Risk Factors Comparison 2025-03-13 to 2024-03-14 Form: 10-K

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Below is a summary of the principal factors that make an investment in our securities speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factors summary, and other risks that we face, can be found in Part I, Item 1A " Risk Factors " and should be carefully considered, together with other information in this Annual Report and our other filings with the SEC before making investment decisions regarding our securities. Investing in our securities involves substantial risk. The risks described under Part I, Item 1A " Risk Factors " of this Annual Report may cause us to not realize the full benefits of our strengths or may cause us to be unable to successfully execute all or part of our strategy. Some of the more significant risks we face include the following: • We may encounter substantial delays and other challenges in our ongoing or planned clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities; • If we are unable to successfully complete or otherwise advance clinical development, obtain regulatory or marketing approval for, or successfully commercialize our therapeutic product candidates, including efzofitimod, or experience significant delays in doing so, our business will be materially harmed; • There is no established FDA regulatory pathway for approval of a drug in pulmonary sarcoidosis. As a result, our Phase 3 randomized, double- blind, placebo- controlled clinical trial to evaluate the efficacy and safety of efzofitimod in patients with pulmonary sarcoidosis (the EFZO- FIT study), even if successful, may not be sufficient to support FDA approval, which would materially and adversely harm our business **; • We may face contracted development and manufacturing organization (CDMO) manufacturing stoppages and other CDMO challenges associated with the clinical or commercial manufacture of our product candidates** ; • Our current product candidates and any other product candidates that we may develop from our discovery platform represent novel therapeutic approaches, which may cause significant delays or may not result in any commercially viable drugs; • Our therapeutic product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any; • We will need to raise additional capital or enter into strategic partnering relationships to fund our operations; • We are a pre- commercial biotherapeutics company and have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; • We depend on our existing collaborations and may depend on collaborations with additional third parties for the development and commercialization of certain of our product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates; • If we are unable to obtain, maintain or protect intellectual property rights related to our product candidates, or if the scope of such intellectual property protection is not sufficiently broad, we may not be able to compete effectively in our markets; • Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel; • Unfavorable macroeconomic conditions could adversely affect our business, financial condition or results of operations; and • The market price of our common stock historically has been highly volatile and is likely to continue to be volatile, and you could lose all or part of your investment. PART I Item 1. Business. We are a clinical stage biotechnology company leveraging evolutionary intelligence to translate tRNA synthetase biology into new therapies for fibrosis and inflammation. tRNA synthetases are ancient, essential proteins that have evolved novel domains that regulate diverse pathways extracellularly in humans. Our discovery platform is focused on unlocking hidden therapeutic intervention points by uncovering signaling pathways driven by our proprietary library of domains derived from all 20 tRNA synthetases. Efzofitimod Our lead therapeutic candidate is efzofitimod, a first- in- class biologic immunomodulator in clinical development for the treatment of interstitial lung disease (ILD), a group of immune- mediated disorders that can cause inflammation and fibrosis, or scarring, of the lungs. Efzofitimod is a tRNA synthetase derived therapy that selectively modulates activated myeloid cells through neuropilin- 2 (NRP2) to resolve aberrant inflammation without immune suppression and potentially prevent the progression of fibrosis. ILDs are predominantly immune- mediated disorders that are characterized by chronic inflammation, which can lead to progressive fibrosis of the lung. There are limited treatment options for ILD and there remains a high unmet medical need. Sarcoidosis and systemic sclerosis (SSc, also known as scleroderma)- associated ILD (SSc- ILD) are two major forms of ILD. The U. S. Food and Drug Administration (FDA) has granted efzofitimod orphan drug designations for the treatment of sarcoidosis and for the treatment of SSc, and Fast Track designations for the treatment of pulmonary sarcoidosis and for the treatment of SSc- ILD. The European Commission (EC) has granted efzofitimod orphan drug designations for the treatment of sarcoidosis and for the treatment of SSc, based on the opinion of the European Medicines Agency (EMA) Committee for Orphan Medicinal Products (COMP). **The Pharmaceutical and Medical Devices Agency (PMDA) has granted efzofitimod orphan drug designation for the treatment of sarcoidosis to Kyorin Pharmaceutical Co., Ltd. (Kyorin), our partner in Japan.** In September 2021, we announced positive results and clinical proof- of- concept from a double- blind, placebo- controlled Phase 1b / 2a clinical trial in 37 patients with pulmonary sarcoidosis. The study was designed to evaluate the safety, tolerability, immunogenicity and preliminary efficacy of three doses of intravenous (IV) efzofitimod, 1. 0, 3. 0 and 5. 0 mg / kg, in the context of a forced steroid taper. Efzofitimod was safe and well- tolerated at all doses administered with no serious drug- related adverse events or signal of immunogenicity. Additionally, the study demonstrated consistent dose response for efzofitimod on key efficacy endpoints and improvements compared to placebo, including measures of steroid reduction, lung function, pulmonary sarcoidosis symptom measures and inflammatory biomarkers. These data were subsequently presented at the American Thoracic Society (ATS) International Conference and published in the peer- reviewed journal CHEST during 2022. In **October 2024, the same published data for efzofitimod was**

featured in the Best of CHEST Journals session at the CHEST 2024 Annual Meeting. In February 2022, we met with the FDA in an end- of- Phase 2 meeting to discuss our plans for subsequent clinical development and path to registration for efzofitimod for pulmonary sarcoidosis. Subsequently, we initiated a global pivotal Phase 3 randomized, double- blind, placebo- controlled clinical trial to evaluate the efficacy and safety of efzofitimod in patients with pulmonary sarcoidosis (the EFZO- FIT study). The EFZO- FIT study is a 52- week study consisting of three parallel cohorts randomized equally to either 3. 0 mg / kg or 5. 0 mg / kg of efzofitimod or placebo dosed intravenously once a month for a total of 12 doses. ~~The~~ **We expected the** study ~~is currently enrolling and intends~~ to enroll up to 264 subjects with pulmonary sarcoidosis at multiple centers in the United States, Europe, Brazil, and Japan. The study design incorporates a forced steroid taper. The objective of the study is to evaluate the efficacy and safety of efzofitimod in patients with pulmonary sarcoidosis. The primary endpoint of the study is steroid reduction. Secondary endpoints include measures of lung function assessed by forced vital capacity (FVC) and health- related quality of life assessments and questionnaires (KSQ lung score). In September 2022, we dosed the first patient in ~~this~~ **the** study. ~~Additionally, during~~ **During** 2023 **and 2024** , we **have** had ~~a~~ data and safety monitoring board (DSMB) ~~review~~ **reviews** of our EFZO- FIT study. The DSMB **reviews** concluded that the study could continue unmodified. ~~We expect to~~ **In July 2024, we** ~~complete~~ **completed** enrollment ~~in~~ **of 268 patients, exceeding target enrollment. Topline data from** the study **are anticipated** in the ~~second~~ **third** quarter of ~~2024~~ **2025** . In February 2024, we announced an Individual Patient Expanded Access Program (**Individual Patient** EAP). The Individual Patient EAP has been initiated based on blinded EFZO- FIT study investigator and patient participant feedback. The program is designed to allow access for patients who complete the Phase 3 EFZO- FIT study and wish to receive treatment with efzofitimod outside of the clinical trial. The administration of efzofitimod as part of the Individual Patient EAP will occur independent of the EFZO- FIT study protocol, and we, principal investigators and patients will remain blinded to the treatment that occurred as part of the EFZO- FIT study. As this Individual Patient EAP will occur independent of the EFZO- FIT study, this program is not an open- label extension (OLE) and no long- term data will be collected by us. Based on the results of the Phase 1b / 2a clinical trial, we believe efzofitimod has potential applications in the treatment of other ILDs, such as chronic hypersensitivity pneumonitis (CHP) and connective tissue disease related ILD (CTD- ILD), including SSc- ILD and rheumatoid arthritis- associated ILD. As such, we designed a focused Phase 2 proof- of- concept clinical trial of efzofitimod (the EFZO- CONNECT study) in patients with SSc- ILD. The EFZO- CONNECT study is a randomized, double- blind placebo- controlled proof- of- concept study to evaluate the efficacy, safety and tolerability of efzofitimod in patients with SSc- ILD. This is a 28- week study with three parallel cohorts randomized 2: 2: 1 to either 270 mg or 450 mg of efzofitimod or placebo dosed intravenously monthly for a total of six doses. The study intends to enroll up to 25 patients at multiple centers in the United States. The objective of the study is to evaluate the efficacy of multiple doses of IV efzofitimod on pulmonary, cutaneous **(limited or diffuse)** and systemic manifestations in patients with SSc- ILD. The primary endpoint is reduction in FVC. Secondary endpoints include certain measures regarding safety and tolerability. ~~The~~ **In July 2024, we amended the** study ~~was initiated in~~ **to add an OLE to patients. Patients who complete** the ~~third~~ **study and wish to receive ongoing treatment with efzofitimod are eligible to participate in the 24- week OLE. Based on current enrollment projections, we expect to report interim data from the study in the second** quarter of ~~2023~~ **2025** ~~, and in October 2023, we dosed the first patient in this study~~ . In January 2020, we entered into a collaboration and license agreement (Kyorin Agreement) with Kyorin ~~Pharmaceutical Co., Ltd. (Kyorin)~~ for the development and commercialization of efzofitimod for the treatment of ILD in Japan. Under **the terms of** the Kyorin Agreement, Kyorin received ~~an~~ exclusive ~~right~~ **rights** to develop and commercialize efzofitimod in Japan for all forms of ILD, and is obligated to fund all research, development, regulatory, marketing and commercialization activities in Japan **. We are responsible for supplying all drug product for Japan, as well as supporting development activities for efzofitimod** . In 2020, Kyorin conducted and funded a Phase 1 clinical trial of efzofitimod (known as KRP- R120 in Japan). The Phase 1 clinical trial was a placebo- controlled clinical trial to evaluate the safety, pharmacokinetics (PK) and immunogenicity of efzofitimod in 32 healthy Japanese male volunteers. Efzofitimod was observed to be generally well- tolerated with no drug- related serious adverse events, and PK findings were consistent with previous studies of efzofitimod. Kyorin is also participating in the EFZO- FIT study as the local sponsor in Japan. In February 2023, Kyorin dosed the first patient in Japan in the EFZO- FIT study which triggered a $ 10. 0 million milestone payment to us. To date, the Kyorin Agreement has generated $ 20. 0 million in upfront and milestone payments to us and we are eligible to receive up to an additional $ 155. 0 million in the aggregate upon achievement of certain development, regulatory and sales milestones, as well as tiered royalties on any net sales in Japan. Discovery Platform Using efzofitimod as a model, we have developed a process to advance novel tRNA synthetase domains from a concept to therapeutic candidate. This process leverages our early discovery work as well as current scientific understanding of tRNA synthetase evolution, protein structure, gene splicing and tissue- specific regulation to identify potentially active protein domains. Screening approaches are employed to identify target cells and extracellular receptors for these tRNA synthetase- derived proteins. These cellular systems can then be used in mechanism- of- action studies to elucidate the role these proteins play in cellular responses and their potential therapeutic utility. We are working to identify new tRNA synthetase based drug candidates through our internal discovery efforts and external collaboration efforts. Therapeutic Candidate Pipeline Strategy Key elements of our strategy include the following: Advance efzofitimod toward regulatory approval in pulmonary sarcoidosis. Based on the positive results and clinical proof- of- concept from our efzofitimod Phase 1b / 2a clinical trial in September 2021, we believe we can expedite development of efzofitimod for pulmonary sarcoidosis toward regulatory approval. ~~During~~ **In July 2024, we completed enrollment of the EFZO- FIT study. Topline data from the EFZO- FIT study are anticipated in** the third quarter of ~~2022~~ **2025** , ~~we initiated~~ **and our strategy for the advancement of efzofitimod includes submitting data from** the EFZO- FIT study **to the FDA** , **which we expect to serve as the basis for U. S. regulatory approval. Transition from** a ~~global pivotal Phase 3 randomized, double- blind, placebo- controlled~~ clinical ~~trial~~ **stage biotech** to ~~evaluate~~ **a commercial pharmaceutical company. We anticipate that positive topline data from** the ~~efficacy and safety~~ **EFZO- FIT study could be a significant catalyst for**

potential future commercial development of efzofitimod ~~in~~ **for** patients with pulmonary sarcoidosis. ~~Our strategy for~~ **We have begun pre- commercialization efforts in the U. S. market and intend to expand** ~~the~~ **these** ~~advancement of efzofitimod includes completing the EFZO~~ **efforts with positive topline data. We are focusing our pre** - ~~FIT study which we expect will serve as the basis for regulatory approval~~ **commercialization efforts in marketing, commercial operations and commercial supply, including general and administrative support** . Develop efzofitimod to address unmet medical needs in other ILDs. In addition, we believe the positive results from our efzofitimod Phase 1b / 2a clinical trial, as well as data from numerous preclinical studies we have conducted to date, will give us the opportunity to potentially launch additional ~~Phase 2~~ clinical trials of efzofitimod in other forms of ILD. As part of this strategy, we **have** initiated **and progressed** the EFZO- CONNECT study of efzofitimod in patients with SSc- ILD ~~and dosed the first patient in this study in October 2023~~ . Build a diverse pipeline of biologics product candidates based on our understanding of extracellular tRNA synthetase biology. Utilizing our unique drug discovery approach through internal research efforts and external collaboration efforts, we intend to continue to advance novel tRNA synthetase domains from concept to product candidates in the areas of fibrosis and inflammation. We have advanced two ~~additional~~ tRNA synthetase programs, ATYR0101 and ATYR0750, into preclinical development. We plan to further elucidate the therapeutic potential of these candidates through mechanistic investigations, including in vitro and in vivo preclinical studies. Background and Mechanism of Action Efzofitimod is a novel immunomodulatory Fc fusion protein in development for the treatment of ILD. Efzofitimod is a selective modulator of NRP2 that downregulates innate immune responses at a cellular level in uncontrolled inflammatory disease states to resolve chronic inflammation and prevent subsequent fibrosis. Efzofitimod is a novel molecular entity comprised of a human 59 amino acid protein fused to the Fc region of human immunoglobulin 1 (IgG1). It acts as an extracellular immunomodulator. The amino acid sequence of the active moiety corresponds identically to the extracellularly active immunomodulatory domain of histidyl- tRNA synthetase (HARS) amino acids 2 to 60 (HARS 2- 60). The gene for HARS gives rise to a number of splice variants, and though most of these have lost their catalytic activity, they all retain the N- terminal domain (HARS amino acids 1- 60). This N- terminal domain, non- essential for the enzyme' s protein synthesis activity that is required in all living organisms, was appended to HARS during the evolutionary development of multicellular organisms and retained with high sequence identity across mammalian species, but is not found in lower organisms. One splice variant (SV9), which encodes only the N- terminal domain of the protein, is enriched in human lung tissue. Expression of this HARS splice variant is increased following inflammatory cytokine stimulation (interferon gamma (IFN- g) and TNF alpha (TNF- a), two key players in the initiation of lung inflammation and fibrosis) followed by subsequent secretion, indicating it is being regulated in response to local inflammation. Furthermore, HARS, specifically the N- terminal domain, is targeted by autoantibodies in a rare autoimmune disorder (known as anti- Jo- 1 syndrome). Anti- Jo- 1 syndrome is characterized by extensive activation and migration of immune cells into lung and muscle and is classically associated with the triad of ILD, myositis, and arthritis. It is hypothesized that the sequestration of HARS may play a causal role through disruption of its homeostatic immune- regulatory effects. NRP2 was identified as the sole binding partner for efzofitimod through screening via a cell microarray system in which over 4, 500 cell surface proteins are represented. This screening approach identified two NRP2 isoforms (Neuropilin 2A and 2B) as the only convincing and specific binding partners of efzofitimod. The binding site was confirmed to be within the " turn " of the helix- turn- helix structure of the HARS N- terminal domain comprised within efzofitimod. Binding of efzofitimod is specific to NRP2 with no observable cross- reactivity to NRP1, which is the most closely related cell surface receptor in both protein sequence and structure. A domain that is structurally similar (but divergent in protein sequence) to the HARS N- terminal domain (termed the WHEP domain) is found in other amino- acyl tRNA synthetases, yet these domains do not exhibit binding to NRP2, indicating this is a highly specific interaction. Interestingly, binding of efzofitimod occurs in a manner distinct from the more well- characterized ligands of NRP2 including VEGF and semaphorin 3F (SEMA3F), and does not interfere with NRP2 dimerization with their co- receptors. Thus, the HARS N- terminus appears to be a newly discovered ligand for NRP2, as opposed to an antagonist. The discovery of the HARS N- terminus / NRP2 signaling axis represents a previously unknown mechanism of biological regulation, in which this novel ligand of NRP2 may act as a homeostatic regulator of aberrant immune responses. NRP2 is a cell surface receptor that is present on multiple immune cell types, including certain myeloid cells and subsets of T- cells. NRP2 expression is often upregulated upon inflammatory insult or stimulation. Growing evidence indicates that NRP2 predominantly influences myeloid cell biology such as activation and recruitment to inflammatory sites. For instance, NRP2 expression on alveolar macrophages regulates airway inflammatory responses to inhaled lipopolysaccharide. In sarcoidosis, NRP2 expression has been shown to be localized within the sarcoid granulomas, highly expressed in Langhans giant cells which are myeloid in nature. Efzofitimod has been shown to significantly reduce lung inflammation and fibrosis, reduce immune cell trafficking to the lung and improve respiratory function parameters in multiple animal models of lung fibrosis. Furthermore, efzofitimod has demonstrated consistent downregulatory effects on inflammatory and pro- fibrotic cytokines and chemokines in both animal disease models and human clinical trials. Efzofitimod appears to primarily impact interleukin- 6 (IL- 6), TNF- ?, IFN- ?, MCP- 1 and IP- 10, markers that have been implicated in the pathology of ILD. Preclinical Development Our preclinical estate of translational animal models was selected to help inform and de- risk clinical development of efzofitimod. We have evaluated the biological activity and safety of efzofitimod across a diverse set of experimental fibrotic lung disease models, representative of the four major forms of ILD (sarcoidosis, CHP, CTD- ILD and idiopathic pulmonary fibrosis (IPF)), as well as in normal animals, looking for signals of activity and potential biomarkers, while confirming tolerability and a favorable safety profile. In these models, efzofitimod has significantly reduced histological lung fibrosis and inflammation, restored normal lung function, reduced lung protein levels of several inflammation and fibrosis- related cytokines and chemokines (e. g. IFN- γ, MCP- 1 / CCL2, IL- 6) and reduced counts of immune cells in bronchoalveolar lavage (BAL) central to ILD pathology (e. g., neutrophils). These data have been presented in posters at key respiratory conferences over the past several years (e. g. the ATS International Congress) and are available for review on our website. Efzofitimod and NRP2 receptor NRP2 is known to be expressed on a number of different immune cell

types that play a key role in regulating inflammatory responses. Efzofitimod is a fusion protein combining a novel immunomodulatory domain from HARS and a human IgG1 Fc. Efzofitimod inhibits cytokines and chemokines involved in the regulation of inflammatory and fibrotic responses and reduces inflammation and fibrosis in animal models of ILD. Efzofitimod has previously demonstrated potent immunomodulatory activity in vitro and in vivo. We sought to characterize the molecular basis for efzofitimod' s immunomodulatory properties and demonstrated that efzofitimod specifically and selectively binds to NRP2 on the cell surface. These findings indicate that modulation of the NRP2 signaling pathway with efzofitimod could be a novel therapeutic approach to immune- mediated and fibrotic diseases such as pulmonary sarcoidosis. Sarcoidosis is characterized by the formulation of granulomas, clumps of inflammatory cells found in one or more organs of the body and denoted by the presence of Langhans giant cells which are myeloid in nature. NRP2 was shown to be expressed in samples obtained from lung and skin of sarcoidosis patients with high NRP2 expression detected on key immune cells known to play an important role in inflammation and granuloma formation, including the Langhans giant cells. In work carried out in collaboration with Dr. Elliot Crouser' s laboratory at The Ohio State University utilizing an established ex vivo assay of granuloma formation, it was demonstrated that an efzofitimod analog containing the identical immunomodulatory HARS domain exhibited statistically significant reduction of granuloma formation generated from sarcoid peripheral blood mononuclear cells (PBMCs). Given the importance of granulomas in the pathology and progression of pulmonary sarcoidosis and the known ability of efzofitimod to disrupt inflammatory responses, we hypothesize that efzofitimod may play a role in regulating sarcoid granuloma formation. These findings highlight the potential of efzofitimod to exert its effect on various immune cells directly related to the pathology of the target patient population. These data were presented in posters at the ATS International Virtual Meeting in 2020 and the European Society International Congress in 2021. As an extension of this work, a highly selective and sensitive antibody was developed for immunohistochemical detection of the target receptor for efzofitimod, NRP2, in patient tissue samples. Development and characterization of the antibody, as well as detection of NRP2 on key immune cells in granulomas of sarcoidosis patient lung and skin biopsy samples was highlighted in a poster presentation at the European Respiratory Society (ERS) International Congress 2022 in Barcelona, Spain. SSc- ILD is an autoimmune disease characterized by chronic inflammation and fibrosis with common involvement of the skin and lungs. As in sarcoidosis, myeloid cells are centrally involved in driving this cycle of chronic inflammation and fibrosis in SSc- ILD. One aspect of this is the production by these cells of inflammatory cytokines, including IL- 6. Based on our translational biology program, which demonstrated activity across distinct experimental animal models either driven by direct lung injury or systemic pathology, along with our understanding of efzofitimod' s mechanism of action, we decided to move the program forward into patient clinical trials in ILD. ILD and the Role of Immunology The current primary target population for efzofitimod is ILD, a group of predominantly immune- mediated disorders which can cause progressive fibrosis of the lung. There are over 200 different types of ILD, of which the four major forms are: pulmonary sarcoidosis, CHP, CTD- ILD, and IPF. These four types comprise roughly 80 % of the total ILD population. We have focused our development efforts on progressive, immune- mediated forms of ILD, with limited therapeutic options, where we believe efzofitimod can have disease modifying effects. These lung conditions are recognized as having a measurable immune- mediated pathology, involving both innate and adaptive immune mechanisms that contribute to pathogenesis, and can result in progressive disease leading to fibrosis and death. Pulmonary Sarcoidosis Sarcoidosis is an inflammatory disease of unknown cause, characterized by the formation of granulomas, clumps of inflammatory cells in one or more organs in the body. Sarcoidosis affects people of all ages, with the incidence peaking at ~~20 to 39~~ **30- 50** years of age. The disorder ~~usually begins in the lungs, skin or lymph nodes, but~~ can ~~affect~~ **occur in** almost any organ **, but primarily affects the lungs** . Sarcoidosis in the lungs is called pulmonary sarcoidosis and occurs in over 90 % of sarcoidosis patients. Approximately 200, 000 Americans are currently living with ~~pulmonary~~ sarcoidosis. The prognosis for patients with pulmonary sarcoidosis ranges from benign and self- limiting to chronic, debilitating fibrotic disease and death. The immunopathogenesis of sarcoidosis is not yet well understood, but a hallmark of the disease is the presence of granulomas, or clumps of immune cells. Granulomas consist of epithelioid cells, lymphocytes (both T and B cells) and myeloid cells, with macrophages and multinucleated giant cells (formed by fusion of macrophages), both of myeloid origin, playing a central role in their formation and persistence. A leading hypothesis is that granuloma formation involves the interplay between antigen, human leukocyte antigen class II molecules, and T- cell receptors: a presumptive sarcoid antigen is engulfed by circulating antigen- presenting cells (APCs; macrophages, dendritic cells) and the subsequent interplay between APCs and CD4 T- cells initiates granuloma formation. This process is accompanied by the release of inflammatory cytokines such as **MCP- 1, IL- 6,** IFN- g and TNF- a from myeloid cells. For patients with pulmonary sarcoidosis, the primary goal of treatment is to improve quality of life and avoid damage to organs. Efzofitimod may provide a therapeutic benefit in pulmonary sarcoidosis by resolving chronic inflammation, alleviating symptoms such as cough and shortness of breath and preventing disease progression towards fibrosis and permanent organ damage. Efzofitimod may also improve patient quality of life by allowing patients to reduce or completely avoid the need for oral corticosteroids (OCS), which are associated with debilitating side effects when used chronically. Efzofitimod targets the immune cells, primarily of myeloid lineage (monocytes, macrophages and dendritic cells), that drive the cellular pathology observed in pulmonary sarcoidosis. In preclinical studies, efzofitimod has been observed to inhibit cytokines involved in regulation of inflammatory and immune responses, modulating the reaction of myeloid cells at the sites of inflammation and attenuating T- cell activation. We have also discovered that efzofitimod' s receptor target NRP2 is up- regulated during differentiation and activation of myeloid cells including macrophages, dendritic cells and neutrophils. Furthermore, efzofitimod has been observed to significantly reduce lung inflammation and fibrosis and improve respiratory function parameters in bleomycin- induced animal models of ILD. We believe that by inhibiting the chronic inflammatory response in these patients, efzofitimod may be able to restore immune balance and prevent progressive fibrosis, without toxicity associated with current treatment options, thereby providing a safer, potentially more effective alternative to OCS and other immunosuppressive therapies that currently comprise the standard of care for patients with symptomatic pulmonary sarcoidosis.

Systemic Sclerosis Systemic sclerosis (SSc, or scleroderma) is a chronic, progressive, autoimmune disease characterized by inflammation and fibrosis of connective tissues throughout the body, including the skin and other internal organs. SSc that occurs in the lungs is called SSc- ILD. It is estimated that approximately 100, 000 people in the U. S. are affected by SSc and **over 50** ~~up to 80~~ % may develop ILD. SSc- ILD is caused by chronic inflammation in the lungs and, if left untreated, can result in scarring, or fibrosis, that causes permanent loss of lung function. ILD is the primary cause of death in patients with SSc. Current treatment options are limited. They mainly focus on slowing lung function decline, do not improve patient symptoms and are associated with significant toxicity. New treatments are needed that can stabilize or improve lung function and improve patient quality of life. Efzofitimod has been shown to reduce lung and skin fibrosis in an animal model of SSc. Certain cytokines central to the immune pathology of SSc- ILD, including IL- 6 **and MCP- 1** , were also downregulated in both animal models of ILD and in humans in an adjacent ILD, pulmonary sarcoidosis, in our Phase 1b / 2a study. Furthermore, NRP2 is expressed in the skin of patients with SSc. This data in both animal and human systems, along with our current understanding of the role of efzofitimod' s target receptor NRP2 and the manner with which this novel ligand can modulate the immune response at the sites of inflammation, suggest it is a promising therapeutic candidate for SSc- ILD. Clinical Development Efzofitimod Phase 3 Clinical Trial – Pulmonary Sarcoidosis We are conducting the EFZO- FIT study, which is a global Phase 3, multicenter, randomized, double- blind, placebo- controlled study to evaluate the efficacy and safety of IV efzofitimod 3. 0 mg / kg and 5. 0 mg / kg versus placebo in patients with symptomatic pulmonary sarcoidosis. It is a 52- week study with patients receiving either efzofitimod or placebo once a month for a total of 12 doses. The study ~~is currently enrolling and intends to enroll~~ **enrolled 268** adults with histologically confirmed pulmonary sarcoidosis receiving stable treatment with OCS, with or without immunosuppressant therapy **,** ~~. The study intends to enroll up to 264 patients~~ at centers throughout the United States, Europe, Brazil and Japan. The study incorporates a forced steroid taper. The objective of the study is to evaluate the efficacy and safety of efzofitimod in patients with pulmonary sarcoidosis. The primary endpoint of the study is steroid reduction. Secondary endpoints include measures of lung function assessed by FVC and health- related quality of life assessments and questionnaires (KSQ lung score). This study consists of three periods: a screening period, a 48- week placebo- controlled treatment period with the primary endpoint being measured at week 48, and a four- week follow- up period. Within the study, ~~up to 264~~ patients will be randomized 1: 1: 1 to efzofitimod 3. 0 mg / kg (N = 88), efzofitimod 5. 0 mg / kg (N = 88) or placebo (N = 88). Study drug is administered via IV infusion every four weeks for a total of 12 doses (48 weeks of treatment). Starting on Day 15 patients begin a taper (reduction) in OCS according to specific guidelines from their starting dose of 7. 5- 25 mg / day of prednisone (or equivalent) to a target dose of 0. 0 mg / day. Patients will be followed for the remainder of the study to determine their ability to remain off of OCS. Patients who require an increase in OCS dose at any time in the study will continue to receive blinded study drug and be followed through to the end of the study. In September 2022, we dosed the first patient in this study. Additionally, during 2023 **and 2024** , we had ~~a~~ **DSMB reviews of our EFZO- FIT study. Following each** DSMB review **, the** ~~of our EFZO- FIT study. The~~ DSMB concluded that the study could continue unmodified. ~~We expect to~~ **In July 2024, we** ~~complete~~ **completed** enrollment ~~in~~ **of 268 patients, exceeding target enrollment of 264 patients. Topline data from** the study **are anticipated** in the ~~second~~ **third** quarter of ~~2024~~ **2025** . In February 2024, we announced an Individual Patient EAP. The Individual Patient EAP has been initiated based on blinded EFZO- FIT study investigator and patient participant feedback. The program is designed to allow access for patients who complete the Phase 3 EFZO- FIT study and wish to receive treatment with efzofitimod outside of the clinical trial. The administration of efzofitimod as part of the Individual Patient EAP will occur independent of the EFZO- FIT study protocol, and we, principal investigators and patients will remain blinded to the treatment that occurred as part of the EFZO- FIT study. As this Individual Patient EAP will occur independent of the EFZO- FIT study, this program is not an ~~open- label extension (~~ OLE ~~)~~ and no long- term data will be collected by us. Efzofitimod Phase 1b / 2a Clinical Trial – Pulmonary Sarcoidosis We designed a proof- of- concept Phase 1b / 2a clinical trial for efzofitimod in patients with pulmonary sarcoidosis. The Phase 1b / 2a clinical trial was a randomized, double- blind, placebo- controlled multiple- ascending dose, first- in- patient study with IV efzofitimod in 37 patients. The study was conducted in patients with pulmonary sarcoidosis undergoing an OCS tapering regimen, in three cohorts of 12 patients each, at dose levels of 1. 0 mg / kg, 3. 0 mg / kg and 5. 0 mg / kg. The primary objective of the study was to evaluate safety and tolerability of multiple ascending doses of efzofitimod. Secondary objectives included assessment of the potential steroid- sparing effects of efzofitimod. In addition, efzofitimod' s PK and immunogenicity following multiple dose administration were evaluated. Additional endpoints of interest included the exploratory assessment of the efficacy of efzofitimod for the treatment of pulmonary sarcoidosis by evaluating changes over time in: lung function assessed by forced vital capacity (FVC) and diffusing capacity of the lungs for carbon monoxide (DLCO); health- related quality of life assessments and questionnaires; and serum biomarkers of interest. This study consisted of three staggered dose cohorts. Each cohort consisted of three periods: a screening period, a 20- week placebo- controlled treatment period, and a four- week follow- up period ending with final study assessments at Week 24. Within each cohort, 12 patients were randomized 2: 1 to efzofitimod (N = 8) or placebo (N = 4). Study drug was administered via IV infusion every four weeks for a total of six doses (20 weeks of treatment). The efzofitimod doses levels being evaluated were 1 mg / kg, 3 mg / kg and 5 mg / kg. Starting on Day 15 patients began a taper (reduction) in OCS according to specific guidelines from their starting dose of 10- 25 mg / day of prednisone (or equivalent) to a target dose of 5. 0 mg / day, to be completed on or before Day 50. The OCS dose was tapered through Week 24 and patients were followed for the remainder of the study to determine their ability to maintain on this 5 mg dose. Optionally, further reductions in the OCS dose to below 5. 0 mg / day may be attempted after the Week 16 visit, if determined by the investigator to be feasible. Patients who required an increase in OCS dose at any time in the study were to continue to receive blinded study drug and be followed through to the end of the study. In September 2021, we announced positive results and clinical proof- of- concept from the Phase 1b / 2a clinical trial in 37 patients with pulmonary sarcoidosis. These data were subsequently presented at the ATS International Conference and published in the peer reviewed journal CHEST in 2022. Efzofitimod was safe and well- tolerated at all doses with no drug- related serious

adverse events or signal of immunogenicity. Additionally, the study demonstrated consistent dose response for efzofitimod on key efficacy endpoints and improvements compared to placebo, including measures of steroid reduction, lung function, sarcoidosis symptom measures and inflammatory biomarkers. Key safety and clinical efficacy findings for efzofitimod from the study include: • Safe and well- tolerated at all doses: • No dose- relationship with most common adverse events associated with underlying disease; • No drug- related serious adverse events; and • No signal of immunogenicity. • Dose response and consistent positive findings across key efficacy endpoints: • Steroid reduction of 58 % overall from baseline and 22 % relative reduction compared to placebo in steroid usage post taper in the 5. 0 mg / kg treatment group; • Complete steroid taper to 0 mg achieved and maintained for 33 % of patients in the 5. 0 mg / kg treatment group compared to no patients in any other group; • Absolute improvement in FVC as a measure of lung function at week 24 of 3. 3 % in the 5. 0 mg / kg treatment group compared to placebo, with an improvement in FVC of > 2. 5 %, considered clinically meaningful; • Clinically meaningful improvement over placebo observed for dyspnea (shortness of breath), cough, fatigue and the King' s Sarcoidosis Scores for Lung and General Health in 5. 0 mg / kg treatment group; • Dose dependent trends of improvement in key inflammatory biomarkers compared to placebo including IL- 6, MCP- 1, IFN- γ, IP- 10 and TNF- ? as well as key sarcoidosis markers including ACE, IL- 2Ra and SAA with tightest control in the 5. 0 mg / kg treatment group; and • FDG- PET- CT was not evaluable due to incomplete data primarily caused by operational issues related to the COVID- 19 pandemic. **We have** ~~In 2023, we~~ published additional analyses of data from this study. ~~This included a positive exposure~~ **The study demonstrated consistent dose** response ~~demonstrated~~ for efzofitimod **on key efficacy** ~~across multiple clinically relevant~~ endpoints **and improvements compared to placebo, including measures of steroid reduction, lung function, pulmonary sarcoidosis symptom measures and inflammatory biomarkers. These data were presented at the American Thoracic Society (ATS) International Conference and** published in the peer- reviewed journal **CHEST during 2022. In October 2024** ~~Frontiers in Pharmacology and a post- hoc analysis demonstrating statistically significant improvement in time to relapse~~ , **the same published data** ~~FVC and patient reported outcomes~~ for efzofitimod ~~presented~~ **was featured in the Best of CHEST Journals session** at the **CHEST 2024 Annual Meeting** ~~European Respiratory Society (ERS) International Congress~~ . Efzofitimod Phase 2 Clinical Trial – SSc- ILD During 2023, we initiated the EFZO- CONNECT study, a Phase 2 study of efzofitimod in patients with SSc- ILD. The EFZO- CONNECT study is a Phase 2 randomized, double- blind placebo- controlled proof- of- concept study to evaluate the efficacy, safety and tolerability of efzofitimod in patients with SSc- ILD. The study is a 28- week study with three parallel cohorts randomized 2: 2: 1 to either 270 mg or 450 mg of efzofitimod or placebo dosed IV monthly for a total of six doses. The study intends to enroll up to 25 patients at multiple centers in the United States. The objective of the study is to evaluate the efficacy of multiple doses of IV efzofitimod on pulmonary, cutaneous **(limited or diffuse)** and systemic manifestations in patients with SSc- ILD. The primary endpoint is reduction of FVC. Secondary endpoints include certain measures regarding safety and tolerability. ~~The~~ **In July 2024, we amended the** study ~~was initiated in~~ **to add an OLE to patients. Patients who complete** the ~~third~~ **study and wish to receive ongoing treatment with efzofitimod are eligible to participate in the 24- week OLE. Based on current enrollment projections, we expect to report interim data from the study in the second** quarter of ~~2023~~ **2025** ~~, and in October 2023, we dosed the first patient in this study~~ . Efzofitimod Phase 2 Clinical Trial – COVID- 19 with Severe Respiratory Complications In response to the COVID- 19 pandemic, we conducted a Phase 2 clinical trial of efzofitimod in patients with COVID- 19 related severe respiratory complications. The study was designed to evaluate the safety and preliminary efficacy of efzofitimod compared to placebo through the assessment of key clinical outcome measures. In early 2021, we reported positive data which showed that the trial met its primary endpoint of safety, demonstrating that a single, IV dose of efzofitimod was observed to be generally safe and well- tolerated in both the 1. 0 and 3. 0 mg / kg treatment groups. The study also showed a signal of activity in the 3. 0 mg / kg cohort. In addition, patients treated with efzofitimod demonstrated a trend of overall improvement in key biomarkers analyzed compared to placebo. We are leveraging these data for our mechanistic understanding of efzofitimod and for its application in ILD. Efzofitimod Phase 1 Clinical Trial – Healthy Volunteers In June 2018, we announced results of our first- in- human Phase 1 clinical trial of efzofitimod conducted in Australia. This randomized, double- blind, placebo- controlled study evaluated the safety, tolerability, immunogenicity, and PK of IV efzofitimod in healthy volunteers. The Phase 1 clinical trial enrolled 36 healthy volunteers who were randomized to one of six sequential cohorts and received a single infusion of IV efzofitimod or placebo. Ascending efzofitimod doses by cohort ranged from 0. 03 mg / kg to 5. 0 mg / kg. The results indicate that the drug was observed to be generally well- tolerated at all dose levels tested, with no significant adverse events or induction of anti- drug antibodies observed following efzofitimod dosing or throughout the one- month follow- up period. The PK profile of efzofitimod following single- dose administration was linear across the evaluated dose range. Higher efzofitimod doses yielded sustained serum concentrations through the end of the one- month follow- up period that were above the predicted therapeutic threshold, supporting the potential for a once- monthly dosing regimen. In January 2020, we entered into the Kyorin Agreement for the development and commercialization of efzofitimod for the treatment of ILD in Japan. Under the terms of the Kyorin Agreement, Kyorin received exclusive rights to develop and commercialize efzofitimod in Japan for all forms of ILD and is obligated to fund all research, development, regulatory, marketing and commercialization activities in Japan. We are responsible for supplying all drug product for Japan, as well as supporting development activities for efzofitimod. In 2020, Kyorin conducted and funded a Phase 1 clinical trial of efzofitimod (known as KRP- R120 in Japan). The Phase 1 trial was a placebo- controlled study to evaluate the safety, PK and immunogenicity of efzofitimod in 32 healthy Japanese male volunteers. Efzofitimod was observed to be generally well- tolerated with no drug- related serious adverse events, and PK findings were consistent with previous studies of efzofitimod. Kyorin is also participating in the EFZO- FIT study as the local sponsor in Japan. In February 2023, Kyorin dosed the first patient in Japan in the EFZO- FIT study which triggered a $ 10. 0 million milestone payment to us. To date, the Kyorin Agreement has generated $ 20. 0 million in upfront and milestone payments to us and we are eligible to receive up to an additional $ 155. 0 million in the aggregate upon achievement of certain development, regulatory and sales milestones, as well

as tiered royalties on any net sales in Japan. Unless earlier terminated, the term of the Kyorin Agreement continues until the expiration of the royalty obligations. Either party may terminate the Kyorin Agreement in the event that the other party breaches the agreement and fails to cure the breach, becomes insolvent or challenges certain of the intellectual property rights licensed under the agreement. Our Discovery Platform tRNA Synthetase Biology Extracellular tRNA synthetase biology represents a novel set of potential physiological modulators and therapeutic targets. **Using efzofitimod as a model, we have developed a process to advance novel tRNA synthetase domains from a concept to therapeutic candidate. This process leverages our early discovery work as well as current scientific understanding of tRNA synthetase evolution, protein structure, gene splicing and tissue- specific regulation to identify potentially active protein domains. Screening approaches are employed to identify target cells and extracellular receptors for these tRNA synthetase- derived proteins. These cellular systems can then be used in mechanism- of- action studies to elucidate the role these proteins play in cellular responses and their potential** therapeutic utility. We are working to identify new tRNA synthetase based drug candidates through our internal discovery efforts and ~~other external collaboration efforts, including our collaboration with Dualsystems Biotech AG (Dualsystems). Dualsystems has agreed to utilize their proprietary receptor screening technology and research expertise to attempt to identify and validate new target receptors for tRNA synthetases. Through our internal research efforts, the Dualsystems collaboration and other external collaboration efforts, we~~ intend to continue to advance our product development efforts within our tRNA synthetase biology platform. tRNA Synthetase Candidates Utilizing our novel approach, we have identified target receptors for domains of two additional tRNA synthetases, gaining insights into their potential biological activity in immunology and fibrosis. These fragments form the basis of our additional pipeline candidates. We plan to further elucidate the therapeutic potential of these candidates through mechanistic investigations, including in vitro and in vivo preclinical studies. ATYR0101 is a fusion protein derived from a domain of aspartyl- tRNA synthetase (DARS). ATYR0101 binds directly to latent- transforming growth factor beta- binding protein 1 (LTBP1), which regulates transforming growth factor beta (TGFβ), which is at the apex of fibrotic signaling. Derived from a naturally occurring tRNA synthetase, ATYR0101 interacts with LTBP1 in a unique way that presents a differentiated approach to targeting fibrosis. Early data suggest ATYR0101 exerts its antifibrotic effects by inducing apoptosis of myofibroblasts in a TGFβ dependent manner. We believe ATYR0101 may have broad therapeutic applications in multiple fibrotic diseases, such as pulmonary fibrosis, SSc, liver fibrosis and kidney fibrosis. ATYR0750 is a fusion protein derived from a domain of alanyl- tRNA synthetase (AARS). ATYR0750 is a novel ligand to fibroblast growth factor receptor 4 (FGFR4), which is involved in many cellular processes, including cell proliferation, differentiation, and tissue repair. FGFR4 is known to play a role in diseases related to inflammation and fibrosis, particularly in the liver. As a novel ligand, ATYR0750 interacts with FGFR4 in a differentiated way to other approaches targeting the receptor, which may lead to improved therapeutic benefit. ~~Impact of Geopolitical and Macroeconomic Conditions Global economic and business activities continue to face widespread macroeconomic uncertainties, including global geopolitical tension, armed conflicts, potential future health pandemics, labor shortages, inflation and monetary supply shifts, liquidity concerns at, and failures of, banks and other financial institutions or other disruptions in the banking system or financing markets, higher interest rates and financial and credit market fluctuations, volatility in the capital markets and recession risks, disruptions to trade, commerce, pricing stability, credit availability and supply chain continuity globally. The ultimate long-term impact of these evolving geopolitical and macroeconomic conditions on our business is uncertain, although we continue to actively monitor the impact of these factors on our results of operations, financial condition and cash flows. The extent of the impact of these factors on our operational and financial performance, including our ability to execute our business strategies and initiatives in the expected timeframe, will depend on future developments, which are uncertain and cannot be predicted; however, any continued or renewed disruption resulting from these factors could negatively impact our business.~~ Competition The biotechnology and pharmaceutical industries are intensely competitive. We will face competition with respect to our current product candidates and any other therapeutics we may develop or commercialize in the future, from pharmaceutical companies, biotechnology companies, universities and other research institutions. Our competitors may have substantially greater financial, technical and other resources, such as larger research and development staff and established marketing, sales and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, drug products that are more effective, safer or less costly than any product candidate that we may develop. Although we believe we are the only company engaged in the discovery and development of therapeutics based on novel functions of tRNA synthetases, we are aware of other companies that could compete with our product candidates as described below. Our lead indication for efzofitimod is pulmonary sarcoidosis. For patients with pulmonary sarcoidosis, the primary goal of treatment is to improve the patient' s quality of life and avoid danger to organs, such as development of scarring or fibrosis caused by chronic inflammation. Currently, the only FDA- approved therapies for the treatment of sarcoidosis are glucocorticoids approved by **the** FDA in the 1950s, prior to current regulatory standards. The consensus standard of care for pulmonary sarcoidosis is immunomodulatory therapy. First line treatment is typically with OCS that act mainly by suppressing inflammatory genes. OCS therapy has been shown to stabilize or improve disease symptoms in some patients, although relapse commonly occurs once OCS therapy is tapered or discontinued. Long-term OCS use is associated with significant side effects including substantial weight gain, development of insulin resistance, osteoporosis, and risk of infection. Alternatives, such as cytotoxic immunosuppressive agents (e. g., methotrexate) have been used as steroid- sparing agents, however, these therapies can also have significant side effects and toxicities, including serious infections and liver toxicity. Patients who have progressive disease despite OCS or other immunosuppressive therapy are sometimes given biologic immunomodulators, such as the tumor necrosis factor (TNF) inhibitors infliximab or adalimumab. These therapies are not approved by the FDA or other regulatory agencies for the treatment of sarcoidosis, and are also

associated with serious potential side effects, including malignancy. The efficacy of these agents **in sarcoidosis** has not been well established clinically. Given the known toxicities of long- term OCS, immunosuppressive and immunomodulatory biologic therapeutic regimens, treatment of patients with sarcoidosis is limited to those who are symptomatic and whose disease is considered active. The presence of granulomas from sarcoidosis define the disease as active, and granulomatous inflammation is the major cause of fibrosis in pulmonary sarcoidosis. Studies to date have not clearly demonstrated that OCS or other immunomodulatory therapies prevent disease progression or formation of fibrosis. We believe there remains a substantial unmet need for safer, more effective therapies for sarcoidosis that could reduce or replace the requirement for long- term OCS or other immunosuppressive therapy. To our knowledge, efzofitimod is the most advanced drug candidate currently in development for the treatment **of** pulmonary sarcoidosis. Our second indication for efzofitimod is SSc- ILD. SSc- ILD is very difficult to treat, with limited options. Few randomized studies have been conducted, and first line standard of care remains off- label immunosuppressive agents, whose impact is modest and associated with significant side effects including malignancies. Despite not being approved for SSc- ILD, the immunosuppressants mycophenolate mofetil and cyclophosphamide are typically used as first- line treatment. Two products were recently approved for the treatment of SSc- ILD. Ofev ® (nintedanib) marketed globally by Boehringer Ingelheim International GmbH, received FDA approval in 2019 for slowing the rate of decline in pulmonary function in patients with SSc- ILD. ~~In 2020, the approval was further expanded to include patients with chronic fibrosing ILD with a progressive phenotype.~~ Actemra ® (tocilizumab) marketed globally by F. Hoffmann- La Roche Ltd. and Chugai Pharmaceutical Co Ltd., was approved by the FDA in 2021 for slowing the rate of decline in pulmonary function in adult patients with SSc- ILD. These therapies have demonstrated the ability to slow decline in lung function as measured by FVC in controlled clinical studies but **did not improve underlying systemic disease in these trials and** are associated with significant side effects ~~, continued symptoms, and progressive disease in the majority of patients~~ . Rituximab, a biologic immunosuppressant targeting B- cells, is also used, but there is little clinical evidence supporting its efficacy in this indication. If efzofitimod is successful for the treatment of pulmonary sarcoidosis and SSc- ILD, we believe it may have applications in other ILD indications and potentially in other severe immune disorders. Based on ~~an analysis~~ **analyses** from ~~an~~ independent ~~consultant~~ **consultants** that we **have** engaged ~~during 2022~~ **and our own modeling** , we estimate that there is a $ 2- ~~3~~ **5** billion ~~dollar~~ global market opportunity in pulmonary sarcoidosis and ~~Ssc~~ **SSc** - ILD ~~and our own modeling~~ . There are a number of companies engaged in the clinical development of potential new treatments for ILD, including Boehringer Ingelheim International GmbH, F. Hoffman- La Roche Ltd., Merck & Co., Sanofi- Aventis LLC, **and** ~~Amgen Inc., GSK plc , and Kinevant Sciences GmbH~~ , among others. Sales and Marketing We intend, where strategically appropriate, to build the commercial infrastructure necessary to effectively support the commercialization of our product candidates, if and when we believe a regulatory approval of the first of such product candidates in a particular geographic market appears imminent. We may elect to utilize strategic partners, distributors, or contract sales forces to assist in the commercialization of our product candidates in selected geographic locations or for particular indications. For example, we have licensed the rights to Kyorin to develop and commercialize efzofitimod in Japan. ~~Additional capabilities important to the marketing of therapeutics include the management of key stakeholders such as managed care organizations, group- purchasing organizations, specialty pharmacies, and government accounts.~~ To develop the appropriate commercial infrastructure **to prepare our products and markets for commercial entry, and to support the engagement and management of key stakeholders** , we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that any of our product candidates will be approved. Manufacturing We currently contract with third parties for the manufacturing and testing of our product candidates, including efzofitimod, to support preclinical studies and clinical trials, and we intend to do so in the future. We do not own or operate manufacturing or testing facilities for the clinical or commercial production of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. The use of ~~contracted development and manufacturing organizations (~~ CDMOs ~~)~~ is cost- efficient and has eliminated the need for our direct investment in manufacturing facilities and additional resources early in development. Although we rely on CDMOs, we employ personnel with extensive biologics development and manufacturing experience to oversee such CDMOs. Efzofitimod is a fusion protein that is expressed in recombinant E. coli. We have worked with CDMOs in the United States and internationally on the development and manufacture of products using current Good Manufacturing Practices (cGMP) to produce drug substance and drug product to support preclinical and clinical development. We have also contracted with CDMOs to conduct the labeling, storage and distribution of our drug product candidates to clinical sites. To date, our CDMOs have met our manufacturing and testing requirements for clinical development and we expect that our current supply chain is capable of providing sufficient quantities of our product candidates to meet our anticipated clinical development needs. Currently we have sufficient efzofitimod on hand to meet our projected needs for the EFZO- FIT (and related Individual Patient EAP) and EFZO- CONNECT studies. Additionally, during 2023, the CDMO that we engaged during late 2021 completed its first and second full, commercial- scale bulk drug substance GMP runs. Quality release testing **was** ~~has been~~ completed and all release specifications were met, supporting the CDMO' s ability to produce bulk drug substance of efzofitimod for commercial purposes if we receive regulatory approval for efzofitimod. **During 2024, we initiated preparatory work with the CDMO on process performance qualification batches that will be required as part of our potential BLA submission for efzofitimod. During the first quarter of 2025, the first of three upstream batches did not meet process performance qualification specifications, and will need to be replaced. The replacement batch has been scheduled with our CDMO. The deviation of this first batch was due to operational errors at the CDMO and not related to the underlying process nor the drug substance. We believe this deviation should not impact the timing of our potential BLA submission. However, future operational errors in these batches could negatively impact the timing of our potential BLA submission and could require significant additional funding.** We will **also** need to demonstrate that the drug substance manufactured by this CDMO is comparable in quality, safety and potency to the drug substance manufactured by our previous CDMO, which is currently being used in the

EFZO- FIT and EFZO- CONNECT studies **. We have completed a comparability study and are awaiting regulatory feedback** . Patents and Proprietary Rights We strive to protect the proprietary technologies that we believe are important to our business, including seeking and maintaining patent protection intended to cover the composition of matter of our product candidates, their methods of use, related technology and other inventions that are important to our business. We own, or have exclusive licenses to, over 300 issued patents or allowed patent applications with predicted expiration dates ranging from 2026 to 2034. In addition to patent protection, we also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know- how related to our business, defend and enforce our patents, maintain our licenses to use intellectual property owned by third parties, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and other proprietary rights of third parties. We also rely on know- how, continuing technological innovation and in- licensing opportunities to develop, strengthen, and maintain our proprietary position in the field of extracellular tRNA synthetase biology, their receptors and associated signaling pathways, including, for example, antibody diagnostics and therapeutics to NRP2. A third party may hold intellectual property, including patent rights, which is important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially. We plan to continue to expand our intellectual property estate by filing patent applications directed to new methods of treatment, therapeutics and additional new product forms thereof with new therapeutic or pharmacokinetic properties. Specifically, we seek patent protection in the United States and internationally for novel compositions of matter covering our protein therapeutics, antibody therapeutics, next generation product forms and the use of these compositions in a variety of therapies. The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties. Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office (USPTO), or a foreign patent office to determine priority of invention or in post- grant challenge proceedings, such as oppositions, that challenge priority of invention or other features of patentability. Such proceedings could result in us incurring substantial costs, even if the eventual outcome is favorable to us. Our efzofitimod patent portfolio is comprised of a number of patent families related to derivatives of HARS, including the HARS amino 1- 60, related splice variants, combinations with other therapeutics, and next- generation product forms with modified therapeutic activity or pharmacokinetic characteristics. Our efzofitimod patent portfolio includes a patent family that is jointly owned by us and our 98 % owned subsidiary, Pangu BioPharma, and includes issued patents in the United States, Australia, Canada, China, Europe, Hong Kong and Japan, and pending patent applications in the United States. The U. S. patents are expected to expire between 2030 and 2031, absent any patent term extension for regulatory delays, and the ex- U. S. patents, and patents that issue from these patent applications, if any, are expected to expire in 2030, absent any patent term extension. The efzofitimod patent portfolio includes another patent family jointly owned by us and Pangu BioPharma, which includes patent applications directed to related splice variants of HARS. This patent family includes issued patents in the United States, Australia, Canada, China, Europe, Hong Kong, Japan and New Zealand. The issued patents are expected to expire in 2031, absent any patent term extension. Also included within the efzofitimod patent portfolio are issued patents and pending patent applications directed to specific product forms of efzofitimod, and other HARS splice variants, including patent families directed to Fc fusion proteins, and combinations for treating lung inflammation, among other indications. One family directed to specific Fc fusion proteins includes issued or allowed patents in the United States, Australia, Canada, Europe, Hong Kong, India and Japan, and pending patent applications in the United States and Japan. A patent family directed to combination therapies includes ~~an~~ issued ~~patent~~ **patents** in the United States, **Europe and Hong Kong** and pending patent applications in the United States, Australia, Canada ~~, China, Europe, Hong Kong~~ and Japan. If issued, the patents that derive from the patent applications are predicted to expire between 2034 and 2038, absent any patent term extensions. tRNA Synthetases Our pipeline of extracellular tRNA synthetase proteins is covered by a series of patent families, which are directed to all 20 human cytosolic tRNA synthetases. Numerous patents are issued in the United States and elsewhere, including issued U. S. patents directed to specific therapeutic protein compositions, the corresponding protein polynucleotide sequences, and certain antibody compositions to specific splice variants. These cases are jointly owned by us and Pangu BioPharma, and include issued patents and / or pending applications in the United States, Australia, Canada, Europe, China and Japan. Patents that issue from these applications, if any, would be expected to expire in 2031, absent any patent term extension. Additional patent applications have also been separately filed (or are in preparation) on the splice variants, and optimized sequences derived from GARS (Glycyl- tRNA synthetase), DARS, YARS (tyrosyl- tRNA synthetase), and other tRNA synthetases, and any patents issuing from these patent applications are expected to expire between 2026 and 2030, absent any patent term extension **. A separate provisional application has been filed on specific DARS mutants, and any patents issuing from this patent application are expected to expire in 2045** . The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is generally 20 years from the earliest date of filing the non- provisional patent application from

which the patent issued. In the United States, the patent term of a patent that covers a drug approved by the FDA, may also be eligible for patent term extension, which permits patent term restoration as compensation for 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 expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other non- United States jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We intend to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. We also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual' s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. Government Regulation Government authorities in the United States, including federal, state, and local authorities, and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, storage, distribution, post-approval monitoring and reporting, advertising and promotion, and export and import of biological products, such as those we are developing. Pricing of such products is also subject to regulation in many countries. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources. U. S. Government Regulation In the United States, the FDA regulates biologics under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act and their implementing regulations. FDA approval is required before any new unapproved biologic or dosage form, including a new use of a previously approved biologic, can be marketed in the United States. Biologics are also subject to other federal, state, and local statutes and regulations. If we fail to comply with applicable FDA or other requirements at any time during the product development process, clinical testing, approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA' s refusal to approve pending applications, license suspension or revocation, untitled or warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us. The process required by the FDA before product candidates may be marketed in the United States generally involves the following: • completion of extensive preclinical laboratory tests and preclinical animal studies, performed in accordance with the good laboratory practice regulations, where applicable; • submission to the FDA of an IND which must become effective before human clinical trials may begin and must be updated annually; • approval by an independent institutional review board (IRB) or ethics committee representing each clinical site before each clinical trial may be initiated; • performance of adequate and well- controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication and conducted in accordance with good clinical practice (GCP) requirements; • preparation of and submission to the FDA of a biologics license application (BLA) after completion of all pivotal clinical trials; • potential review of the product application by an FDA advisory committee, where appropriate and if applicable; • a determination by the FDA within 60 days of its receipt of a BLA to file the application for review; • satisfactory completion of an FDA pre- approval inspection of the manufacturing facilities where the proposed product is produced to assess compliance with cGMP; • potential FDA audit of the clinical trial sites that generated the data in support of the BLA; and • FDA review and approval of a BLA prior to any commercial marketing or sale of the product in the United States. The preclinical and clinical testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all. An IND is a request for authorization from the FDA to administer an investigational new drug or biologic product to humans in clinical trials. The IND submission includes the general investigational plan and the protocol (s) for human trials. The IND also includes results of preclinical testing, including animal and in vitro studies, to assess the toxicology, PK, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational new drug. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trials. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical trials can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence. The FDA may impose a clinical hold at any time during a clinical trial and may impose a partial clinical hold that would apply certain limits to the trial, for example, imposing dosage limitations or restricting the timeframe of the trial. Clinical Trials Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCPs which include the requirement 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 study, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. Additionally, approval must also be obtained from each clinical trial site' s IRB before the clinical trials may be initiated, and the IRB must monitor the trial until it is completed. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries. The clinical investigation of a drug is generally divided into three phases. Although the phases are usually conducted sequentially, they may overlap or be combined. • Phase 1. The drug is initially introduced into a relatively small number of healthy human subjects or patients with the target disease or condition. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational new drug in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness. • Phase 2. The drug is administered to a limited patient population to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks, and preliminarily evaluate efficacy. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. • Phase 3. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites to generate enough data to evaluate dosage, clinical effectiveness and safety, and establish the overall benefit- risk relationship of the investigational new drug product. A well- controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a drug: such Phase 3 studies are referred to as " pivotal. " In some cases, the FDA may condition approval of a BLA for a product candidate on the sponsor' s agreement to conduct additional clinical trials after approval. In other cases, a sponsor may voluntarily conduct additional clinical trials after approval to gain more information about the drug. Such post- approval studies are typically referred to as Phase 4 clinical trials. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials that the FDA requires as a condition of approval could result in FDA withdrawing approval for the product. A clinical trial sponsor must submit written IND safety reports to the FDA and the investigators for serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator' s brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the product candidate within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor' s initial receipt of the information. The FDA, the IRB, or the clinical trial sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. 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 or not a trial may move forward at designated check points based on access to certain data from the trial. We may also suspend or terminate a clinical trial based on evolving business objectives or competitive climate. BLA Submission Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed information about the investigational biologic product is submitted to the FDA in the form of a BLA requesting approval to market the product for one or more indications. Efzofitimod and our other potential product candidates are proteins that will be regulated as biological products subject to the BLA marketing pathway. Under federal law, the submission of most BLAs is subject to an application user fee, and the sponsor of an approved BLA is also subject to an annual prescription drug product program fee. These fees typically increase annually. Applications for orphan drug products are exempted from the BLA user fees, unless the application includes an indication for other than a rare disease or condition. A BLA must include all relevant data available from pertinent preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product' s chemistry, manufacturing, controls, and proposed labeling, among other things. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational new drug product to the satisfaction of the FDA. FDA approval of a BLA must be obtained before a biologic may be marketed in the United States. Before approving a BLA, the FDA typically will conduct a pre- approval inspection of 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 assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA may refer any NDA or BLA, including applications for novel biologic candidates **or drug candidates** which present difficult questions of safety or efficacy, to an advisory committee. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that 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. The FDA' s Decision on a BLA The FDA evaluates a BLA to determine whether the data demonstrate that the biologic is safe, pure, and potent, or effective. After the FDA evaluates the BLA and conducts inspections of manufacturing facilities where the product will be produced, it may issue an approval letter or a Complete Response Letter (CRL). An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A CRL indicates that the review cycle of the application is complete and the application is not ready for approval. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. A CRL may require additional clinical data or an additional pivotal Phase 3 clinical trial (s), or other significant, expensive and time- consuming requirements related to clinical trials, preclinical studies or manufacturing. Even with the submission of this additional information, however, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval and issue a denial. The FDA could also approve the BLA with a Risk Evaluation and Mitigation Strategy

plan to mitigate risks associated with the product, 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. The FDA may also condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post- market studies or clinical trials. Such post- market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product' s safety and effectiveness after commercialization. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA' s policies may change, which could delay or prevent regulatory approval of our products under development. Expedited Review and Accelerated Approval Programs A sponsor may seek approval of its product candidate under programs designed to accelerate FDA' s review and approval of NDAs and BLAs. For example, Fast Track designation may be granted to a drug or biologic intended for treatment of a serious or life- threatening disease or condition that has potential to address unmet medical needs for the disease or condition by providing a therapy where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The key benefits of Fast Track designation are more frequent interactions with the FDA during development and testing and eligibility for priority review. The FDA may also review sections of the NDA or BLA for a Fast Track product on a rolling basis before the complete application is submitted, if the sponsor and the FDA agree on a schedule for the submission of the application sections, and the sponsor pays any required user fees upon submission of the first section of the application. Based on results of the Phase 3 clinical trial (s) submitted in a BLA, the FDA may grant the BLA a priority review designation, which sets the target date for FDA action on the application at six months after the FDA accepts the application for filing. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific / medical standard for approval or the quality of evidence necessary to support approval. Fast Track designation may be withdrawn by the sponsor or rescinded by the FDA if the designation is no longer supported by data emerging in the clinical trial process. Under the accelerated approval program, the FDA may approve a BLA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit or, on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that 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. Drugs and biologics granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval. Post- marketing trials or completion of ongoing trials after marketing approval are generally required to verify the drug' s clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, a sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, 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. If so designated, the FDA shall act to expedite the development and review of the product' s marketing application, including by meeting with the sponsor throughout the product' s development, providing timely advice to the sponsor to ensure that the development program to gather preclinical and clinical data is as efficient as practicable, involving senior managers and experienced review staff in a cross-disciplinary review, and assigning a cross- disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor. Post- Approval Requirements Drugs 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 or some changes to the manufacturing process, are subject to prior FDA review and approval. Drug manufacturers are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements. We rely, and expect to continue to rely, on third parties for the production of clinical quantities of our product candidates, and expect to rely in the future on third parties for the production of commercial quantities. Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved BLA, including withdrawal or recall of the product from the market or other voluntary, FDA- initiated or judicial action that could delay or prohibit further marketing, or result in the imposition of post- market studies or trials to assess new safety risks. The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Drugs 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. Orphan Designation and Exclusivity The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200, 000 individuals in the United States, or if it affects more than 200, 000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug for this type of disease or condition will be recovered from sales in the United States. 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, but it entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user- fee waivers. In addition,

if a product is the first to receive FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity. Orphan drug exclusivity, however, also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA for treatment of the same indication or disease. Pediatric Trials and Exclusivity Under the Pediatric Research Equity Act of 2003, as amended, BLAs or supplement to a BLA must contain data that are adequate to assess the safety and effectiveness of an investigational drug or biologic product for the claimed indications in all relevant pediatric populations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. A sponsor who is planning to submit a marketing application for a drug product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan (PSP) within sixty 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 clinical trial. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers if certain criteria are met. The FDA and the sponsor must reach 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. The requirements for pediatric data do not apply to any drug or biologic for an indication for which orphan designation has been granted, except under certain circumstances. Pediatric exclusivity is another type of non- patent exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including orphan exclusivity. This six- month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. Rest of World Government Regulation In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. The cost of establishing a regulatory compliance system for numerous varying jurisdictions can be very significant. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union and in other jurisdictions, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. 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. Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the EU, for example, a clinical trial authorization application (CTA) must be submitted for each clinical protocol to each country' s national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is accepted in accordance with a country' s requirements, the clinical trial may proceed. The requirements and process governing the conduct of clinical trials vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP the applicable regulatory requirements, and the ethical principles that have their origin in the Declaration of Helsinki. Pharmaceutical Coverage, Pricing and Reimbursement Significant uncertainty exists as to the coverage and reimbursement status of any products for which we obtain regulatory approval. In the United States and in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third- party payors. Third- party payors include government authorities, managed care providers, private health insurers and other organizations. Private payors often follow Centers for Medicare & Medicaid Services (CMS' s) determinations relating to Medicare and Medicaid with respect to coverage policy and payment limitations in setting their own reimbursement policies. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third- party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Moreover, a payor' s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third- party reimbursement may not be available or sufficient to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Third- party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost- effectiveness of our products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost- effective. If third- party payors do not consider a product to be cost- effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. The U. S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government- paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of

example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA) contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. There have been **amendments and** executive, judicial and Congressional challenges to certain aspects of the ACA. For example ~~, legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act of 2017, included a provision which repealed, effective January 1, 2019, the tax- based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the " individual mandate. " On June 17, 2021, the Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the " individual mandate " was repealed by Congress. Further~~ , on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022 (IRA) **was signed** into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the " donut hole " under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out- of- pocket cost and creating a new manufacturer discount program. It is possible that the ACA will be subject to **additional amendments and** judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the **current** ~~Biden administration will impact the ACA and our business. Prior to the Supreme Court ruling, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the Biden~~ administration will impact the ACA and our business. In addition, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example ~~, in July 2021, the Biden administration released an executive order, " Promoting Competition in the American Economy, " with multiple provisions aimed at prescription drugs. In response to Biden' s executive order, on September 9, 2021, the Department of Health and Human Services (HHS) released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In addition~~ , the IRA, among other things (i) directs **the U. S. Department of Health and Human Services (** HHS **)** to negotiate the price of certain high- expenditure, single- source drugs and biologics **that have been on the market for at least 7 years** covered under Medicare **(the Medicare Drug Price Negotiation Program)** and (ii) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions ~~take~~ **took** effect progressively starting in fiscal year 2023. On August ~~29~~ **15** , ~~2023~~ **2024** , HHS announced the ~~list~~ **agreed- upon prices** of the first ten drugs that **were** ~~will be~~ subject to price negotiations **, which take effect in January 2026. HHS will select up to fifteen additional products covered under Part D for negotiation in 2025** , although the Medicare drug price negotiation program is currently subject to legal challenges. **Each year thereafter more Part B and Part D products will become subject to the Medicare Drug Price Negotiation Program.** In response to **an** ~~the Biden administration' s~~ October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023, ~~the Biden administration announced~~ an initiative to control the price of prescription drugs through the use of march- in rights under the Bayh- Dole Act **was announced** . On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March- In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march- in rights. While march- in rights have not previously been exercised, it is uncertain if that will continue under the new framework. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Additional state and federal healthcare reform measures may be adopted in the future. In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost- effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly higher barriers are being erected to the entry of new products. In addition, in some countries, cross- border imports from low- priced markets exert a commercial pressure on pricing within a country. The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third- party payors fail to provide adequate coverage and reimbursement. In addition, an increasing

emphasis on cost containment measures in the United States and other countries has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third- party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. Other Healthcare Laws and Compliance Requirements If we obtain regulatory approval for any of our product candidates, we may be 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, marketing and education programs. 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 our ability to operate include: • the federal Anti- Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs; • federal civil and criminal false claims laws and civil monetary penalty laws, including the civil False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third- party payors that are false or fraudulent; • the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters; • the federal transparency laws, including the provision of the ACA referred to as the federal Physician Payments Sunshine Act, that requires certain drug and biologics manufacturers to disclose payments and other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors), certain other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals and ownership interests of physicians and their immediate family members; • HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, which imposes certain requirements on HIPAA covered entities, their business associates and their covered subcontractors relating to the privacy, security and transmission of individually identifiable health information; and • state law equivalents of each of the above federal laws, such as anti- kickback and false claims laws that may apply to items or services reimbursed by any third- party payor, including commercial insurers, and state laws governing transparency, marketing and drug pricing reporting, and the privacy and security of health 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. The ACA broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and certain other criminal healthcare fraud statutes. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the ACA provides that 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 civil False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti- Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs. We are also subject to the U. S. Foreign Corrupt Practices Act (FCPA), which prohibits improper payments or offers of payments to foreign governments and their officials for the purpose of obtaining or retaining business. Safeguards we implement to discourage improper payments or offers of payments by our employees, consultants, and others may be ineffective, and violations of the FCPA and similar laws may result in severe criminal or civil sanctions, or other liabilities or proceedings against us, any of which would likely harm our reputation, business, financial condition and result of operations. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including significant administrative, civil and criminal penalties, exclusion from participation in government healthcare programs, such as Medicare and Medicaid and imprisonment, disgorgement, damages, fines, additional reporting requirements and regulatory oversight and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Employees and Human Capital Resources As of December 31, ~~2023~~ **2024**, we had 59 employees, 56 of which were full- time employees. Of our full- time employees, 36 serve in roles related to research and development, clinical, manufacturing and regulatory affairs, and 20 serve in general and administrative capacities. As of December 31, ~~2023~~ **2024**, all of our employees were based in the United States. We also engage temporary consultants and contractors. All of our employees are " at – will, " which means that each employee can terminate his or her relationship with us and we can terminate our relationship with him or her, at any time. None of our employees are represented by a labor union or covered by collective bargaining agreements. We consider our relationship with our employees to be good. We compete in the highly competitive biotechnology industry. Attracting, developing and retaining talented employees is crucial to executing our strategy and our ability to compete effectively. Our ability to recruit and retain such talent depends on several factors, including compensation and benefits, talent development and career opportunities, and work environment. To that end, we invest in our employees to be an employer of choice. Our Code of Business Conduct and Ethics (Code of Conduct) ensures that our core values of respect, integrity, collaboration, innovation, trust, and excellence are applied throughout our operations. Our Code of Conduct serves as a critical tool to help all of us recognize and report unethical conduct, while preserving and nurturing our culture of honesty and accountability. The physical health, financial wellbeing, work- life balance and mental health of our employees is vital to our success. Our environmental, health and safety team stays abreast of local, regional and global concerns and trends and ensures safety procedures are in place to mitigate workplace injuries and safety risks. Our employees are required to complete training in various safety procedures for the laboratories and manufacturing facilities and specialized safety training based on particular job duties. Our Designated Safety Officers and response teams oversee safety- related initiatives and a safety committee that provides input on safety procedures, practices, and policies. Our employees are required to wear personal protective equipment relevant for their particular job duties. Occupational injuries at

our facilities are extremely low and are always investigated to determine if any environmental or other changes need to be implemented. Financial Information about Segments We operate in a single accounting segment. Refer to Note 1 to our consolidated financial statements included elsewhere in this Annual Report. Corporate Information We were incorporated under the laws of the State of Delaware in September 2005. Our principal executive office is located at 10240 Sorrento Valley Road, Suite 300, San Diego, California 92121, and our telephone number is (858) 731- 8389. Our website address is www. atyrpharma. com. You are advised to read this Annual Report in conjunction with other reports and documents that we file from time to time with the SEC. Our Annual Reports on Form 10- K, Quarterly Reports on Form 10- Q, Current Reports on Form 8- K, and amendments to these reports filed or furnished pursuant to Section 13 (a) or 15 (d) of the Exchange Act, are available free of charge on our website as soon as reasonably practicable after such reports and amendments are electronically filed with, or furnished to, the SEC. You may obtain copies of these reports directly from us or from the SEC. In addition, the SEC maintains information for electronic filers (including aTyr Pharma, Inc.) at its website at www. sec. gov. We also make available copies of our news releases and other financial information and updates with respect to our business on our website. We do not incorporate the information on or accessible through our website into this Annual Report, and you should not consider any information on, or that can be accessed through, our website as part of this Annual Report. Item 1A. Risk Factors You should carefully consider the following risk factors, as well as the other information in this Annual Report on Form 10- K (Annual Report) and in our other public filings with the SEC. The occurrence of any of these risks could harm our business, financial condition, results of operations and / or growth prospects or cause our actual results to differ materially from those contained in forward- looking statements we have made in this Annual Report and those we may make from time to time. You should consider all of the risk factors described in our public filings when evaluating our business. Risks related to the discovery, development and regulation of our product candidates We may encounter substantial delays and other challenges in our ongoing or planned clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical trials are expensive, time- consuming, often delayed and uncertain as to outcome. We cannot guarantee that our ongoing **clinical trials, including our EFZO- FIT study and our Phase 2 study in systemic sclerosis (SSc, also known as scleroderma) associated- interstitial lung disease (ILD) (SSc- ILD) (the EFZO- CONNECT study),** or planned clinical trials will be initiated or conducted as planned or completed on schedule, if at all. We cannot assure you that our product candidates will not be subject to new clinical holds or significant delay in the future. For example, we may experience delays in site initiation and patient enrollment, failures to comply with study protocols, delays in the manufacture of study drug for clinical testing and other difficulties in starting or completing our ~~Phase 3 randomized, double- blind, placebo- controlled clinical trial to evaluate the efficacy and safety of efzofitimod in patients with pulmonary sarcoidosis (the EFZO- FIT study) and our Phase 2 study in systemic sclerosis (SSc also known as scleroderma) associated- ILD (SSc- ILD) (the EFZO- CONNECT study) or future~~ clinical trials. Any inability to initiate or complete clinical trials of our product candidates in the United States, as a result of clinical holds or otherwise, would delay our clinical development plans, may require us to incur additional clinical development costs and could impair our ability to obtain U. S. regulatory approval for such product candidates. A failure of one or more clinical trials can occur at any stage of testing, and our clinical trials may not be successful. Events that may prevent successful or timely completion of clinical development include, but are not limited to: • our inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation of human clinical trials, including clinical trials of certain dosages; • delays in reaching consensus with regulatory agencies on trial design, including the endpoints for our ~~global pivotal Phase 3 study of efzofitimod in patients with pulmonary sarcoidosis (the~~ EFZO- FIT study ~~)~~, and prioritization of outcome measurements that would best support the evaluation of efzofitimod' s efficacy; • delays in reaching agreement on acceptable terms with prospective clinical contract research organizations (CROs) and clinical trial sites, including any delays resulting from changes in CROs; • delays in obtaining required institutional review board or Ethics Committee approval at each clinical trial site; • delays in recruiting suitable patients to participate in our clinical trials, or delays that may result if the number of patients required for a clinical trial is larger than we anticipate; • imposition of a clinical hold by regulatory agencies, which may occur at any time before or during a clinical trial, including after our submission of data to these agencies or an inspection of our clinical trial operations or trial sites; • failure by our CROs, investigators, other third parties or us to adhere to clinical trial requirements; • failure to perform in accordance with the good clinical practices (GCPs) of the U. S. Food and Drug Administration (FDA) or applicable regulatory requirements in other countries; • delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites; • delays in having patients complete participation in a trial or return for post- treatment follow- up; • disagreements with regulators regarding our interpretation of data from preclinical studies or clinical trials; • occurrence of adverse events associated with a product candidate that are viewed to outweigh its potential benefits; or • changes in regulatory requirements and guidance that require amending or submitting new clinical protocols. Any delay in or inability to successfully complete preclinical and clinical development (including any delays resulting from any changes in a CRO) could result in additional costs to us and impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates (including our technology transfer to another contract development manufacturing organization (CDMO) for bulk drug substance and production capacity changes for efzofitimod), we will need to conduct additional comparability studies to bridge our modified product candidates to earlier versions, and the data generated from these comparability studies will need to be reviewed and accepted by the FDA or other regulatory authorities. If the results of our clinical trials are perceived to be negative or inconclusive, or if there are safety concerns or adverse events associated with our product candidates, we may be required to perform additional clinical trials to support approval or be subject to additional post- marketing testing requirements; be delayed in obtaining marketing approval for our product candidates, if at all; obtain approval for indications or patient populations that are not as broad as intended or desired;

obtain approval with labeling that includes significant use or distribution restrictions or safety warnings; be subject to changes in the way the product is manufactured or administered; have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy; be subject to litigation; or experience damage to our reputation. To date, the safety and efficacy of efzofitimod has only been studied in a limited number of humans. Accordingly, efzofitimod and any future product candidates could potentially cause unexpected adverse events. In addition, the inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to the natural progression of the disease. Further, if patients drop out of our ongoing or future clinical trials, miss scheduled doses or follow- up visits or otherwise fail to follow trial protocols, or if our clinical trials are otherwise disrupted due to global geopolitical tension, armed conflicts, potential future health pandemics or other adverse macroeconomic and geopolitical events, the integrity of data from our clinical trials may be compromised or not accepted by the FDA or other regulatory authorities, which would represent a significant setback for the applicable program. In addition, the COVID- 19 pandemic previously impacted clinical trials broadly, including our completed efzofitimod Phase 1b / 2a trial in patients with pulmonary sarcoidosis, where many sites stopped enrollment and patients chose not to enroll or continue participating in the trial due to the impact of COVID- 19. While we completed the clinical trial, the availability of results from the Phase 1b / 2a clinical trial was delayed until September 2021. If we are unable to successfully complete or otherwise advance clinical development, obtain regulatory or marketing approval for, or successfully commercialize our therapeutic product candidates, including efzofitimod, or experience significant delays in doing so, our business will be materially harmed. To date, we have expended significant time, resources and effort on the discovery and development of product candidates related to the extracellular proteins derived from the histidyl tRNA synthetase (HARS) family, including conducting preclinical studies and clinical trials. We have not yet completed any evaluation of our product candidates in human clinical trials designed to demonstrate efficacy to the satisfaction of the FDA. Before we can market or sell our therapeutic candidates in the United States or foreign jurisdictions, we will need to commence and complete additional clinical trials ~~(including our EFZO- CONNECT study)~~ and larger, pivotal trials ~~(like the EFZO- FIT study)~~, manage clinical and manufacturing activities, obtain necessary regulatory approvals from the FDA in the United States and from similar regulatory authorities in other jurisdictions, obtain adequate clinical and commercial manufacturing supplies, build commercial capabilities, which may include entering into a marketing collaboration with a third party, and in some jurisdictions, obtain reimbursement authorization, among other things. We cannot assure you that we will be able to successfully complete the necessary clinical trials, obtain regulatory approvals, secure an adequate commercial supply for, or otherwise successfully commercialize our therapeutic candidates. If we do not receive regulatory approvals for our product candidates, and even if we do obtain regulatory approvals, we may never generate significant revenues, if any, from commercial sales. If we fail to successfully commercialize our therapeutic candidates, we may be unable to generate sufficient revenues to sustain and grow our company, and our business, prospects, financial condition and results of operations will be adversely affected. There is no established FDA regulatory pathway for approval of a drug in pulmonary sarcoidosis. As a result, the EFZO- FIT study, even if successful, may not be sufficient to support FDA approval, which would materially and adversely harm our business. During the third quarter of 2022, we initiated the EFZO- FIT study. The only FDA- approved therapies for the treatment of sarcoidosis are glucocorticoids which were approved by the FDA in the 1950s, prior to current regulatory standards. As such, the most appropriate efficacy endpoints to demonstrate clinically meaningful treatment effects have not been established. In this instance, without regulatory precedent for established endpoints, the FDA has not endorsed a specific **primary endpoint nor a specific** means for measurement of steroid reduction. ~~Therefore, we~~ **We have selected steroid reduction as our primary endpoint and** are measuring steroid reduction in multiple ways in an effort to support an approval. Our rationale for selecting endpoints for the EFZO- FIT study is based on the anticipated effects of efzofitimod in pulmonary sarcoidosis consistent with the results of our completed Phase 1b / 2a study in patients with pulmonary sarcoidosis. The FDA has highlighted the risk of proceeding with a larger study of longer duration based on our limited Phase 1b / 2a data **and without FDA endorsement of a specific primary endpoint**, and our inability to replicate the findings in our Phase 1b / 2a study **or the FDA' s refusal to accept our selected primary endpoint** would not support FDA approval and will adversely affect our business, prospects, financial condition and results of operations. In addition, the FDA has substantial discretion in the approval process and may refuse to accept ~~any~~ **our** application or decide that our data are insufficient for approval and require additional preclinical, clinical or other trials, which would be costly and significantly delay the potential for regulatory approval. In particular, even if we were to receive positive data from the EFZO- FIT study, the FDA may determine that the data is not compelling enough for approval **or may not accept our selected primary endpoint**. The FDA may also require a panel of experts, referred to as an Advisory Committee, to deliberate on the adequacy of the safety and efficacy data to support approval. The opinion of the Advisory Committee, although not binding, may have a significant impact on our ability to obtain approval of efzofitimod based on the completed clinical trials. Interim, top- line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data. From time to time, we may publicly disclose preliminary or top- line data from our clinical studies, which are based on a preliminary analysis of then- available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. 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. Top- line data 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, top- line data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our clinical studies. In addition, we may report interim analyses of only certain endpoints rather than all

endpoints. Interim data 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. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock. 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 program, the approvability or commercialization of a 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 material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate or our business. If the top- line 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, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition. We have encountered and may continue to encounter delays and difficulties enrolling patients in our clinical trials for a variety of reasons, including the limited number of patients who have the diseases for which certain of our product candidates are being studied, which could delay or halt the clinical development of our product candidates. Identifying and qualifying patients to participate in clinical trials for our product candidates is critical to our success. Certain of the conditions for which we may elect to evaluate our product candidates may be rare diseases with limited patient pools from which to draw for clinical trials. **We may be unable to identify and enroll a sufficient number of patients with the disease in question and who meet the eligibility criteria for, and are willing to participate in, our clinical trials.** For example ~~, we are conducting the EFZO- FIT study in patients with pulmonary sarcoidosis. While estimates of pulmonary sarcoidosis prevalence vary, we estimate that pulmonary sarcoidosis affects an estimated 200, 000 patients in the United States. Of that population, however, we estimate that approximately 70 % experience symptomatic disease such that our targeted population is smaller. The eligibility criteria for any of our clinical trials may further limit the pool of available participants in our clinical trials. For example, if patients have been previously prescribed certain other medications to treat pulmonary sarcoidosis or if they have not been on steroids for a certain period of time, they may not be eligible to participate in the EFZO- FIT study, thus further reducing our patient pool. We may be unable to identify and enroll a sufficient number of patients with the disease in question and who meet the eligibility criteria for, and are willing to participate in, the clinical trials. Once enrolled, patients may decide or be required to discontinue from the clinical trial due to inconvenience, burden of trial requirements, adverse events associated with efzofitimod, limitations required by trial protocols or other reasons. Additionally~~ , we are conducting the EFZO- CONNECT study in patients with SSc- ILD ~~. It~~ **, where it** is estimated that approximately 100, 000 people in the United States are affected by SSc and up to 80 % may develop ~~interstitial lung disease (~~ILD ~~)~~ **. In addition to the limited potential patient population, the eligibility criteria may further limit the pool of available participants in the EFZO- CONNECT study. Once enrolled, patients may decide or be required to discontinue from the clinical trial due to inconvenience, burden of trial requirements, adverse events associated with efzofitimod, limitations required by trial protocols or other reasons** . Our ability to identify, recruit, enroll and maintain a sufficient number of patients, or those with required or desired characteristics to achieve diversity in our clinical trials in a timely manner may also be affected by other factors, including, but not limited to: • proximity and availability of clinical trial sites for patients; • severity of the disease under investigation; • design of the study protocol and the burdens to patients of compliance with our study protocol; • perceived risks and benefits of the product candidate under study; • availability of competing therapies and clinical trials for the patient populations and indications under study; • efforts to facilitate timely enrollment in clinical trials; • patient referral practices of physicians; and • ability to monitor patients adequately during and after treatment. We plan to seek initial marketing approval in the United States. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA or other regulatory agencies. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including, but not limited to: • difficulty in establishing or managing relationships with or changes in CROs and physicians; • different requirements and standards for the conduct of clinical trials; • our inability to locate qualified local consultants, physicians and partners; and • the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of biotechnology products and treatment. Additionally, if patients are unwilling to participate in our clinical trials because of negative publicity from adverse events in our clinical trials or in the biotechnology or protein therapeutics industries or for other reasons, including competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product development or termination of our clinical trials altogether. If we have difficulty enrolling and maintaining a sufficient number of patients to conduct our clinical trials as planned for any reason, we may need to delay, limit or terminate clinical trials, any of which would have an adverse effect on our business, prospects, financial condition and results of operations. Furthermore, clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to obtain orphan exclusivity and successfully commercialize our product candidates and may have an adverse effect on our business, financial condition and results of operations. Our current product candidates and any other..... financial condition and results of operations. We have previously conducted and we or our third - party collaborators may conduct additional clinical trials of efzofitimod outside of the United States. The FDA, however, may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business. In June 2018, we completed a Phase 1 clinical

trial of efzofitimod in healthy subjects in Australia. This randomized, double- blind, placebo- controlled study investigated the safety, tolerability, immunogenicity, and pharmacokinetics (PK) of intravenous efzofitimod in 36 healthy volunteers. In addition, we or our third - party collaborators may choose to conduct additional clinical trials for efzofitimod in countries outside the United States, subject to applicable regulatory approval. For example, our partner, Kyorin Pharmaceutical Co., Ltd. (Kyorin), conducted and funded an efzofitimod Phase 1 clinical trial in 32 healthy Japanese male volunteers and is participating in the EZFO- FIT study. ~~We are enrolling subjects in~~ **In July 2024, we completed enrollment of** the ~~EZFO -~~ **EFZO** - FIT study **with a total of 268 subjects** in centers in the United States, Europe ~~and ,~~ Brazil ~~and~~ **, as well as centers in Japan where our partner** Kyorin **led** ~~is enrolling subjects in~~ the **enrollment effort** ~~EZFO- FIT study in centers in Japan~~ . Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of such study data is generally subject to certain conditions. For example, in cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable in the U. S. population and U. S. medical practice; and (ii) the clinical trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations. Additionally, the FDA' s clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. In addition, when studies are conducted only at sites outside of the United States, the FDA generally does not provide advance comment on the clinical protocols for the studies, and therefore there is an additional risk that the FDA could determine that the study design or protocol for a non- U. S. clinical trial was inadequate, which would likely require us to conduct additional clinical trials, in which case our development plans will be delayed, which could materially harm our business. Conducting clinical trials outside the United States also exposes us to additional risks, including risks associated with: • additional foreign regulatory requirements; • foreign exchange fluctuations; • compliance with foreign manufacturing, customs, shipment and storage requirements; • cultural differences in medical practice and clinical research; • evolving global geopolitical tension, armed conflicts and macroeconomic developments ~~,~~; and • diminished protection of intellectual property in some countries. Further, the integrity of data from any clinical trials conducted outside of the United States may not be acceptable to the FDA. Our therapeutic product candidates may cause undesirable..... financial condition and results of operations. We may not be successful in our efforts to..... and results of operations. We may face **CDMO** manufacturing stoppages and other **CDMO** challenges associated with the clinical or commercial manufacture of our product candidates. All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our ~~existing~~ CDMOs for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or use in late- stage clinical trials must be manufactured in accordance with cGMPs. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our CDMOs must supply all necessary documentation in support of a biologics license application (BLA) on a timely basis and must adhere to the FDA' s Good Laboratory Practices and cGMP regulations enforced by the FDA through its facilities inspection program. The facilities and quality systems of our CDMOs and other CROs must pass a pre- approval inspection for compliance with applicable regulations as a condition of regulatory approval of our product candidates. If these facilities do not pass a pre- approval plant inspection, FDA approval of the products will not be granted. If anything were to prevent the FDA or other regulatory authorities from conducting their regular inspections, it could impact the ability of our CDMOs to provide us with product for clinical trials. The regulatory authorities also may, at any time following approval of a product for sale, audit the facilities in which the product is manufactured. If any such inspection or audit of our facilities or those of our CDMOs and CROs identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independently of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly or time- consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business. If we or any of our CDMOs and CROs fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new biologic product, or revocation of a pre- existing approval. Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in clinical or commercial supply. An alternative manufacturer would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. In addition, the manufacture of our product candidates presents challenges associated with biologics production, including the inherent instability of larger, more complex molecules and the need to ensure uniformity of the drug substance produced in different facilities or across different batches. The process of manufacturing biologics is extremely susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing and distribution processes for any of our product candidates could result in reduced production yields, product defects, and other supply disruptions. Furthermore, although tRNA synthetases represent a class of proteins that may share immunomodulatory properties in various physiological pathways, each tRNA synthetase has a different structure and may have unique manufacturing requirements that are not applicable across the entire class. For example, fusion proteins, such as efzofitimod, include an additional antibody domain to improve PK characteristics, and may therefore require a more complex and time- consuming manufacturing process than other tRNA synthetase- based therapeutic candidates. Currently, we are producing our efzofitimod molecule in E. coli. The manufacturing processes for one of our product candidates may not be readily adaptable to other product candidates that we develop, and we

may need to engage multiple third- party manufacturers to produce our product candidates. For example, we engaged an additional CDMO to manufacture efzofitimod and completed a technology transfer and validation process before the ~~new~~ CDMO was able to produce additional bulk drug substance. **During 2023, the CDMO completed its first and second full, commercial- scale bulk drug substance GMP runs. Quality release testing was completed and all release specifications were met, supporting the CDMO' s ability to produce bulk drug substance of efzofitimod for commercial purposes if we receive regulatory approval for efzofitimod. During 2024, we initiated preparatory work with the CDMO on process performance qualification batches that will be required as part of our potential BLA submission for efzofitimod. During the first quarter of 2025, the first of three upstream batches did not meet process performance qualification specifications, and will need to be replaced. The replacement batch has been scheduled with our CDMO. The deviation of this first batch was due to operational errors at the CDMO and not related to the underlying process nor the drug substance. Future operational errors in these batches could negatively impact the timing of our potential BLA submission and could require significant additional funding.** Any **additional** adverse developments affecting manufacturing operations for our product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls or other interruptions in the supply of our drug substance and drug product which could delay the development of our product candidates **, the timing of our potential BLA submission for efzofitimod and could require significant additional funding** . We may also have to write off inventory, incur other charges and expenses for supply of drug product that fails to meet specifications or expires, undertake costly remediation efforts, or seek more costly manufacturing alternatives. Any manufacturing stoppage or delay, or any inability to consistently manufacture adequate supplies of our product candidates for our clinical trials or on a commercial scale will harm our business, prospects, financial condition and results of operations. Even if we complete the necessary preclinical studies and clinical trials, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate, and the scope of any approval may be narrower than we expect. We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA advisory committee or regulatory authority recommends non- approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested, may impose restrictions on dosing or may grant approval subject to the performance of post- marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. Although we have obtained orphan drug designation for efzofitimod for the treatment of sarcoidosis and systemic sclerosis in the United States and for the treatment of sarcoidosis **,** in the European Union (EU) **and in Japan** we may not receive orphan drug designation for efzofitimod in other jurisdictions or for other indications that we may pursue, or for any other product candidates we may develop under any new applications for orphan drug designation that we may submit, and any orphan drug designations that we have received or may receive may not confer marketing exclusivity or other expected commercial benefits. The FDA granted orphan drug designation to efzofitimod for the treatment of sarcoidosis in January 2022 and SSc in April 2022. The European Commission, on the basis of the opinion of the European Medicines Agency (EMA) Committee for Orphan Medicinal Products (COMP) granted orphan drug designation to efzofitimod for the treatment of sarcoidosis in January 2023 and for the treatment of SSc in June 2023. **In Japan, the Pharmaceutical and Medical Devices Agency (PMDA) has granted efzofitimod orphan drug designation for the treatment of sarcoidosis to Kyorin, our partner in Japan in August 2023.** We may apply for orphan drug designation for efzofitimod for other indications and product candidates in the United States and the EU. Under the Orphan Drug Act, the FDA may designate a drug or biologic product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200, 000 in the United States, or a patient population greater than 200, 000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the EU, the EMA' s COMP grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life- threatening or chronically debilitating condition affecting not more than five in 10, 000 persons in the EU. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life- threatening, seriously debilitating or serious and chronic condition when, without incentives, it is unlikely that sales of the drug in the EU would be sufficient to justify the necessary investment in developing the drug or biological product or where there is no satisfactory method of diagnosis, prevention, or treatment, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition. Orphan drug status confers up to ten years of marketing exclusivity in Europe, and up to seven years of marketing exclusivity in the United States, for a particular product in a specified indication. Obtaining an orphan drug designation can be difficult and we cannot assure you that we will be able to obtain orphan drug designation in other jurisdictions or for other indications, or rely on orphan drug or similar designations to exclude other companies from manufacturing or selling products using the same principal mechanisms of action for the same indications that we pursue beyond these timeframes. Furthermore, marketing exclusivity in Europe can be reduced from ten years to six years if the initial designation criteria have significantly changed since the market authorization of the orphan product. Even if we are the first to obtain marketing authorization for an orphan drug indication, there are circumstances under which a competing product may be approved for the same indication during the period of marketing exclusivity, such as if the later product is shown to be clinically superior to the orphan product, or if the later product is deemed a different product than ours. Further, the marketing exclusivity would not prevent competitors from obtaining approval of the same product candidate as ours for indications other than those in which we have been granted orphan drug designation, or for the use of other types of products in the same indications as our orphan product. A breakthrough therapy or

Fast Track designation by the FDA, including the Fast Track designation we received for efzofitimod, may not lead to expedited development or regulatory review or approval. In 2022, the FDA granted Fast Track designation to efzofitimod for the treatment of pulmonary sarcoidosis and for the treatment of SSc- ILD. We may seek, from time to time, breakthrough therapy or Fast Track designation for our product candidates. A breakthrough therapy designation is for a product candidate intended to treat a serious or life- threatening condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement on a clinically significant endpoint (s) over available therapies. A Fast Track designation is for a product candidate that treats a serious or life- threatening condition, and preclinical or clinical data demonstrate the potential to address an unmet medical need. The FDA has broad discretion whether or not to grant these designations. Accordingly, even if we believe a particular product candidate is eligible for breakthrough therapy or Fast Track designation, we cannot assure you that the FDA would decide to grant it. Even if we receive breakthrough therapy or Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw breakthrough therapy or Fast Track designation if it believes that the product no longer meets the qualifying criteria. In addition, the breakthrough therapy program is a relatively new program. As a result, we cannot be certain whether any of our product candidates can or will qualify for breakthrough therapy designation. Our business may be harmed if we are unable to avail ourselves of these or any other expedited development and regulatory pathways. Disruptions at the FDA and other government agencies caused by **layoffs,** funding shortages or global health concerns could negatively impact our business. The ability of the FDA to review and approve proposed clinical trials or new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA' s ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA' s ability to perform routine functions. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, **including executive and congressional priorities, the impacts of** which ~~is~~ **are** inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including for 35 days beginning on December 22, 2018, the U. S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities **. In addition, the current administration has proposed substantial reductions in force at various government agencies that, if applied to the FDA in a material way, could significantly reduce the FDA' s capacity to perform its functions in a manner consistent with its past practices and could negatively impact our business** . Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny. Even if we obtain regulatory approval for a product candidate, such product will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post- marketing studies, adverse event reporting and submission of safety, efficacy, and other post- market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities. We and our CDMOs will be subject to continual review and inspections to assess compliance with cGMPs and adherence to commitments made in any BLA or marketing authorization application (MAA). Accordingly, we and others with whom we work will need to continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control. Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post- marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. If new safety issues emerge, we may be required to change our labeling. Any new legislation addressing drug safety or efficacy issues could result in delays in product development or commercialization, or increased costs to assure compliance. We will have to comply with requirements concerning advertising and promotion for our products. Violations, including actual or alleged promotion of our products for unapproved, or off- label, uses are subject to enforcement letters, inquiries and investigations, and civil and criminal sanctions. Any actual or alleged failure to comply with labeling and promotion requirements may have a negative impact on our business. In the United States, engaging in impermissible promotion of our products for off- label uses can also subject us to false claims litigation under federal and state statutes, which can lead to civil and criminal penalties and fines, agreements that would materially restrict the manner in which we promote or distribute our drug products and exclusion from Medicare, Medicaid and other federal and state healthcare programs. These false claims statutes include the federal False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government prevails in the lawsuit, the individual will share in any fines or settlement funds. If we do not lawfully promote our approved products, we may become subject to such litigation and, if we are not successful in defending against such actions, those actions could compromise our ability to become profitable. The holder of an approved BLA or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post- marketing clinical trials to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval were obtained through an accelerated approval pathway, we could be required to conduct a successful post- marketing clinical trial to confirm clinical benefit for our products. An unsuccessful post- marketing study or failure to complete such a trial could result in the withdrawal of marketing approval. If a regulatory agency discovers 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 disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement

authority may, among other things: • issue untitled or warning letters; • impose civil or criminal penalties; • suspend or withdraw regulatory approval; • suspend any of our ongoing clinical trials; • refuse to approve pending applications or supplements to approved applications submitted by us; • impose restrictions on our operations, including closing our CDMOs' facilities; or • seize or detain products, or require or request a product recall. Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected. ~~results of operations.We may~~ not be successful in our efforts to identify or discover additional product candidates.A key element of our strategy is to expand applications of efzofitimod to additional immune-mediated diseases and leverage our discovery platform to identify the therapeutic potential of extracellular proteins derived from tRNA synthetases to help identify or discover additional product candidates.A significant portion of the research that we are conducting involves new compounds and drug discovery methods,including our proprietary technology.Our drug discovery activities using our proprietary technology may not be successful in identifying product candidates that are useful in treating diseases.Our research programs may initially show promise in identifying potential product candidates,yet fail to yield product candidates for clinical development for a number of reasons,including:• the research methodology used may not be successful in identifying appropriate potential product candidates;or • potential product candidates may,on further study,be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be product candidates that will receive marketing approval and achieve market acceptance.Research programs to identify new product candidates require substantial technical,financial and human resources.We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful.If we are unable to identify suitable product candidates for preclinical and clinical development and regulatory approval,we will not be able to generate product revenues,which would have an adverse impact on our business,prospects,financial condition and **results of operations.We may** Risks related to our financial condition and need for additional capital We will need to raise additional capital or enter into strategic partnering relationships to fund our operations. The development of therapeutic product candidates is expensive, and we expect our research and development expenses to fluctuate. As of December 31, ~~2023~~ **2024** , our cash, cash equivalents, restricted cash and available- for- sale investments were approximately $ ~~101~~ **75** . ~~7~~ **1** million. We believe that our current cash, cash equivalents, restricted cash and available- for- sale investments, will be sufficient to meet our material cash requirements for known contractual and other obligations for a period of at least one year from the date of this Annual Report. However, our operating plans may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through equity or debt offerings, grant funding, collaborations, strategic partnerships and / or licensing arrangements. Our future funding requirements are difficult to forecast and will depend on many factors, including but not limited to: • the type, number, scope progress, expansions, results, costs and timing of, our clinical trials and preclinical studies for our product candidates or other potential product candidates or indications which we are pursuing or may choose to pursue in the future, including changes in our CROs or CDMOs; • the costs, timing and outcome of regulatory review of our product candidates; • potential delays of our planned clinical trials of efzofitimod; • cost increases related to the manufacturing of preclinical study and clinical trial materials, including cost increases related to technology transfers to additional CDMOs and any delays in the manufacturing of study drug; • cost increases as a result of global geopolitical tension, armed conflicts, potential future health pandemics, liquidity concerns at, and failures of, banks and other financial institutions or other disruptions in the banking system or financing markets **, tariffs and trade tensions** , higher interest rates and financial and credit market fluctuations, volatility in the capital markets, labor shortages, economic slowdowns, recessions or market corrections, inflation and monetary supply shifts and tightening of credit markets; • the number and characteristics of product candidates that we pursue; • the scope, progress, results and costs of preclinical development, and clinical trials for other product candidates; • our ability to maintain existing and enter into new collaboration and licensing arrangements and the timing of any payments we may receive under such arrangements; • the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property- related claims; and • the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval. In any event, we will require additional capital to complete additional clinical trials, to obtain regulatory approval for, and to commercialize, our product candidates, such as efzofitimod. Raising funds in the current and future economic environment may present additional challenges. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidates, or we may be unable to expand our operations, maintain our current organization and employee base or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. The terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would cause dilution to all of our stockholders. The incurrence of indebtedness would result in fixed payment obligations and may require us to agree to certain restrictive covenants, such as limitations on our ability to incur debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. As a result of global geopolitical and macroeconomic conditions, liquidity concerns at, and failures of, banks and other financial institutions or other disruptions in the banking system or financing markets, **tariffs and trade tensions,** higher interest rates and financial and credit market fluctuations, volatility in the capital markets, the global credit and financial markets have experienced volatility and disruptions, including severely diminished

liquidity and credit availability, declines in consumer confidence, declines in economic growth, volatility in unemployment rates, inflation, higher interest rates and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. In addition, any fundraising efforts may divert our management from their day- to- day activities, which may adversely affect our ability to develop and commercialize our product candidates ~~. Additionally, financial markets around the world experienced volatility following the invasion of Ukraine by Russia in February 2022. In response to the invasion, the United States, United Kingdom and European Union (EU), along with others, imposed significant new sanctions and export controls against Russia, Russian banks and certain Russian individuals and may implement additional sanctions or take further punitive actions in the future. The full economic and social impact of the sanctions imposed on Russia (as well as possible future punitive measures that may be implemented), as well as the counter measures imposed by Russia, in addition to the ongoing Ukraine- Russian conflict, which could conceivably expand into the surrounding region, remains uncertain; however, both the conflict and related sanctions have resulted and could continue to result in disruptions to trade, commerce, pricing stability, credit availability and / or supply chain continuity in both Europe and globally, and has introduced significant uncertainty into global markets. In particular, the ongoing Ukraine- Russia conflict has contributed to rapidly rising costs of living (driven largely by higher energy prices) in Europe and other advanced economies. Similarly, the conflict in the Middle East has resulted, and may continue to result, in disruptions to trade and supply chain continuity, and has increased supply chain costs, the full effects of which remains uncertain. Further, a weak or declining economy could strain our suppliers and manufacturers, possibly resulting in additional supply disruption for the production of efzofitimod. As a result, our business and results of operations may be adversely affected by the ongoing Ukraine- Russia conflict, particularly to the extent it escalates to involve additional countries, further economic sanctions or wider military conflict. In addition, global economic and business activities continue to face widespread macroeconomic uncertainties, including liquidity concerns at, and failures of, banks and other financial institutions or other disruptions in the banking system or financing markets, higher interest rates and financial and credit market fluctuations, volatility in the capital markets, labor shortages, inflation and monetary supply shifts, and recession risks, which has resulted in further volatility in the U. S. and global financial markets and which has led to, and may continue to lead to, additional disruptions to trade, commerce, pricing stability, credit availability and supply chain continuity globally. The ultimate long- term impact of the ongoing Ukraine- Russia conflict, the conflict in the Middle East, and other evolving geopolitical and macroeconomic conditions on our business is uncertain, although we continue to actively monitor the impact of these factors on our results of operations, financial condition and cash flows. The extent of the impact of these factors on our operational and financial performance, including our ability to execute our business strategies and initiatives in the expected time frame, will depend on future developments, which are uncertain and cannot be predicted; however, any continued or renewed disruption resulting from these factors could negatively impact our business ~~. We are a pre- commercial biotherapeutics company and have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We are a pre- commercial biotherapeutics company, and we have not yet generated any revenues from product sales. We have incurred net losses in each year since our inception in 2005, including consolidated net losses of $ ~~50~~ **64** . ~~4~~ **0** million for the year ended December 31, ~~2023~~ **2024** . As of December 31, ~~2023~~ **2024** , we had an accumulated deficit of $ ~~468~~ **532** . 0 million. We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through the sale of equity securities and convertible debt and through venture debt, term loans and license and collaboration agreement revenues. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity offerings, grant funding, collaborations, strategic partnerships and / or licensing arrangements. We have not completed registrational clinical trials for any product candidate to date and it will be several years, if ever, before we have a product candidate ready for commercialization. Even if we obtain regulatory approval to market a product candidate, our future revenues will depend, in part, upon the size of any markets in which our product candidates have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third- party payors and adequate market share for our product candidates in those markets. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will fluctuate in connection with our ongoing activities as we: continue our research and preclinical and clinical development of efzofitimod or any other product candidates that we may develop; obtain clinical trial materials and further develop the manufacturing process for our product candidates; seek regulatory approvals for our product candidates that successfully complete clinical trials; ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; seek to identify and validate additional product candidates; maintain, protect and expand our intellectual property portfolio; acquire or in- license other product candidates and technologies; attract and retain skilled personnel; and create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts. Our revenues, expenses and income or losses may fluctuate significantly from quarter to quarter and year to year, such that a period- to- period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline. We have never generated any revenue from product sales and may never be profitable. Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize our product candidates. We do not anticipate generating revenues from product sales for the foreseeable future, if ever. Our ability to generate future revenues from product sales depends heavily on our success in: • completing research, preclinical development and clinical development of our product candidates, potentially with a strategic partner; • seeking and obtaining regulatory approvals for product candidates for which we complete clinical trials; • developing a sustainable, scalable, reproducible, and transferable manufacturing process for our product candidates and establishing supply and manufacturing

relationships with third parties; • launching and commercializing product candidates for which we obtain regulatory approval, either by collaborating with a partner or, if launched independently, by establishing a sales force, marketing and distribution infrastructure; • maintaining, protecting and expanding our intellectual property portfolio; • obtaining market acceptance of our product candidates as viable treatment options for our target indications; • identifying and validating new therapeutic product candidates; • attracting, hiring and retaining qualified personnel; and • negotiating favorable terms in any licensing, collaboration or other arrangements into which we may enter. Even if one of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any such approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA or other regulatory agencies, domestic or foreign, to perform clinical trials and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Risks related to our reliance on third parties We depend on our existing collaborations and may depend on collaborations with additional third parties for the development and commercialization of certain of our product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates. We have entered into, and may continue to enter into, research collaborations for the research and development of specified product candidates. Our sole source of revenue depends upon the performance by these collaborators of their responsibilities under these arrangements. For example, while we are eligible to receive up to an additional $ 155. 0 million in milestone payments under the Kyorin Agreement, as well as tiered royalties ranging from the mid- single digits to mid- teens on any net sales in Japan, whether and when we receive these payments will depend on Kyorin' s development and commercialization of efzofitimod in Japan, over which we have limited control. The development efforts of our collaborators are subject to the same risks and uncertainties described above with respect to our independently developed product candidates. Some collaborators may not succeed in their product development efforts. It is possible that our collaborators may be unable to obtain regulatory approval of our product candidates or successfully market and commercialize any such products for which regulatory approval is obtained. For example, while we have received $ 20. 0 million in upfront and milestone payments from Kyorin to date, if Kyorin' s operations are limited as a result of global geopolitical and macroeconomic conditions or other reasons, the development of efzofitimod in Japan may be significantly delayed and adversely affected, which may in turn delay or limit our receipt of any additional payments under the Kyorin Agreement. Other collaborators may not devote sufficient time or resources to the programs covered by these arrangements, and we may have limited or no control over the time or resources allocated by these collaborators to these programs. The occurrence of any of these events may cause us to derive little or no revenue from these arrangements, lose opportunities to validate our product candidates, or force us to curtail or cease our development efforts in these areas. Our collaborators may breach or terminate their agreements with us, including termination without cause, subject to certain prior written notice requirements, and we may be unsuccessful in entering into and maintaining other collaborative arrangements for the development of product candidates. For example, Kyorin has the right to terminate the agreement for any reason upon 90 days advance written notice to us. In addition, if we are unable to maintain existing collaboration arrangements or enter into new ones, our ability to generate licensing, milestone or royalty revenues would be materially impaired. We may decide to enter into additional strategic partnerships, including collaborations with pharmaceutical and biotechnology companies, to enhance and accelerate the development and potential commercialization of our product candidates. We face significant competition in seeking appropriate partners, and the negotiation process is time- consuming and complex. Moreover, we may not be successful in our efforts to establish any new strategic partnership or other collaborative arrangement for any of our product candidates and programs for a variety of reasons, including strategic fit with partners and differences in analysis of commercial value and regulatory risk. We may not be able to negotiate strategic partnerships on a timely basis, on acceptable terms or at all. We are unable to predict when, if ever, we will enter into any new strategic partnership because of the numerous risks and uncertainties associated with establishing strategic partnerships. Even if we are successful in our efforts to establish new strategic partnerships, the terms that we agree upon may not be favorable to us and we may not be able to maintain such strategic partnerships if, for example, we encounter unfavorable results or delays during development or approval of a product candidate or sales of an approved product are lower than expectations. We rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, protocol development, research and preclinical and clinical testing, and these third parties may not perform satisfactorily. We currently rely, and expect to continue to rely, on third parties to conduct some or all aspects of product manufacturing, protocol development, research and preclinical and clinical testing with respect to our product candidates. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For example, for any product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable study plan and protocols and GCPs so long as we continue to develop and commercialize on our own. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our research and development activities, including clinical trials, in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical studies and clinical trials required to support future BLA submissions and approval of our product candidates. We rely and intend to rely on third parties to produce preclinical, clinical and commercial supplies of our product candidates. Other than some internal capacity to support preclinical activities, we do not have, nor do we plan to acquire, the infrastructure or capability internally to manufacture our preclinical and clinical quantities of our product candidates, and we lack the internal resources and capability to manufacture any of our product candidates on a clinical or commercial scale. Reliance on CDMOs entails risks to which we would not be subject if we manufactured the product candidates ourselves, including: • the inability to negotiate manufacturing agreements with third

parties under commercially reasonable terms; • reduced control as a result of using third- party CDMOs for all aspects of manufacturing activities; • termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; and • disruptions to the operations of our CDMOs or suppliers caused by conditions unrelated to our business or operations, including the insolvency or bankruptcy of the CDMOs or suppliers. Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production. Additionally, each CDMO may require licenses to manufacture our product candidates or components thereof if the applicable manufacturing processes are not owned by the CDMO or in the public domain, and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities. These factors could cause the delay of clinical development, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. We do not have long- term contracts with our CDMOs, and our CDMOs may terminate their agreements with us for a variety of reasons including technical issues or our material breach of our obligations under the applicable agreement. Furthermore, our CDMOs may reallocate resources away from the production of our product candidates if we delay manufacturing under certain circumstances, and the manufacturing facilities in which our product candidates are made could be adversely affected by earthquakes and other natural disasters, labor shortages, power failures, economic slowdowns, higher interest rates, inflation and monetary supply shifts, evolving global geopolitical tension and numerous other factors. If our CDMOs fail to meet contractual requirements, and we are unable to secure one or more replacement CDMOs capable of production at a substantially equivalent cost, our clinical development activities may be delayed, or we could lose potential revenue. Manufacturing biologic drugs is complicated and tightly regulated by the FDA and comparable regulatory authorities around the world, and although alternative CDMOs with the necessary manufacturing and regulatory expertise and facilities exist, it could be expensive and take a significant amount of time to arrange for alternative CDMOs, transfer manufacturing procedures to these alternative CDMOs, and demonstrate comparability of material produced by such new CDMOs. New CDMOs of any product would be required to comply with applicable regulatory requirements. These CDMOs may not be able to manufacture our product candidates at costs, or in quantities, or in a timely manner necessary to complete the clinical development of our product candidates or make commercially successful products. We previously relied on a single CDMO for process development and scale- up of efzofitimod, including the manufacture of bulk drug substance for our projected needs for planned clinical trials. We have entered into an agreement with another CDMO for the transfer of the process, scale- up and manufacturing of bulk drug substance. If we want to eventually utilize product manufactured by the new CDMO for commercial purposes, the FDA will require us to demonstrate that the product manufactured by the new CDMO is comparable in quality, safety and efficacy to the product that is being used in the EFZO- FIT and EFZO- CONNECT studies. The current supply of efzofitimod being used in the EFZO- FIT and EFZO- CONNECT studies was produced by a prior CDMO. We have transitioned to a new CDMO that completed its first two commercial- scale cGMP runs during 2023. Full quality release testing has been completed and all release specifications were met, supporting the new CDMO' s ability to produce bulk drug substance of efzofitimod for commercial purposes if we receive regulatory approval for efzofitimod. Because the change in CDMO has been introduced at an advanced stage of development of efzofitimod, the FDA will require a comparability assessment, including additional nonclinical or clinical studies utilizing the product manufactured by the new CDMO. These requirements could result in substantial delays and additional costs for clinical development, and commercialization of efzofitimod, or our inability to obtain approval for efzofitimod. We **have completed a comparability study and are awaiting regulatory feedback. We** rely, and expect to continue to rely, on third parties to conduct, supervise and monitor our clinical trials, and if these third parties perform in an unsatisfactory manner, it may harm our business. We have relied, and expect to continue to rely, on third- party CROs, clinical investigators and clinical trial sites to ensure our clinical trials are conducted properly and on time. While we have and will continue to enter into agreements governing their activities, we will have limited influence over their actual performance. We will control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements, and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our investigators and CROs are required to comply with GCPs for conducting, recording and reporting the results of clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA enforces GCPs through periodic inspections of study sponsors, principal investigators and clinical trial sites. If we or our investigators and CROs fail to comply with applicable GCPs, the clinical data generated in our future clinical trials may be deemed unreliable and the FDA may require us to perform additional unanticipated clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCPs. In addition, our future clinical trials will require a sufficient number of test subjects to evaluate the safety and effectiveness of our product candidates. Accordingly, if our investigators and CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process. Our investigators and CROs are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and preclinical programs. They may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If our investigators or CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any 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. As a result, enrollment and data integrity from monitoring of the trial may suffer, our financial results could

be harmed, our costs could increase, our ability to generate revenues could be delayed and the commercial prospects for our product candidates could be adversely affected. 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 third parties to manufacture our product candidates, and we collaborate with both industry and various academic institutions in the development of our discovery platform for therapeutic applications based on tRNA synthetase biology. In connection with these activities, we are required, at times, to share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information 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. Given that our proprietary position is based, in part, on our know- how and trade secrets, a competitor' s discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business, prospects, financial condition and results of operations. In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure intellectual property rights to which we are entitled arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor' s discovery of our trade secrets would impair our competitive position and have an adverse impact on our business, prospects, financial condition and results of operations. Risks related to our intellectual property If we are unable to obtain, maintain or protect intellectual property rights related to our product candidates, or if the scope of such intellectual property protection is not sufficiently broad, we may not be able to compete effectively in our markets. We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies and product candidates. Our success depends in large part on our and our licensors' abilities to obtain and maintain patent and other intellectual property protection in the United States and in other countries for our proprietary technology and product candidates. We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates that are important to our business. This process is expensive and time consuming, and we may not be able to file and prosecute 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. The patentability of inventions, and the validity, enforceability and scope of patents in the biotechnology and pharmaceutical fields involves complex legal and scientific questions and can be uncertain. As a result, patent applications that we own or in- license may not issue as patents with claims that cover our product candidates, or at all, in the United States or in foreign countries for many reasons. For example, there is no assurance that we were the first to invent or the first to file patent applications in respect of the inventions claimed in our patent applications or that our patent applications claim patentable subject matter. We may also be unaware of potentially relevant prior art relating to our patents and patent applications, and this prior art, if any, may be used by third parties as grounds to seek to invalidate a patent or to prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents disclose aspects of our product candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications 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 the patents and patent applications we hold, license or pursue with respect to our product candidates is threatened, it could threaten our ability to commercialize our product candidates. Further, if we encounter delays in our clinical trials, the period of time during which we could market any of our product candidates under patent protection, if approved, would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we were the first to file any patent application related to our product candidates. Changes to the patent laws in the United States and other jurisdictions could also diminish the value of our patents and patent applications or narrow the scope of our patent protection. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse effect on our business. If the patent applications we own or have in- licensed that relate to our programs or product candidates do not issue as patents, if their breadth or strength of protection is threatened, or if they fail to provide exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize future products. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patents or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. In addition, patents have a limited term. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if a patent does issue for any of our pending patent applications, possible delays in regulatory approvals could mean that the period of time during which we could market a product

candidate under patent protection could be reduced from what we generally would expect. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by a third party to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Even if patents covering aspects of our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications. In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know- how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know- how, information or technology that is not covered by patents. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems, but it is possible that these security measures could be breached. Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know- how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. For example, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps we take to maintain the confidentiality of our trade secrets are inadequate, we may have insufficient recourse against third parties for misappropriating our proprietary information and processes. 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. If due to the effects on our operations of general political and economic conditions, including global geopolitical tension, armed conflicts, potential future health pandemics, labor shortages, economic slowdowns, recessions or market corrections, inflation and monetary supply shifts, **tariffs and trade tensions,** higher interest rates and tightening of credit markets, or another cause, we are unable to generate new animal, or in vitro data, in time to support new, or updated patent application filings, or prior to patent conversion deadlines, it could materially impact the enforceability or scope of those patent filings. If we are unable to prevent material disclosure of the non- patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition. Further, 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 United States. As a result, we may encounter significant problems in preventing third parties from practicing our inventions in countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Claims that our product candidates or the manufacture, sale or use of our future products infringe the patent or other intellectual property rights of third parties could result in costly litigation or could require substantial time and money to resolve, even if litigation is avoided. Our commercial 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 patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter partes reexamination proceedings before the United States Patent and Trademark Office (USPTO) and corresponding foreign patent offices. 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 pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Third parties may assert that we are employing their proprietary technology without authorization. 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. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third- party patents were held by a court of competent jurisdiction to cover the formulations for, or the manufacturing process or methods of use of, any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to develop and commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. In either case, such a license may not be available on commercially reasonable terms or at all. Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may not be able to be obtained on reasonable commercial terms or at all, or require substantial

time and monetary expenditure. Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time. Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U. S. non- provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. We may not be successful in obtaining or maintaining necessary rights to our therapeutic product candidates and processes for our development pipeline through acquisitions and in- licenses. We believe that we have rights to intellectual property, through licenses from third parties and under patents that we own, that is necessary or useful to develop our product candidates. Because our programs may involve additional product candidates that may require the use of 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 any compositions, methods of use, processes or other third- party intellectual property rights from third parties that we identify on reasonable commercial terms or at all. The licensing and acquisition of third- party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third- party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities. We sometimes collaborate with U. S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. These institutions may provide us with an option to negotiate a license to the institution' s rights in technology resulting from the collaboration. Regardless of any such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. 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. If we are unable to successfully obtain rights to required third- party intellectual property rights, our business, financial condition and prospects for growth could suffer. 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 are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable commercial terms, if at all. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business significantly. In some cases, patent prosecution of our licensed technology is controlled by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using such intellectual property. In certain cases, we may control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensors. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may arise regarding intellectual property subject to a license agreement, including: • the scope of rights granted under the license agreement and other interpretation- related issues; • the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement; • the sublicensing of patent and other rights under our collaborative development relationships; • our diligence obligations under the license agreement and what activities satisfy those diligence obligations; • the ownership of inventions and know- how resulting from the joint creation or use of intellectual property by our licensors and us and our sublicensees or partners, if any; and • the priority of invention of patented technology. If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates. We may become involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time- consuming and unsuccessful. Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time- consuming. Any claims that we assert against perceived infringers could also provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property rights. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. Interference or

derivation proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions or other matters of inventorship with respect to our patents or patent applications or those of our licensors. We may also become involved in other proceedings, such as re- examination or opposition proceedings, before the USPTO or its foreign counterparts relating to our intellectual property or the intellectual property rights of others. An unfavorable outcome in any such proceedings could require us to cease using the related technology or to attempt to license rights to it from the prevailing party, or could cause us to lose valuable intellectual property rights. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms, if any license is offered at all. 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. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market. We may also become involved in disputes with others regarding the ownership of intellectual property rights. For example, we jointly develop intellectual property with certain parties, and disagreements may therefore arise as to the ownership of the intellectual property developed pursuant to these relationships. If we are unable to resolve these disputes, we could lose valuable intellectual property rights. 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. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers. We employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee' s former employer or other third parties. 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 impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We may be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership, or 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. 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. Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non- compliance with these requirements. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non- U. S. patent agencies. The USPTO and various non- U. S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which non- compliance 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 and this circumstance would have a material adverse effect on our business. Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court. If we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non- enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re- examination, post grant review, and equivalent proceedings in foreign jurisdictions (e. g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and

the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection would have a material adverse effect on our business. Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our products. As is the case with many other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and therefore obtaining, maintaining and enforcing biotechnology patents is costly, time- consuming and inherently uncertain. In addition, recent legislative and judicial developments in the United States and elsewhere have in some cases removed the protection afforded to patent owners, made patents more difficult to obtain, or increased the uncertainty regarding the ability to obtain, maintain and enforce patents. For example, Congress has recently passed, and the United States is currently implementing, wide- ranging patent reform legislation, and may pass further patent reform legislation in the future. Recent U. S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. For example, in Association for Molecular Pathology v. Myriad Genetics, Inc., the U. S. Supreme Court held that certain claims to naturally occurring substances are not patentable. Although we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, Congress, or the USPTO may impact the value of our patents. 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 generally, once obtained. Depending on decisions and actions by Congress, the federal courts, the USPTO and their respective foreign counterparts, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to maintain and enforce our existing patents and patents that we might obtain in the future. Patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the validity or defense of our issued patents. On September 16, 2011, the Leahy- Smith America Invents Act (the Leahy- Smith Act) was signed into law. The Leahy- Smith 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 administration of the Leahy- Smith Act, and many of the substantive changes to patent law associated with the Leahy- Smith Act, and in particular, the first to file provisions, were enacted March 16, 2013. Although it is not clear what, if any, impact the Leahy- Smith Act will have on the operation of our business, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our 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. We may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state 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, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement 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. 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 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 our patent applications at risk of not issuing 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. Risks related to our business operations We may use our financial and human resources to pursue a particular business strategy, research program or product candidate and fail to capitalize on strategies, programs or product candidates that may be more profitable or for which there is a greater likelihood of success. Because we have limited resources, we may forego or delay pursuit of certain strategic opportunities or opportunities with certain programs, product candidates or indications that later prove to have greater commercial potential. We may focus on or pursue one indication over another potential indication and such development efforts may not be successful, which would cause us to delay the clinical development and approval of efzofitimod and other product candidates. In addition, our decisions as to which of our discovery programs to advance into preclinical and clinical development could preclude us from advancing others. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. For example, based ~~on~~ **upon** ~~analysis~~ **analyses** from ~~an~~ independent ~~consultant~~ **consultants** that we **have** engaged ~~during 2022~~ **and our own modeling**, we estimate that there is a $ 2- ~~3~~ **5** billion ~~dollar~~ market opportunity in pulmonary sarcoidosis and SSc- ILD ~~in our own modeling~~. Depending on the accuracy of this estimate, we may not be most efficiently allocating resources toward the advancement of efzofitimod versus the advancement of other development efforts. In addition, we may elect to pursue a research, clinical or commercial strategy that ultimately does not yield the results that we desire. Our spending on current and future research and development programs for product candidates may not result in any commercially viable products. If we do

not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area or market in which it would have been more advantageous to enter into a partnering arrangement. Any failure to allocate resources or capitalize on strategies in a successful manner will have an adverse impact on our business. Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel. We are highly dependent on principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are " at will " employees. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. In response to competition, higher rates of inflation and labor shortages, we may need to adjust employee cash compensation, which would affect our operating costs and our margins, or equity compensation, which would affect our outstanding share count and cause dilution to existing stockholders. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, the available pool of skilled employees may be further reduced if immigration laws change in a manner that increases restrictions on immigration. Further, failure to succeed in preclinical studies or clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives. We may undertake internal restructuring activities in the future that could result in disruptions to our business or otherwise materially harm our results of operations or financial condition. From time to time we may undertake internal restructuring activities as we continue to evaluate and attempt to optimize our cost and operating structure in light of developments in our business strategy and long- term operating plans ~~. For example, we implemented a corporate and program prioritization plan in May 2018 that included a reduction in our workforce~~ . Any such restructuring activities may result in write- offs or other restructuring charges. There can be no assurance that any restructuring activities that we have undertaken or undertake in the future will achieve the cost savings, operating efficiencies or other benefits that we may initially expect. Restructuring activities may also result in a loss of continuity, accumulated knowledge and inefficiency during transitional periods and thereafter. In addition, internal restructurings can require a significant amount of time and focus from management and other employees, which may divert attention from commercial operations. If any internal restructuring activities we have undertaken or undertake in the future fail to achieve some or all of the expected benefits therefrom, our business, results of operations and financial condition could be materially and adversely affected. We are subject to a variety of risks associated with international operations that could materially adversely affect our business. We currently conduct **certain** research activities through Pangu BioPharma Limited, in collaboration with the Hong Kong University of Science and Technology. Additionally, we have conducted clinical trials in the EU and in Australia and may conduct future clinical trials internationally. Our partner, Kyorin, conducted and funded an efzofitimod Phase 1 clinical trial in healthy volunteers in Japan, and has joined the EFZO- FIT study, a global Phase 3 clinical trial ~~designed to~~ **in which we have** ~~enroll~~ **enrolled 268** ~~up to 264~~ subjects at multiple centers in United States, Europe, Brazil and Japan. ~~If~~ **Some countries, such as Brazil, require that clinical trial participants receive the product candidate at no cost even after the clinical trial has ended. We would not be able to recover any profit for these patients and depending on the number of patients, duration of the treatment and numerous other factors, such regulations could harm our business, prospects, financial condition and results of operations significantly. Further, if** any of our product candidates are approved for commercialization outside of the United States, we expect to either use our own sales organization or selectively enter into agreements with third parties to market our products on a worldwide basis or in more limited geographical regions, as with Kyorin and efzofitimod in Japan. We are, and we expect that we will continue to be, subject to a variety of risks related to international operations, including, but not limited to: liquidity concerns at, and failures of, banks and other financial institutions or other disruptions in the banking system or financing markets ~~,~~ **; tariffs and trade tensions;** different regulatory requirements for approval of drugs and biologics in foreign countries; reduced or uncertain protection for intellectual property; unexpected changes in tariffs, trade barriers and regulatory requirements; economic weakness, including labor shortages, economic slowdowns, recessions, inflation ~~and~~ **,** monetary supply shifts, higher interest rates and tightening of credit markets **;** ~~, or~~ political instability in particular foreign economies and markets, including global geopolitical tension and armed conflicts; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in reduced revenues ~~,~~ and other obligations incident to doing business in another country; and the global impacts of potential future health pandemics. Any failure to continue our international operations or to commercialize our product candidates outside of the United States may impair our ability to generate revenues and harm our business, prospects and results of operations. Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements and insider trading. We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. 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 healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare 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. Such misconduct could also involve the improper use of information obtained in the course of clinical

trials, which could result in significant regulatory sanctions and cause serious harm to our reputation. We have adopted a code of business conduct and ethics applicable to all of our employees, but 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, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions. We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use of our product candidates harm patients, or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims. The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in: • impairment of our business reputation; • withdrawal of clinical trial participants; • costs due to related litigation; • distraction of management' s attention from our primary business; • substantial monetary awards to patients or other claimants; • the inability to commercialize our product candidates; and • decreased demand for our product candidates, if approved for commercial sale. We carry product liability insurance for our clinical trials covering $ 10. 0 million per occurrence and up to $ 10. 0 million in the aggregate, subject to certain deductibles and exclusions. Although we believe the amount of our insurance coverage is typical for companies similar to us in our industry, we may not have adequate insurance coverage or be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and adversely affect our reputation and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. Patients with the diseases targeted by our product candidates are often already in severe and advanced stages of disease and may have both known and unknown significant pre- existing and potentially life- threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time- consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations. We **(and the third- parties with whom we work)** are, or may become, subject to stringent and evolving U. S. and foreign laws, regulations, rules, policies, contractual obligations, industry standards, and other obligations related to data privacy and security. Our **(or the third- parties with whom we work)** actual or perceived failure to comply with such obligations could have a material adverse effect on our business and financial condition, including a disruption of clinical trials or commercialization of products; regulatory investigations or actions; litigation (including class claims) and mass arbitration demands; fines and penalties; reputational harm; loss of revenue or profits; and other adverse business consequences. We collect, receive, store, process, use, generate, transfer, disclose, make accessible, protect, secure, dispose of, transmit and share (Process or Processing) personal data and other sensitive information, including information we or ~~our~~ **the** third ~~party partners~~ **parties with whom we work** (such as CROs and clinical trial sites) collect about patients and healthcare providers in connection with clinical trials necessary to operate our business. Therefore, our data Processing activities subject us to numerous data privacy and security laws, regulations, rules, guidance, and industry standards as well as external and internal data privacy and security policies, contractual requirements and other obligations that apply to the Processing of personal (and other sensitive) data both by us and ~~on our behalf~~ **the third parties with whom we work** (collectively, Data Protection Requirements). The number and scope of the Data Protection Requirements are changing, becoming increasingly stringent, creating uncertainty, subject to differing applications and interpretations, and may be inconsistent between jurisdictions. These Data Protection Requirements may require us to change our business model. New Data Protection Requirements may be proposed or enacted. Additionally, given the breadth and evolving nature of Data Protection Requirements (and consumers' data privacy expectations), preparing for and complying with these requirements is rigorous, time- intensive and requires significant resources and a review of our technologies, systems and practices, as well as those of any third **parties with whom we work** ~~party collaborators, service providers, contractors or consultants that Process personal data on our behalf~~. We may at times fail (or be perceived to have failed) in our efforts to comply with our Data Protection Requirements. Moreover, despite our efforts, our personnel or third parties ~~upon~~ **with** whom we ~~rely~~ **work** may fail to comply with such obligations, which could negatively impact our business operations and compliance posture. If we or the third parties ~~upon which~~ **with whom** we ~~rely~~ **work** fail, or are perceived to have failed, to address or comply with Data Protection Requirements, this could result in government enforcement actions against us that could include investigations, fines, penalties, audits and inspections, additional reporting requirements and / or oversight, temporary or permanent bans on all or some Processing of personal data, or orders to destroy or

not use personal data. Further, individuals or other relevant stakeholders could bring a variety of claims (including class claims and mass arbitration demands) against us for our actual or perceived failure to comply with the Data Protection Requirements. In particular, plaintiffs have become increasingly more active in bringing privacy- related claims against companies, including class claims and mass arbitration demands. Some of these claims allow for the recovery of statutory damages on a per violation basis, and, if viable, carry the potential for monumental statutory damages, depending on the volume of data and the number of violations. Any of these events could have a material adverse effect on our reputation, business, or financial condition, and could lead to a loss of actual or prospective customers, ~~collaborators~~ or **third** ~~partners~~ **parties with whom we work** ; interrupt or stop our clinical trials; result in an inability to Process personal data or to operate in certain jurisdictions; limit our ability to develop or commercialize our products; require us to revise, restructure or substantially change our operations; or otherwise materially adversely affect our operations (each, a Material Adverse Impact). In the United States, federal, state and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, consumer protection laws (e. g., Section 5 of the Federal Trade Commission Act). and other similar laws (e. g. wiretapping laws). **Numerous U. S. states have enacted comprehensive information privacy laws that impose certain obligations on covered businesses, including providing specific disclosures in privacy notices and affording residents with certain rights concerning their personal data. These state laws allow for statutory fines for noncompliance.** For example, the California Consumer Privacy Act of 2018, as amended by the California Privacy Rights Act of 2020 (CPRA), (collectively, CCPA) applies to personal data of consumers, business representatives, and employees who are California residents, and requires businesses to provide specific disclosures in privacy notices and honor requests of California residents to exercise certain privacy rights, such as those noted below. The CCPA provides for fines **for** ~~of up to $ 7, 500 per~~ intentional violation and allows private litigants affected by certain data breaches to recover significant statutory damages. Although the CCPA exempts some data Processed in the context of clinical trials, the CCPA may increase compliance costs and potential liability with respect to other personal data maintained about California residents. In addition, the CPRA expanded the CCPA' s requirements and established a regulatory agency to implement and enforce the law. Other states have also passed or are considering comprehensive privacy laws, with actions also being considered at the federal and local levels **, and we expect more states to pass similar laws in the future** . These state laws and the CCPA provide individuals with certain rights concerning their personal data, including the right to access, correct, or delete certain personal data, and opt- out of certain data Processing activities, such as targeted advertising, profiling, and automated decision- making. The exercise of these rights may impact our business and ability to provide our products and services. While these states, like the CCPA, also exempt some data Processed in the context of clinical trials, these developments may further complicate compliance efforts, and may increase legal risk and compliance costs for us and the third parties ~~upon~~ **with** whom we ~~rely~~ **work** . Outside the United States, an increasing number of laws, regulations, and industry standards may govern data privacy and security. For example, the European Union' s General Data Protection Regulation (EU GDPR), the United Kingdom' s GDPR (UK GDPR), Brazil' s General Data Protection Law (Lei Geral de Proteção de Dados Pessoais, or LGPD) (Law No. 13, 709 / 2018) and China' s Personal Information Protection Law (~~"~~ PIPL ~~"~~) impose strict requirements for Processing personal data. We may become subject to an increasing number of foreign privacy laws, particularly as we have begun to sponsor clinical trials in foreign jurisdictions, including in Europe. For example, failure to comply with the requirements of the EU and UK GDPR may result in warning letters, litigation, orders banning the Processing of personal data, mandatory audits and financial penalties, including fines of up to 4 % of the total worldwide annual turnover, or € 20, 000, 000 under the EU GDPR (17, 500, 000 British Pounds under the UK GDPR), in either case, whichever is greater; or private litigation related to Processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. Kyorin has also enrolled clinical trial patients in Japan and may be subject to local laws and regulations regarding data privacy, including Japan' s Act on the Protection of Personal Information. As another example, the LGPD broadly regulates Processing personal data of individuals in Brazil and imposes compliance obligations and penalties comparable to those of the EU GDPR. In the ordinary course of business, we may transfer personal data from Europe and other jurisdictions to the United States or other countries. Europe and other jurisdictions have enacted laws requiring data to be localized or limiting the transfer of personal data to other countries. In particular, the EEA and the UK have significantly restricted the transfer of personal data to the United States and other countries whose privacy laws it generally believes are inadequate. Other jurisdictions may adopt **or have already adopted** similarly stringent ~~interpretations of their~~ data localization and cross- border data transfer laws. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA ~~and UK~~ ' s standard contractual clauses, the UK' s International Data Transfer Agreement / Addendum, and the EU- U. S. Data Privacy Framework and the UK extension thereto (which allows for transfers for relevant U. S.- based organizations who self- certify compliance and participate in the Framework), these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If there is no lawful manner for us to transfer personal data from the EEA, the UK, or other jurisdictions to the United States, or if the requirements for a legally- compliant transfer are too onerous, we could face significant adverse consequences, including the interruption or degradation of our operations, the need to relocate part of or all of our business or data processing activities to other jurisdictions (such as Europe) at significant expense, increased exposure to regulatory actions, substantial fines and penalties, the inability to transfer data and work with ~~partners, vendors and other~~ third parties, and injunctions against our processing or transferring of personal data necessary to operate our business. Additionally, companies that transfer personal data out of the EEA and UK to other jurisdictions, particularly to the United States, are subject to increased scrutiny from regulators, individual litigants, and activities groups. Some European regulators have ordered certain companies to suspend or permanently cease certain transfers of personal data out of Europe for allegedly violating the EU and UK GDPR' s cross- border data transfer limitations. Our employees and personnel use generative artificial intelligence (AI) technologies to perform their work, and the

disclosure and use of personal data in generative AI technologies is subject to various privacy laws and other privacy obligations. Governments have passed and are likely to pass additional laws regulating generative AI. Our use of this technology could result in additional compliance costs, regulatory investigations and actions, and lawsuits. If we are unable to use generative AI, it could make our business less efficient and result in competitive disadvantages. In addition to data privacy and security laws, we are contractually subject to industry standards adopted by industry groups and, we are, or may become subject to such obligations in the future. We are also bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. For example, certain privacy laws, such as the EU and UK GDPR and the CCPA, may require our customers to impose specific contractual restrictions on their service providers. We also publish privacy policies, marketing materials **, white papers,** and other statements, ~~such as~~ **related to,** compliance with certain certifications, ~~regarding~~ **concerning** data privacy and security. ~~If~~ **Regulators in the United States are increasingly scrutinizing these statements, and if** these policies, materials or statements are found to be deficient, lacking in transparency, deceptive, unfair, **misleading** or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators or other adverse consequences. Unfavorable macroeconomic conditions could adversely affect our business, financial condition or results of operations. Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the global financial crisis caused volatility and disruptions in the capital and credit markets. In addition, due to general political and economic conditions, including global geopolitical tension, armed conflicts, **including the ongoing Ukraine- Russia conflict and conflicts in the Middle East, increasing tensions between the U. S. and China,** liquidity concerns at, and failures of, banks and other financial institutions or other disruptions in the banking system or financing markets **, tariffs and trade tensions** , higher interest rates and financial and credit market fluctuations, volatility in the capital markets, the global credit and financial markets have experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, volatility in unemployment rates, inflation and uncertainty about economic stability. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including inability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our CDMOs and CROs, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business. We or the third parties upon whom we depend may be adversely affected by earthquakes, droughts, floods, fires, hurricanes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster. We are located in San Diego, California and our manufacturing activities are conducted by CDMOs and our clinical trials are conducted at various locations in the United States and abroad. Some of these geographic locations have in the past experienced natural disasters, including severe earthquakes. Earthquakes, droughts, floods, fires, hurricanes, disease epidemics or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our facilities, that damaged critical infrastructure, such as the manufacturing facilities of our CDMOs and clinical sites utilized by our CROs, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, as well as limits on our insurance coverage, which could have a material adverse effect on our business, prospects, financial condition and results of operations. Risks related to the commercialization of our product candidates If we are unable to establish sales, marketing and distribution capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenues. We do not currently have any infrastructure for the sales, marketing and distribution of pharmaceutical products. In order to market our product candidates, if approved by the FDA or any other regulatory body, we must build our sales, marketing, distribution, managerial and other non- technical capabilities or make arrangements with third parties to perform these services. There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. If we enter into arrangements or collaborations with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market, sell or distribute any medicines that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our medicines effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates. We rely on third- party manufacturers to produce our product candidates, but we have not entered into agreements with any such manufacturers to support commercialization. We have not yet secured manufacturing capabilities for commercial quantities of any of our product candidates. Although we intend to rely on third- party manufacturers for commercialization, we have not yet entered into a long- term commercial supply agreement to support full scale commercial production, and we or our CDMOs may be unable to process validation activities necessary to enter into commercial supply agreements or otherwise negotiate agreements with the manufacturers to support our commercialization activities at commercially reasonable terms. We may run into technical or scientific issues related to development or manufacturing that we

may be unable to resolve in a timely manner or with available funds. For example, we engaged an additional CDMO to manufacture efzofitimod bulk drug substance. If the new CDMO experiences ~~delays~~ **additional issues** in validating the manufacturing process, particularly delays in producing efzofitimod in compliance with cGMP regulations, we could be forced to delay future clinical trials or the submission of regulatory approval applications to the FDA. In addition, due to the fact that all prior cGMP batches of efzofitimod, including those that we intend to use in the EFZO- FIT study, have been produced by our ~~existing~~ **prior** CDMO, we will be required to complete comparability studies prior to using efzofitimod produced at the new CDMO' s facilities in subsequent clinical trials or submitting regulatory approval applications to the FDA. If we are unable to demonstrate such comparability to the satisfaction of the FDA, it may result in delays to future clinical trials or a deficiency in future regulatory applications **. We have completed a comparability study and are awaiting regulatory feedback** . If we or our CDMOs are unable to scale the manufacturing process to produce commercial quantities of our product candidates, or our CDMOs do not pass required regulatory pre- approval inspections, our commercialization efforts will be harmed. In addition, any significant disruption in our relationships with our CDMOs could harm our business. There are a relatively small number of potential manufacturers for our product candidates, and such manufacturers may not be able to supply our drug products at the times we need them or on commercially reasonable terms. Any disruption to our relationship with our current CDMOs and any manufacturers that we contract with in the future will result in delays in our ability to complete the clinical development of, or to commercialize, our product candidates, and may require us to incur additional costs. We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are more advanced or effective than ours, which may adversely affect our financial condition and our ability to successfully commercialize our product candidates. The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors both in the United States and internationally, including major multi- national pharmaceutical companies, biotechnology companies and universities and other research institutions. Although we believe we are the only company engaged in the discovery and development of therapeutics based on novel functions of tRNA synthetases, we are aware of other companies that could compete with our product candidates in their target therapeutic indications, such as our lead candidate, efzofitimod, for the treatment of pulmonary sarcoidosis, SSc- ILD and other ILD. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, products that are more effective, safer, more convenient or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization and market penetration than us. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors. The commercial success of any current product candidate or future product candidates will depend upon the degree of market acceptance by physicians, patients, third- party payors and others in the medical community. Even with the requisite approval from the FDA and comparable foreign regulatory authorities, the commercial success of our product candidates will depend in part on the medical community, patients, and third- party payors accepting our product candidates as medically useful, cost- effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, third- party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be known until after it is launched. Our efforts to educate the medical community and third- party payors on the benefits of the product candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors, and our competitors may have substantially greater resources or brand recognition to effectively market their products. If our product candidates are approved but fail to achieve an adequate level of acceptance by physicians, patients, third- party payors, and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable. The insurance coverage and reimbursement status of newly- approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products **, if approved,** could limit our ability to market those products and decrease our ability to generate revenue. The availability and extent of coverage and adequate reimbursement by third- party payors, including government health administration authorities, private health coverage insurers, managed care organizations and other third- party payors is essential for most patients to be able to afford expensive treatments. Sales of any of our product candidates that receive marketing approval will depend substantially, both in the United States and internationally, on the extent to which the costs of such product candidates will be covered and reimbursed by third- party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize an adequate return on our investment. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services (CMS), as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors often follow CMS with respect to coverage policy and payment limitations in setting their own reimbursement policies. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. One third- party payor' s determination to provide coverage for a product candidate does not assure that other payors will also provide coverage for the product candidate. Further, no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor. As a

result, the coverage determination process is often time- consuming and costly. This process will require us to provide scientific and clinical support for the use of our products to each third- party payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Reimbursement agencies in Europe may be more conservative than third- party payors in the United States. For example, a number of cancer drugs have been approved for reimbursement in the United States, but have not been approved for reimbursement in certain European countries. There may be significant delays in obtaining reimbursement for newly approved medicines, and our inability to promptly obtain coverage and profitable payment rates from third- party payors for any approved medicines could have a material adverse effect on our business, prospects, financial condition and results of operations. Outside the United States, international sales are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that currently restrict imports of medicines from countries where they may be sold at lower prices than in the United States. Moreover, increasing efforts by governmental and third- party payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products and, as a result, they may not cover or provide adequate payment for our product candidates. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA) was passed in March 2010, and substantially changed the way healthcare is financed by both governmental and private insurers. There have been **amendments and** executive, judicial and congressional challenges to certain aspects of the ACA ~~. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modified certain provisions of the ACA such as removing penalties, starting January 1, 2019, for not complying with the ACA' s individual mandate to carry health insurance. On June 17, 2021 the U. S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the " individual mandate " was repealed by Congress~~ . On August 16, 2022, ~~President Biden signed~~ the Inflation Reduction Act of 2022 (IRA) **was signed** into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the " donut hole " under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out- of- pocket cost and through a newly established manufacturer discount program. It is possible that the ACA will be subject to **amendments and** judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the ~~Biden~~ **current** administration will impact the ACA and our business. In addition, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent presidential executive orders, congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, **the IRA** ~~in July 2021~~ , **among** ~~the~~ **other things** ~~Biden administration released an executive order~~ , **(1) directs** ~~" Promoting Competition in the American Economy, " with multiple provisions aimed at prescription drugs. In response to Biden' s executive order, on September 9, 2021,~~ the U. S. Department of Health and Human Services (HHS) ~~released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. Further, the IRA, among other things, (1) directs the HHS~~ to negotiate the price of certain single- source drugs and biologics **that have been on the market for at least 7 years** covered under Medicare **(the Medicare Drug Price Negotiation Program)** and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions ~~take~~ **took** effect progressively starting in fiscal year 2023. On August ~~29~~ **15** , ~~2023~~ **2024** , HHS announced the ~~list~~ **agreed- upon reimbursement prices** of the first ten drugs that **were** ~~will be~~ subject to price negotiations, although the Medicare ~~drug~~ **Drug** ~~price~~ **Price** ~~negotiation~~ **Negotiation** ~~program~~ **Program** is currently subject to legal challenges. HHS ~~has and~~ will ~~continue~~ **select up** to ~~issue and update guidance as these programs are implemented~~ **fifteen additional drugs covered under Part D for price negotiation in 2025** . ~~It is currently unclear how the IRA~~ **Each year thereafter more Part B and Part D products** will **become subject** ~~be implemented but is likely~~ to ~~have a significant impact on~~ the ~~pharmaceutical industry~~ **Medicare Drug Price Negotiation Program** . In addition, in response to **an** ~~the Biden administration' s~~ October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the Center for Medicare and Medicaid Innovation which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023, ~~the Biden administration announced~~ an initiative to control the price of prescription drugs through the use of march- in rights under the Bayh- Dole Act **was announced** . On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March- In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march- in rights. While march- in rights have not previously been exercised, it is uncertain if that will continue under the new framework. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health

maintenance organizations and additional health reform measures. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly higher barriers are being erected to the entry of new products **. Further, the overall funding of certain government programs such as Medicaid and Medicare is uncertain and there is no guarantee that funds approved by the U. S. Congress will be made available by the current administration. We expect additional health reform measures may be implemented in the future, particularly in light of the recent U. S. Presidential and Congressional elections. Further, the current administration is pursuing policies to reduce regulations and expenditures across government including at the HHS, the FDA, CMS and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. These actions may include directives to reduce agency workforce, rescinding a Biden administration executive order tasking the Center for Medicare and Medicaid Innovation (CMMI) to consider new payment and healthcare models to limit drug spending and eliminating the Biden administration' s executive order that directed HHS to establishing an AI task force and developing a strategic plan. Additionally, in its June 2024 decision in Loper Bright Enterprises v. Raimondo (Loper Bright), the U. S. Supreme Court overturned the longstanding Chevron doctrine, under which courts were required to give deference to regulatory agencies' reasonable interpretations of ambiguous federal statutes. The Loper Bright decision could result in additional legal challenges to current regulations and guidance issued by federal agencies applicable to our operations, including those issued by the FDA. Congress may introduce and ultimately pass health care related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program created under the IRA. We cannot predict which additional measures may be adopted or the impact of current and additional measures on the marketing, pricing and demand for our products, if approved, which could have a material adverse effect on our business, financial condition and results of operations** . In addition, drug prices are under significant scrutiny in the markets in which our products may be sold. Drug pricing and other health care costs continues to be subject to intense political and societal pressures which we anticipate will continue and escalate on a global basis. If coverage and reimbursement is available only to limited levels, we may not be able to successfully commercialize our product candidates for which we obtain marketing approval. As a result, we may have difficulty raising capital and our results of operations may be adversely impacted. Our business operations and current and future relationships with investigators, healthcare professionals, consultants, third- party payors and customers may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, transparency laws, health information privacy and security 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. Although we do not currently have any products on the market, our current and future operations may be, directly or indirectly through our prescribers, customers and third- party payors, subject to various federal and state healthcare laws and regulations. The laws that may affect our ability to operate include: • the federal Anti- Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying any remuneration (including any kickback, bribe or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal and state healthcare programs such as Medicare and Medicaid. 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; • the U. S. federal false claims, including the False Claims Act, which can be enforced through whistleblower actions, and civil monetary penalties laws, which, among other things, impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the U. S. federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act; • the federal Health Insurance Portability and Accountability Act (HIPAA), which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services; similar to the U. S. 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 (HITECH), which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by covered entities, i. e. health plans, healthcare clearinghouses and certain healthcare providers, as well as their business associates and covered subcontractors that perform certain services for or on their behalf involving the use or disclosure of individually identifiable health information; • the U. S. federal legislation commonly referred to as Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid or the Children' s Health Insurance Program to report annually to the CMS information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other healthcare professionals (such as physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members; and • analogous state and foreign laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative

penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits, 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 and the delay, reduction, termination or restructuring of our operations. Risks related to the ownership of our common stock The market price of our common stock has been volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this " Risk Factors " section and elsewhere in this Annual Report, these factors include: • adverse results or delays in preclinical studies or clinical trials; • manufacturing sufficient quantities of product candidates for use in clinical trials; • the imposition of a clinical hold on our product candidates or our inability to cause the clinical hold to be lifted; • any delay in filing an investigational new drug application (IND) or BLA for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA' s review of that IND or BLA; • failure of our strategic partners to perform under our collaborations or early termination of collaborations; • failure to successfully develop and commercialize our product candidates; • limited market sizes and pricing for our product candidates; • failure by us or our licensors to prosecute, maintain or enforce intellectual property rights covering our product candidates and processes; • changes in laws or regulations applicable to current or future products; • inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices; • adverse regulatory decisions; • introduction of new products, services or technologies by our competitors; • inability to obtain additional capital; • failure to meet or exceed financial or operational projections we may provide to the public; • failure to meet or exceed the financial or operational projections of the investment community; • the perception of the biopharmaceutical industry by the public, politicians, legislatures, regulators and the investment community; • significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors; • disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies; • additions or departures of key scientific or management personnel; • significant lawsuits, including patent or stockholder litigation; • if securities or industry analysts issue an adverse or misleading opinion regarding our common stock; • changes in the market valuations of similar companies; • changes in the structure of healthcare payment systems; • sales of our common stock by us or our stockholders in the future; • a potential additional reverse stock split if we are unable to maintain a stock price above $ 1. 00 per share of common stock; • trading volume of our common stock; and • general political and macroeconomic conditions, including global geopolitical tension, armed conflicts, potential future health pandemics, liquidity concerns at, and failures of, banks and other financial institutions or other disruptions in the banking system or financing markets, ~~rising~~ **tariffs and trade tensions, higher** interest rates and financial and credit market fluctuations, volatility in the capital markets, and other geopolitical and macroeconomic conditions, including labor shortages, economic slowdowns, recessions, inflation and monetary supply shifts, rising interest rates and tightening of credit markets, and the resulting impacts on our business operations or financial condition. In addition, companies trading in the stock market in general, and on the Nasdaq Capital Market and biotechnology companies in particular, have experienced extreme price and volume fluctuations, and we have in the past experienced volatility that has been unrelated or disproportionate to our operating performance. From January 1, 2023 through March ~~8~~ **7**, ~~2024~~ **2025** the closing price of our common stock has ranged between $ 1. 11 and $ ~~2~~ **4**. ~~57~~ **43** per share. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. Our executive officers, directors, 5 % holders and their affiliates currently own a significant percentage of our stock and will be able to exert significant control over matters submitted to stockholders for approval. As of March ~~8~~ **7**, ~~2024~~ **2025**, based on the latest information available to us, our executive officers, directors, holders known by us to own 5 % of our voting stock and their affiliates own approximately ~~38~~ **33**. ~~5~~ **6** % of our voting stock. Therefore, our executive officers, directors, holders known by us to own 5 % of our voting stock and their affiliates will have the ability to influence us through their ownership positions and may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders. Future sales and issuances of equity securities could result in dilution to our stockholders, impose restrictions or limitations on our business and could cause our stock price to fall. We will need additional capital in the future to continue our planned operations, and we may seek additional funding through a combination of equity offerings, debt, grant funding, collaborations, strategic partnerships and / or licensing arrangements. In February 2023, we completed an underwritten follow- on public offering of 23, 125, 000 shares of our common stock, including the partial exercise of the underwriters' option to purchase additional shares, at a price to the public of $ 2. 25 per share. The total net proceeds from the offering were approximately $ 48. 1 million, after deducting underwriting discounts, commissions and offering expenses payable by us. In April 2022, we entered into an Open Market Sale AgreementSM with Jefferies LLC (Jefferies) implementing an " at- the- market " offering program, (the Jefferies ATM Offering Program) ~~pursuant to which~~ **. In December 2024, we amended the Jefferies ATM Offering Program. Under the Jefferies ATM Offering Program** we may offer and sell, from time to time and at our option, up to an aggregate of $ ~~65~~ **215**. 0 million of shares of our common stock **(inclusive of $ 65. 0 million of sales made prior to the amendment)** through Jefferies, acting as sales agent. Jefferies is entitled to a fixed commission rate of up to 3. 0 % of the gross sales proceeds of shares sold under the Jefferies ATM Offering Program. During **the year ended December 31,** ~~2022~~ **2023**, we sold an aggregate of ~~1~~ **10**, ~~421~~ **530**, ~~627~~ **795** shares of common stock at a weighted- average price of $ ~~3~~ **1**. ~~09~~ **82** per share for net proceeds of approximately $ **18.** 4 ~~. 0~~ million under the Jefferies ATM Offering Program. During the year ended December 31, ~~2023~~ **2024**, we sold an aggregate of ~~10~~ **20**, ~~530~~ **653**, ~~795~~ **450** shares of common stock at a weighted- average price of $ ~~1~~ **2**. ~~82~~ **02** per share for net proceeds of approximately $ ~~18~~ **40**. ~~4~~ **3** million under the Jefferies ATM Offering Program. These financing activities may have an adverse effect on our stockholders' rights, the market price of our common stock and on our

operations, and may require us to relinquish rights to some of our technologies, intellectual property or product candidates, issue additional equity or debt securities, or otherwise agree to terms unfavorable to us. In addition, sales of a substantial number of shares of our common stock by our existing stockholders in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock, even if there is no relationship between such sales and the performance of our business. We have also registered or plan to register all common stock that we may issue under our employee benefits plans as well as shares of common stock underlying options to purchase shares of our common stock that were granted as inducement grants. As a result, once registered, these shares can be freely sold in the public market upon issuance, subject to restrictions under the securities laws. In addition, our directors and executive officers may establish programmed selling plans under Rule 10b5- 1 of the Securities Exchange Act of 1934 (Exchange Act) for the purpose of effecting sales of our common stock. If any of these events cause a large number of our shares to be sold in the public market, the sales could reduce the trading price of our common stock and impede our ability to raise future capital. Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations. We have incurred substantial losses during our history, we do not expect to become profitable in the near future and we may never achieve profitability. Net operating loss **(NOL)** carryforwards ~~(NOLs)~~ that expire unused will be unavailable to offset future income tax liabilities. Under current law, federal **NOLs** ~~net operating losses~~ incurred in tax years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal ~~NOLs~~ **NOL carryforwards in a taxable year** is limited to 80 % of taxable income **in such year** . In addition, under Section 382 of the Internal Revenue Code of 1986, as amended (Code) a corporation that undergoes an " ownership change " (as defined under Section 382 of the Code and applicable Treasury Regulations) is subject to limitations on its ability to utilize its pre- change NOLs to offset post- change taxable income. We have experienced ownership changes in the past, and may experience future ownership changes, under Section 382 of the Code that could affect our ability to utilize our ~~NOLs~~ **NOL carryforwards** to offset our income. Furthermore, our ability to utilize NOLs of companies that we may acquire in the future may be subject to limitations. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs or other unforeseen reasons, portions of our existing NOLs could expire or otherwise be unavailable to reduce future income tax liabilities, including for state tax purposes **. For example, California imposed limits on the usability of California state net operating losses to offset taxable income in tax years beginning after 2023 and before 2027** . For these reasons, we may not be able to utilize a material portion of our NOLs, even if we attain profitability, which could potentially result in increased future tax liability to us and could adversely affect our operating results and financial condition. Uncertainties in the interpretation and application of existing, new and proposed tax laws and regulations could materially affect our tax obligations and effective tax rate. The tax regimes to which we are subject or under which we operate are unsettled and may be subject to significant change. The issuance of additional guidance related to existing or future tax laws, or changes to tax laws or regulations proposed or implemented by the current or a future U. S. presidential administration, Congress, or taxing authorities in other jurisdictions, including jurisdictions outside of the United States, could materially affect our tax obligations and effective tax rate. To the extent that such changes have a negative impact on us, including as a result of related uncertainty, these changes may adversely impact our business, financial condition, results of operations, and cash flows. The amount of taxes we pay in different jurisdictions depends on the application of the tax laws of various jurisdictions, including the United States, to our international business activities, tax rates, new or revised tax laws, or interpretations of tax laws and policies, and our ability to operate our business in a manner consistent with our corporate structure and intercompany arrangements. The taxing authorities of the jurisdictions in which we operate may challenge our methodologies for pricing intercompany transactions pursuant to our intercompany arrangements or disagree with our determinations as to the income and expenses attributable to specific jurisdictions. If such a challenge or disagreement were to occur, and our position was not sustained, we could be required to pay additional taxes, interest, and penalties, which could result in one- time tax charges, higher effective tax rates, reduced cash flows, and lower overall profitability of our operations. Our financial statements could fail to reflect adequate reserves to cover such a contingency. Similarly, a taxing authority could assert that we are subject to tax in a jurisdiction where we believe we have not established a taxable connection, often referred to as a " permanent establishment " under international tax treaties, and such an assertion, if successful, could increase our expected tax liability in one or more jurisdictions. We do not intend to pay dividends on our common stock, and therefore any returns will be limited to the value of our stock. We have never declared or paid any cash dividends on our common stock. We anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock. In addition, future debt instruments may materially restrict our ability to pay dividends on our common stock. Any future determination related to dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, tax considerations, legal or contractual restrictions, business prospects, the requirements of current or then- existing debt instruments, general economic conditions and other factors our board of directors may deem relevant. Provisions in our amended and restated certificate of incorporation and amended and restated bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to remove our current management, acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders. Our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and amended and restated bylaws include provisions that: • authorize " blank check " preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock; • create a classified board of directors whose members serve staggered three- year terms; • specify that special meetings of our stockholders can be called only by our

board of directors, the chairperson of our board of directors, our chief executive officer or our president; • prohibit stockholder action by written consent; • establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors; • provide that our directors may be removed only for cause; • provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum; • specify that no stockholder is permitted to cumulate votes at any election of directors; • expressly authorize our board of directors to modify, alter or repeal our amended and restated bylaws; and • require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated bylaws. These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management. In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15 % of our outstanding voting stock to merge or combine with us. Any provision of our amended and restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock. Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for certain disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees. Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, (iii) any action asserting a claim against our company arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or bylaws, or (iv) any action asserting a claim against our company governed by the internal affairs doctrine. This choice of forum provision does not apply to suits brought to enforce a duty or liability created by the Securities Act of 1933, as amended (Securities Act) or the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction. This choice of forum provision may limit a stockholder' s ability to bring certain claims in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder. If a court were to find this choice of forum provision to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition. General Risk Factors If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business. We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work- related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions. If our information technology systems or data, or those maintained ~~on our behalf~~ **by the third parties with whom we work** , are or were compromised, this could result in a Material Adverse Impact. In the ordinary course of our business, we and the third ~~-~~ parties ~~upon which~~ **with whom** we ~~rely~~ **work** Process (as defined above) proprietary, confidential and sensitive information, including personal data (including key- coded data, health information and other special categories of personal data), intellectual property, trade secrets, and proprietary business information owned or controlled by ourselves or other third **party** ~~parties~~ **partners** (collectively, Sensitive Information). We and ~~our~~ **the** third ~~- party service providers~~ **parties with whom we work** utilize information technology systems to Process Sensitive Information in connection with our business activities, and we face a variety of evolving threats that could cause security incidents. Cyber- attacks, malicious internet- based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity and availability of our Sensitive Information and information technology systems, and those of the third parties ~~upon which~~ **with whom** we ~~rely~~ **work** . Such threats are prevalent, continue to rise, are increasingly difficult to detect and come from a variety of sources, including traditional computer " hackers, " threat actors, " hacktivists, " organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation state supported actors. Some actors now engage and are expected to continue to engage in cyber- attacks, including without limitation nation state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties ~~upon which~~ **with whom** we ~~rely~~ **work** may be vulnerable to a heightened risk of these attacks, including retaliatory cyber- attacks, that could materially disrupt our systems and operations, supply chain, and ability to conduct our business. We and the third parties ~~upon which~~ **with whom** we ~~rely~~ **work** are subject to a variety of evolving threats, including but not limited to software bugs; malicious code (such as viruses and worms); denial- of- service attacks; credential stuffing; credential harvesting; malware (including as a result of advanced persistent threat intrusions; natural disasters; terrorism; war; telecommunication and electrical failures; ransomware attacks; social- engineering attacks (including through deep fakes, which

may be increasingly more difficult to identify as fake, and phishing attacks); server malfunctions; software or hardware failures; supply- chain attacks; loss of data or other computer assets; attacks enhanced or facilitated by AI; and other similar ~~issues~~ **threats** . Particularly, severe ransomware attacks are becoming increasingly prevalent and can lead to significant interruptions, delays, or outages in our operations, disruption of clinical trials, loss of data (including data related to clinical trials), and other Material Adverse Impacts (as defined above). To alleviate the financial, operational and reputational impact of a ransomware attack, it may be preferable to make extortion payments, but we may be unwilling or unable to do so (including, for example, if applicable laws or regulations prohibit such payments). **It may be difficult and / or costly to detect, investigate, mitigate, contain and remediate a security incident. Our efforts to do so may not be successful. Actions taken by us or the third parties with whom we work to detect, investigate, mitigate, contain and remediate a security incident could result in outages, data losses and disruptions of our business. Threat actors may also gain access to other networks and systems after a compromise of our networks and systems.** Additionally, remote work ~~has become more common and~~ has increased the risk to our information technology assets and data, as more of our employees utilize network connections, computers and devices outside of our premises and networks, including working at home, while in transit and public locations. Additionally, future or past business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies. Furthermore, we may discover security issues that were not found during due diligence of such acquired or integrated entities, and it may be difficult to integrate companies into our information technology environment and security program. We use third ~~- party~~ **parties, including** service providers and subprocessors **,** to help us operate our business and engage in Processing ~~on our behalf~~ or otherwise share Sensitive Information with our partners or other third parties in conjunction with our business. These third **parties** ~~party service providers~~ and **their** technologies operate critical business systems to Process Sensitive Information in a variety of contexts, including, without limitation, cloud- based infrastructure, data center facilities, encryption and authentication technology, employee email, and other functions. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If ~~our~~ **the** third ~~- party service providers~~ **parties with whom we work** experience a security incident or other interruption, we could experience Material Adverse Impacts. While we may be entitled to damages if ~~our~~ **the** third ~~- party service providers~~ **parties with whom we work** fail to satisfy their privacy or security- related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award. Similarly, supply chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or ~~our~~ **that of the** third ~~- party partners~~ **parties** ~~' supply chains~~ **with whom we work** have not been compromised. Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our Sensitive Information or our information technology systems, or those of the third parties ~~upon~~ **with** whom we ~~rely~~ **work. Any of the previously identified or similar threats could cause a security incident or other interruption that could result in unauthorized, unlawful, or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of, or access to our sensitive information or our information technology systems, or those of the third parties with whom we work. For example, we have been the target of phishing attempts in the past, and expect such attempts will continue in the future** . A security incident or other interruption could disrupt our ability (and that of third parties ~~upon~~ **with** whom we ~~rely~~ **work**) to provide our services. We may expend significant resources, fundamentally change our business activities and practices, or modify our operations, including our clinical trial activities, or information technology in an effort to protect against security incidents and to mitigate, detect, and remediate actual and potential vulnerabilities. Applicable Data Protection Requirements (as defined above) may require us to implement specific security measures ~~or use industry- standard or reasonable measures~~ to protect against security incidents. While we have implemented security measures designed to protect against security incidents, there can be no assurance that we, or ~~any~~ **the** third ~~- party partner~~ **parties with whom we work** , will be successful in preventing a security incident or mitigating their effects. We take steps designed to detect, mitigate and remediate vulnerabilities in our information technology systems **(such as our hardware and / or software** , ~~but~~ **including that of third parties with whom** we **work). We** may not ~~be able to~~ **, however,** detect and remediate all ~~vulnerabilities because the threats and techniques used to exploit the vulnerability change frequently and are often sophisticated in nature. Therefore,~~ such vulnerabilities **including that of third parties with whom we work, on a timely basis. Further, we may experience delays in developing and deploying remedial measures and patches designed to address identified vulnerabilities. Vulnerabilities** could be exploited **and result in** ~~but may not be detected until after~~ a security incident ~~has occurred~~ . **These** ~~Unremediated high risk or critical~~ vulnerabilities **, bugs, errors or defects alone, or a combination of them, could** pose material ~~risk~~ **risks** to our business ~~. Further, we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities~~ . Furthermore, applicable Data Protection Requirements may require us **, or we may voluntarily choose,** to notify relevant stakeholders of security incidents **, or take other actions, such as providing credit monitoring and identity theft protection services** . Such disclosures ~~are~~ **and related actions can be** costly, and the disclosures or the failure to comply with such **applicable** requirements could lead to Material Adverse Impacts. If we or the third parties ~~upon which~~ **with whom** we ~~rely~~ **work** experience or in the future experience (or are perceived to have experienced) any security incident (s), we could suffer reputational harm, face litigation or adverse regulatory actions, fines, other penalties, audits, inspections, additional reporting requirements and / or oversight, restrictions on Processing Sensitive Information, indemnification obligations, negative publicity, business interruptions, and diversion of funds. For example, the loss of data from completed clinical trials for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs. As a result, we could experience Material Adverse Impacts. Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims

related to our data privacy and security obligations. Furthermore, we cannot be sure that our insurance coverage, will be adequate or otherwise protect us from or adequately mitigate liabilities or damages with respect to claims, costs, expenses, litigation, fines, penalties, business loss, data loss, regulatory actions or Material Adverse Impacts arising out of our Processing operations, data privacy and security practices, or security incidents we may experience. The successful assertion of one or more large claims against us that exceeds our available insurance coverage, or results in changes to our insurance policies (including premium increases or the imposition of large excess or deductible or co- insurance requirements), could have a Material Adverse Impact. In addition to experiencing a security incident, third parties may gather, collect, or infer Sensitive Information about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position. Additionally, Sensitive Information of the Company could be leaked, disclosed, or revealed as a result of or in connection with our employees', personnel' s, or vendors' use of generative AI technologies. We are subject to anti- corruption laws in the jurisdictions in which we operate. We are subject to a number of anti- corruption laws, including the Foreign Corrupt Practices Act of 1977, as amended (FCPA), and various other anti- corruption laws. The FCPA generally prohibits companies and their intermediaries from making improper payments to foreign officials for the purpose of obtaining or keeping business and / or other benefits. Our business relies on approvals and licenses from government and regulatory entities, and as a result, we are subject to certain elevated risks associated with interactions with these entities. Although we have adopted a code of business conduct and ethics that includes provisions governing the interactions of employees with government entities to mitigate these risks, there can be no assurance that this will be successful in preventing violations of anti- corruption laws. If we are not in compliance with anti- corruption laws and other laws governing the conduct of business with government entities (including local laws), we may be subject to criminal and civil penalties and other remedial measures, which could harm our reputation and have a material adverse effect on our business, financial condition, results of operations and prospects. Any investigation of any actual or alleged violations of such laws could also harm our reputation or have an adverse impact on our business, prospects, financial condition and results of operations. We have incurred and will continue to incur significant costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives. As a public company, we have incurred and will continue to incur legal, accounting and other expenses. In addition, the Sarbanes- Oxley Act of 2002 as well as rules subsequently implemented by the SEC and The Nasdaq Stock Market have imposed various requirements on public companies. In July 2010, the Dodd- Frank Wall Street Reform and Consumer Protection Act (the Dodd- Frank Act) was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd- Frank Act that require the SEC to adopt additional rules and regulations in these areas such as " say on pay " and proxy access. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time- consuming and costly. For example, these rules and regulations make it more difficult and more expensive for us to maintain director and officer liability insurance and we have been required to incur substantial costs to maintain our current levels of such coverage. If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline. The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. If no or few analysts commence coverage or continue coverage of us, the trading price of our stock would likely decrease. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline. We could be subject to securities class action litigation. In the past, securities class action litigation has often been brought against companies following a decline in the market price of their securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility. If we face such litigation, it could result in substantial costs and a diversion of management' s attention and resources, which could harm our business and cause our stock price to decline. We have broad discretion in the use of our cash, cash equivalents ~~, restricted cash~~ and available- for- sale investments and are exposed to risks related to the marketable securities we may purchase. We have considerable discretion in the application of our existing cash, cash equivalents ~~, restricted cash~~ and available- for- sale investments. We expect to use our existing cash to fund research and development activities and for working capital and general corporate purposes, including funding the costs of operating as a public company. In addition, pending their use, we may invest our existing cash in certain short- term investments, including but not limited to investment- grade, interest- bearing securities. Historically, investment in these securities has been highly liquid and has experienced only very limited defaults. However, volatility in the financial markets in recent years has created additional uncertainty regarding the liquidity and safety of these investments. Additionally, we may use this cash, cash equivalents ~~, restricted cash~~ and available- for- sale investments for purposes that do not yield a significant return or any return at all for our stockholders.