the SEC rules, subjecting brokers trading our Common Shares to more stringent rules on disclosure and the class of investors to which the broker may sell the Common Shares; limited news and analyst coverage for our Company, in part due to the " penny stock " rules; decreased ability to issue additional securities or obtain additional financing in the future; and potential breaches under or terminations of our agreements with current or prospective large stockholders, strategic investors and banks. The perception among investors that we are at heightened risk of delisting could also negatively affect the market price of our securities and trading volume of our common stock. If compliance is regained, 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. 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~~ **90investment** . 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~~ **2024** , 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~~ **48** . 4 % of our outstanding Common Shares. As a result, these persons, acting together, would be able to significantly ~~87influence~~ -- **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 **, including the rules applicable to us if our public float as of a measuring date preceding the Annual Report is less than $ 75 million, which rules we are currently subject to** . 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~~ **91Our** 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 2 / 3 % 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; ~~88~~ ● 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; **92** ● 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 ~~89of~~ **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~~ **are** 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~~ **93result** 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 FactorsWe 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 ~~90corporate~~ **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~~ **94services** 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, ~~91including~~ **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~~ **95of** 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. ~~92Comprehensive~~ **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. **The U. S. Congress, the Trump administration, or any new administration may make substantial changes to fiscal, tax, and other federal policies that may adversely affect our business In 2017, the U. S. Congress and the Trump administration made substantial changes to U. S. policies, which included comprehensive corporate and individual tax reform. In addition, the Trump administration called for significant changes to U. S. trade, healthcare, immigration and government regulatory policy. Since the start of the Trump Administration in 2025, U. S. policy changes have been implemented at a rapid pace and additional changes are likely. Changes to U. S. policy implemented by the U. S. Congress, the Trump administration or any new administration have impacted and may in the future impact, among other things, the U. S. and global economy, international trade relations, unemployment, immigration, healthcare, taxation, the U. S. regulatory environment, inflation and other areas. Although we cannot predict the impact, if any, of these changes to our business, they could adversely affect our business. Until we know what policy changes are made, whether those policy changes are challenged and subsequently upheld by the court system and how those changes 96impact our business and the business of our competitors over the long term, we will not know if, overall, we will benefit from them or be negatively affected by them.** 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~~ **2023** taxable year and do not expect to have been a PFIC for the ~~2023~~ **2024** 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 93Common 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 **posture** or a natural disaster. Despite the implementation of security measures, our internal computer systems, and those of third parties on which we rely **, we, like others in our industry, have experienced and expect to continue to experience cybersecurity incidents related to our infrastructure. We, like other organizations** , 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. **97** ~~. 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. 94~~