Risk Factors Comparison 2023-03-16 to 2022-03-24 Form: 10-K

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~~Our business is subject to numerous~~ **Investing in our common stock involves a high degree of risk. You should carefully consider the** risks ~~and uncertainties, including those~~ described **below** ~~in Part I~~, **as well as the other information** ~~Item 1A. " Risk Factors "~~ in this Annual Report on Form 10- K ~~. You should carefully consider~~ **, including our consolidated financial statements and** ~~these~~ -- **the** ~~risks~~ **related notes** and ~~uncertainties when~~ **Part II, Item 7 " Management' s Discussion and Analysis of Financial Condition and Results of Operations ", before deciding whether to** ~~investing~~ --- **invest** in our common stock. ~~Principal risks and uncertainties affecting~~ **The occurrence of any of the events or developments described below could harm** our business ~~include~~ **, financial condition, results of operations and growth prospects. In such an event,** the ~~following: •~~ **market price of our common stock could decline, and you may lose all or part of your investment. Risks Related to Our Financial Position and Need for Additional Capital** We are a development- stage company and have incurred significant losses since our inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability. ~~Moreover~~ **Since inception** , ~~our limited~~ **we have incurred significant** operating ~~history may make it difficult to evaluate~~ **losses. Our net loss was $ 114. 5 million and $ 122. 2 million for** the ~~success~~ **years ended December 31, 2022 and 2021, respectively. As** of ~~our business to date~~ **December 31, 2022, we had** ~~and~~ - **an** ~~to assess our future viability~~ **accumulated deficit of $ 529** . ~~• We~~ **2 million. As noted below, we** have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. ~~We will need additional funding in order to complete development of our product candidates and commercialize our products, if approved. If we are unable to raise capital when needed, we will be forced to delay, reduce or discontinue our product development programs or commercialization efforts. • Our product candidates are based on targeting SINTAX ™, the small intestinal axis, which is an unproven approach to therapeutic intervention. • We are dependent on the success of our investigational product candidates. If the investigational product candidates do not successfully complete clinical development or receive regulatory approval, our business may be harmed. • The regulatory approval process is lengthy, expensive and uncertain, and we may be unable to obtain regulatory approval for our product candidates under applicable regulatory requirements of the United States and / or internationally. The denial or delay of any such approval would delay commercialization of our product candidates and adversely impact our ability to generate revenue, our business and our results of operations. • We rely, and will continue to rely, on third parties to conduct the clinical trials for our product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials. • We do not have our own manufacturing capabilities and rely, and will continue to rely, on third parties to produce clinical supplies and, if approved, commercial supplies of our product candidates. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. • If we are unable to establish our own sales, marketing and distribution capabilities, or enter into agreements with third parties to sell and market our product candidates, we may not be successful in commercializing our product candidates if and when they are approved, and we may not be able to generate any revenue. • The successful commercialization of our product candidates will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue. • We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do. • Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, cause us to suspend or discontinue clinical trials, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any. • If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents which are sufficient to protect our product candidates, other companies could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects. • The COVID-19 pandemic has adversely impacted, and may continue to adversely impact, our business, including our preclinical studies and clinical trials, results of operations and financial condition. PART I Item 1. Business Overview Evelo Biosciences is discovering and developing a new class of orally delivered investigational medicines that are intended to act on cells in the small intestine to produce therapeutic effects throughout the body. The target cells in the small intestine play a central role in governing human immune, metabolic and neurologic systems. We refer to this biology as the small intestinal axis, or SINTAX ™. We have built a platform to discover and develop novel oral medicines which target the small intestinal axis. By harnessing the small intestinal axis, we have the potential to transform healthcare via medicines that have the potential to be effective, safe, convenient and affordable and to thereby treat patients at all stages of diseases and to treat patients globally. Our first product candidates are orally delivered pharmaceutical preparations of naturally occurring, specific single strains of microbes or microbial extracellular vesicles. In preclinical models, our product candidates engaged immune cells in the small intestine and drove changes in systemic biology without any observed systemic exposure. We have observed in clinical trials and preclinical studies that our approach led to modulated immune responses throughout the body by acting on the small intestinal axis. Our most advanced product candidate, EDP1815, is being developed for the treatment of inflammatory diseases. Additional product candidates in development include EDP1867 and EDP2939 for the treatment of inflammatory disease. Orally delivered SINTAX medicines have the potential to address patient needs at all stages of disease due to their potentially superior characteristics over current therapies: • In preclinical models, our product candidates have acted through multiple clinically relevant and validated biological~~

pathways. By acting on multiple pathways simultaneously, we believe our product candidates could impact disease in ways that are not possible with current single- target or dual- target therapies. • Our data suggest that our product candidates for inflammatory diseases have the potential to resolve disease causing inflammation whilst preserving immunity, a significant potential benefit. Anti- inflammatory therapies often cause significant immune suppression. • EDP1815 has been administered in approximately 480 human subjects as of March 11, 2022, and been generally well tolerated in clinical trials to date. EDP1815 and our other product candidates are derived from naturally occurring, specific single commensal strains of human bacteria, have not shown systemic exposure in clinical trials to date, and have been observed to be cleared from the body with no colonization of the gut. • Our product candidates are formulated as oral medicines, which most patients prefer over injectable biologics and burdensome application of topical medicines. • We have developed robust manufacturing processes for EDP1815, allowing for large scale production and the potential for global, room- temperature stable distribution of EDP1815 at affordable prices. • We believe our discovery and development of oral SINTAX medicines has the potential to be more efficient than other product classes such as cell therapy, monoclonal antibodies and small molecules. We believe that our product candidates will not require the lengthy target validation and compound discovery requirements of conventional drug discovery. In turn, we believe that SINTAX medicines provide a clear pathway to successfully achieving our mission to treat patients at all stages of disease, across the globe. Our Strategy Our goal is to create and develop a new class of therapies that has the potential to transform the treatment of a broad range of diseases by targeting SINTAX. Key elements of our strategy: • Explore the full potential of SINTAX to create an expansive and diversified product portfolio. We believe targeting SINTAX has applicability across a broad range of disease areas and we are committed to pursuing opportunities in which our platform has the potential to transform their treatment. Our initial focus is on inflammatory diseases and oncology. We intend to expand into other disease areas, such as autoimmune diseases, respiratory diseases, neuro- inflammation and degeneration, allergy, neurobehavior, cardiovascular disease and diseases of metabolism. We also see the potential for early disease intereception and intervention, and the ability to impact inflammation driven aging. • Develop best- in- class therapies to improve outcomes across various stages of disease. We intend to develop best- in- class orally delivered therapies and explore the potential of SINTAX medicines across the full spectrum of disease severity, including in patients with mild and moderate forms of disease. We intend to pursue what we believe to be the inherent advantages of SINTAX medicines to enable use in all stages of disease. • Advance and scale our SINTAX medicine platform. We plan to continue to invest in our platform, which integrates microbiology, immunology and computational biology capabilities. We intend to expand the diversity of our microbial library and enhance our proprietary in vitro and in vivo assays to optimize selection of our future product candidates. Our manufacturing processes are designed to ensure the quality and scalability of our product candidates. We plan to continue to invest in novel methods for process development, manufacturing and formulation for our SINTAX medicine. In the future, we intend to invest in commercial scale manufacturing. We plan to leverage the efficiency of our integrated capabilities to accelerate the clinical development of product candidates. • Expand our intellectual property to protect our platform and product candidates. We have exclusive rights to our technologies including issued composition of matter and method of use patents in the United States relating to some of our product candidates. We intend to pursue patent protection for our scientific innovations and to maintain a strong and broad estate of patents and trade secrets in the United States and other geographies. • Collaborate to realize the potential of SINTAX medicines. We intend to continue to seek collaborations with academic groups, biotech and pharmaceutical companies to realize the value of our broad platform and extend the range of our development activities and disease areas in a timely and cost-effective manner. We plan to commercialize products in multiple geographies both on our own and with collaborators. The Immune System and the Use of Immunotherapy in Disease Immunology and Current Immunotherapy The immune system consists of many different cell types that act together as a coordinated system constantly scanning for, identifying and responding to both human and microbial signals. Immune cells, including different types of T- cells, circulate throughout the body via the lymphatic system searching for signs of disease or infection. When this immune surveillance is functioning correctly, immune cells recognize and destroy both pathogens and cancer cells. However, when the immune system responds excessively, diseases such as psoriasis, rheumatoid arthritis, atopic dermatitis, asthma, inflammatory bowel disease and multiple sclerosis can result. Conversely, an inadequate immune system response may allow various types of cancer and infections to progress unchecked. Advances in our understanding of how the immune system affects a broad spectrum of disease has resulted in the development of immunotherapies, which are medicines that reduce, suppress, elicit or amplify specific immune responses. Antibody- based immunotherapies for inflammatory diseases and oncology have fundamentally changed the treatment landscape for patients. For example, anti- TNFα antibodies are widely used to treat moderate to severe stages of many inflammatory diseases. In 2020, three of the twenty top selling drugs worldwide were anti- TNFα antibodies, with HUMIRA alone generating worldwide annual net sales of $ 20. 4 billion. In oncology, checkpoint inhibitor antibodies, including those targeting the programmed cell death protein / ligand 1, or PD- 1 / PD- L1 pathways, block the tumor' s ability to suppress the immune response. They have improved the treatment of many cancers and are expected as a class to reach peak annual net sales of $ 30 billion by 2025. While existing immunotherapies have been successful in treating inflammatory diseases and oncology, there remains a substantial unmet need for patients. Emergence of a Broad New Opportunity in Immunotherapy Until recently, immunotherapeutic approaches have largely ignored one of the body' s naturally- evolved routine immunological processes and its associated immune organ — the gut, and specifically the small intestine. Immunomodulation through the small intestine has the potential to address certain limitations of current immunotherapies by acting on multiple naturally evolved and clinically relevant pathways. We believe this novel approach presents advantages, including potentially minimizing adverse events, enhancing patient convenience and targeting multiple immune pathways simultaneously. We believe that a novel class of therapeutics with these attributes has the potential to be transformative in treating a broad range of immune- mediated diseases. Furthermore, we believe this approach could also expand the use of immunotherapies for the treatment of patients with earlier stages of disease. SINTAX is Central to Human Biology and Immunology The small intestine is the largest part of the immune

system. Specific types of immune cells, such as dendritic cells and macrophages, are resident in the tissue of the small intestine. They sample specific contents in the interior of the small intestine, which is called the lumen. These immune cells then migrate to lymph nodes where they condition other important immune cells, including T- cells. These conditioned T- cells then travel throughout the body via the lymphatic system to impact disease. We believe SINTAX provides an opportunity for immunomodulation throughout the body after oral delivery of products that remain physically restricted to the lumen and lymphoid tissues of the gut. Immunomodulation via SINTAX may represent an underappreciated opportunity to drive therapeutically relevant immune responses throughout the body. SINTAX, Microbes and Microbial Extracellular Vesicles Microbes in the human gut are single- cell organisms that have co- evolved with the human immune system. Many human immune cells are programmed to sense and respond to microbes that they contact in the small intestine. Research in mucosal immunology has revealed that microbial interactions in the small intestine can drive activity in SINTAX. Multiple mechanisms for direct interactions between microbes and immune cells in the small intestine have been demonstrated. We believe that dendritic cells and macrophages in the lymphoid tissues of the small intestine are key target cells of immunomodulatory microbes. The small intestine has a large surface area and thin and diffuse mucus layer, which allows for close contact between microbes and immune cells. Dendritic cells are a specialized type of immune cell that survey the body' s tissues, detecting and presenting antigens to T- cells. Macrophages can take on many functional forms depending on the conditioning of their environment in the body and are important for both anti- inflammatory and anti- tumor immunity. Immune cells, such as dendritic cells and macrophages, can extend protrusions through junctions between epithelial cells in the lining of the small intestine. These protrusions come into direct contact with and sample the microbial contents of the small intestine lumen. These immune cells then migrate to mesenteric lymph nodes where they come into contact with T- cells. Dendritic cells and macrophages that have been primed by exposure to microbes in the gut, condition T- cells within the mesenteric lymph node and push them towards an inflammatory or immunoregulatory phenotype depending on the specific strain of the microbe. Conditioned T- cells continue to move through the body via the lymphatic system to other parts of the body where they may act in local tissue to modulate an immune response. Several of our academic collaborators have explored the functional consequences of the interactions between immune cells and single strains of microbes in the gut. Veena Taneja, Ph. D. and Joseph Murray M. D. of the Mayo Clinic showed that an orally administered strain of Prevotella histicola modulated immune function in mouse models of rheumatoid arthritis, multiple sclerosis, Type I diabetes, and celiac disease. In the field of immuno- oncology, Thomas Gajewski, M. D., Ph. D. and his group at the University of Chicago conducted an experiment in which a single strain of orally administered Bifidobacterium had equivalent activity to an anti- PD- L1 antibody and additive activity in combination in a mouse model of melanoma. We believe these and other examples from the academic literature support our theory that single strains of microbes can act on SINTAX to suppress or activate immune responses throughout the body. Our clinical data to date also support this theory. As an extension of our platform, we are evaluating microbial extracellular vesicles (" EVs ") as a next- wave of product candidates targeting SINTAX. EVs are lipoprotein nanoparticles that are naturally secreted by multiple cell types, including certain bacterial cells. EVs are a core component of host- microbe communication and contain the pharmacologically active structural motifs that drive activity of single- strain microbes. We believe EVs have the potential to enable stronger SINTAX activation and therapeutic efficacy through their smaller size and diffusion properties. SINTAX medicines as a Potential New Class of Oral Biologic Medicines Our company was founded to discover and develop therapies that act on SINTAX. We aim to develop therapies based on our observations on the central role of the small intestine in modulating immune activity throughout the body and the equally important role of microbes as key modulators of SINTAX. We have developed the tools to isolate, select, and develop specific microbes that have historically been difficult to identify, isolate and culture. This extends from microbial isolation to manufacturing. We have developed proprietary insights and tools that enhance our ability to produce pharmaceutical compositions of microbes at scale. This allows us to deliver potentially therapeutic doses of appropriately formulated strains. We are developing SINTAX medicines- whole, inactivated microbes and microbial EVs- to engage cells in the small intestine and drive changes in systemic biology, by either downregulating or upregulating immune responses for the treatment of disease. SINTAX medicines are orally delivered pharmaceutical compositions of specific strains of microbes or EVs from specific strains of microbes. We believe key features and advantages of our SINTAX medicine candidates are: • Single strain. Our product candidates are pharmaceutical compositions of single strains of microbes or EVs produced by single strains of microbes that we have selected for their specific immunomodulatory properties. We extensively characterize the ability of our product candidates to elicit a desired immunomodulatory effect. • Orally- administered formulation. We intend to deliver our initial product candidates orally in formulations designed for targeted release to specific regions within the small intestine. Patients typically prefer oral administration to intravenous infusion, subcutaneous injection, and topical administration, which we believe will facilitate the adoption of our SINTAX medicines, if approved. • Limited systemic exposure. In preclinical studies, we observed that our product candidates had limited systemic exposure, that they cleared from the gut within 24 to 48 hours and that colonization was not required for beneficial activity. We believe that these factors suggest that SINTAX medicines may have limited systemic off- target side- effects. Our clinical data to date support this potential. • Action on multiple clinically relevant and validated pathways. Our preclinical data have shown that SINTAX medicines may act simultaneously on multiple clinically relevant and validated biological pathways. The diseases we intend to treat are multifactorial, and we believe that our potential therapies will be advantageous over single- target treatments. Additionally, our data suggest that SINTAX medicines resolve inflammation whilst preserving immunity, a significant potential benefit compared to other anti- inflammatory therapies that often cause significant immune suppression. Given these expected features, we believe that SINTAX medicines may have a number of advantages in comparison to other immunotherapies such as antibodies, cell therapies and small molecules. SINTAX Medicine Platform We have developed an integrated platform designed to identify individual strains of microbes capable of modulating the immune system by acting on SINTAX when administered at pharmacologically active doses and appropriately formulated. We use the process development

and formulation capabilities of our platform to develop selected microbes and EVs as product candidates. Our proprietary SINTAX platform is comprised of the following four key areas: Candidate discovery. We have assembled a proprietary library of diverse strains of microbes. The continuing accrual of strains in our library is from human mucosal and small intestinal sources in order to benefit from the co- evolution of microbes and the human immune system. We also add to our library through selective licensing agreements and collaborations with academic partners. The proprietary tools within our platform are designed to identify and characterize selected microbes using in vitro, in vivo and ex vivo assays. Proprietary in vitro assays simulate the interactions between microbes and human immune cells, allowing us to evaluate the immunological activity of each microbial strain in relevant experimental systems. Our in vitro assays can screen hundreds of microbes, producing more than 150 data points per strain, including levels of pro- inflammatory and anti- inflammatory cytokines and chemokines. This assists our comprehensive selection process to identify candidates for testing in relevant animal models. Product form. The activity of our SINTAX medicines observed in preclinical studies has been driven by engagement with and modification of immune cells in the small intestine. This activity has not been reliant on engraftment (or colonization) as we have observed that our SINTAX medicines passed through the gut and did not distribute around the body or engraft in the gut. Furthermore, this preclinical activity was observed to be independent of the ability of our SINTAX medicines to replicate. From this observation, we believe that activity of SINTAX medicines is likely driven by recognition of structural motifs on the surface of microbes or EVs by immune cells in the small intestine. Our candidate selection process may include an additional manufacturing step for our whole- microbe candidates to develop them as non- replicating product candidates, such as EDP1867. We are also developing reduced forms of our whole- microbe product candidates, for example in the form of EVs, to target SINTAX. Preclinical studies suggest that this approach may further improve potency and activity and we anticipate the initiation of clinical development of EDP2939, an EV product candidate, in 2022. Formulation. In our first clinical trials, product candidates were formulated as capsules containing lyophilized powder for targeted release in the small intestine. We have continued to explore potency and dose as it relates to formulation and have developed manufacturing processes that increase the concentration of EDP1815. Additionally, we have developed a tablet formulation with the higher concentration of EDP1815, also for targeted release in the small intestine. We are committed to continuously investing in formulation development to improve the potency and delivery of our product candidates and enhance their ability to target and act on SINTAX. Process development and manufacturing. Process development and manufacturing are critical for the translation of SINTAX medicines into therapies. Our expertise and investments in laboratory and pilot scale development have allowed us to mitigate challenges inherent to manufacturing SINTAX medicines at clinical scale. Process development is integrated into our research activities, combining discovery and downstream development. We believe we have achieved control of quality, identity, purity, and potency throughout the process of strain selection, fermentation, EV purification, formulation, and pharmacology, with high yield. Importantly, we believe our manufacturing processes enable us to produce a drug substance that is pharmacologically active in the form of a lyophilized powder, which is suitable for production in accordance with current Good Manufacturing Practice (" cGMP"), Good Manufacturing Practice (" GMP"), and other similar foreign regulations. For each of our clinical product candidates, we have observed therapeutic activity in lyophilized powder form and in compressed tablet form in relevant preclinical mouse models and, in the case of EDP1815, in clinical trials using lyophilized powder in capsules. We have been able to manufacture SINTAX medicines in a relatively short timeframe compared to other biologic therapies, which we believe may accelerate our speed into the clinic. Additionally, we believe that we may be able to cost- effectively manufacture SINTAX medicines. Product Development Strategy and Portfolio We are advancing SINTAX medicines to potentially treat a spectrum of immune- mediated diseases, with an initial focus on inflammatory diseases. We expect our initial clinical trials for our product candidates to provide information on safety, tolerability, pharmacodynamic responses and biomarkers of immune response in multiple indications with different pathologies and sites of disease. This may allow for expansion into an additional range of clinical indications, which could enable us to capture broader clinical value. Beyond our first wave of product candidates in inflammatory diseases, we are continuing to invest in the discovery of new candidates to build a deep pipeline across a wide range of diseases, including in neuroinflammation, to leverage the broad potential of our platform. We also intend to opportunistically collaborate to expand indications and accelerate development of programs where collaborators can contribute further disease- specific expertise to our platform. In addition to product candidates based on whole and inactivated microbes, which include EDP1815 and EDP1867, we continue to advance the development of orally delivered EVs. EVs are lipoprotein nanoparticles naturally produced by some bacteria. EVs have the potential to enable increased target engagement driven by their small size, as they are approximately 1 / 1, 000th the volume of whole microbes. We have nominated two EV clinical candidates, EDP2939 and EDP1908, for the treatment of inflammatory diseases and cancer, respectively, and anticipate initiating the first- in- human clinical trial of EDP2939 in 2022. Our ongoing and planned clinical trials for our current product candidates are illustrated below. Inflammatory Diseases Portfolio We have three candidates in development for inflammatory diseases. EDP1815 is a whole- microbe product candidate that completed a Phase 2 trial for the treatment of psoriasis in 2021, and is currently in a Phase 2 trial for the treatment of atopic dermatitis. Additionally, we advanced EDP1867, an inactivated, whole- microbe product candidate, into a Phase 1b study in 2021 in patients with atopic dermatitis. EDP2939 is our first product candidate based on EVs, and we anticipate initiation of clinical development of this product candidate in 2022. EDP1815 is an investigational oral biologic being developed for the treatment of inflammatory diseases. It is a single strain of Prevotella histicola, selected for its specific pharmacology. Psoriasis and atopic dermatitis Phase 2 clinical trial in psoriasis In September 2021, we announced positive data from our Phase 2 trial of EDP1815 in psoriasis. This multicenter, randomized, double- blind, placebo- controlled, dose- ranging Phase 2 trial was designed to evaluate three doses of an enteric coated capsule formulation of EDP1815 in adult patients with mild and moderate psoriasis. The trial included a treatment phase (Part A) and an off treatment, follow- up phase (Part B). In Part A of the trial, 249 patients were randomized in a 1: 1: 1 ratio to one of three parallel cohorts: 1 capsule, 4 capsules or 10 capsules. They were then randomized in a 2: 1 ratio to active or placebo prior to the start of dosing. Trial medication was taken once daily for

16 weeks, and patients were followed for 4 weeks after treatment completion to week 20. Psoriasis Area and Severity Index (“ PASI ”) scores were assessed by both mean changes from baseline and responder rates. The primary endpoint was the mean percentage change in PASI scores between treatment and placebo at 16 weeks. Secondary endpoints included the proportion of study patients who achieved at least a 50 % improvement in PASI from baseline at the week 16 timepoint (a" PASI- 50" response), and other clinical measures of disease such as Physicians Global Assessment (" PGA"), Body Surface Area (" BSA"), PGA x BSA, Psoriasis Symptom Inventory (" PSI"), and Dermatology Life Quality Index (" DLQI"). The primary endpoint, the difference in mean percentage change in PASI scores from baseline at week 16 between treatment and placebo, was prespecified as a Bayesian analysis. The Bayesian approach provides an estimate of the probability that EDP1815 was superior to placebo. The 16- week primary endpoint gave probabilities that EDP1815 is superior to placebo ranging from 80 % to 90 % across the prespecified analyses and cohorts. The responder endpoint analysis evaluated the proportion of patients who achieved a PASI- 50 (a meaningful clinical response) or greater reduction in PASI score at week 16. As shown in the figure below, 25 % to 32 % of patients across the three EDP1815 treated cohorts achieved a PASI- 50 or greater reduction at week 16 compared to 12 % on placebo. In cohorts 1 and 2, this difference in response rate was statistically significant ($p < 0. 05$). Cohort 3 was not statistically significant, but directionally similar (25 % vs. 12 %). The pooled PASI- 50 response across all three EDP1815 cohorts, an exploratory analysis, was 29 % vs. 12 % for placebo and was also statistically significant with a p- value of 0. 027. An increase in the number of capsules of EDP1815 did not lead to a dose response. * $p < 0. 05$. PASI- 50 responses at week 16. Statistically significant p- value (< 0. 05) for 2 of the 3 individual dose cohorts, and for all 3 cohorts when pooled Additionally, several patients on EDP1815 achieved a PASI- 75 response or better at week 16. For individuals who had a PASI- 50 response or better, consistent improvements in patient reported outcomes such as DLQI and PSI were observed as seen in the figure below. Responders in active cohort demonstrated improvements across multiple secondary endpoints. A" responder" was defined as an active patient who achieved PASI- 50 or greater. EDP1815 was observed to be well tolerated in Part A (treatment phase) of the Phase 2 trial. The safety data were comparable to placebo. Adverse events (" AEs") classified as “ gastrointestinal ” were comparable between active and placebo groups, with no meaningful differences in rates of diarrhea, abdominal pain, nausea, or vomiting. There were no drug related serious adverse events. All patients in Part A of the Phase 2 trial had the option to enter Part B (extended follow- up phase, off- treatment) of the trial. The objective of Part B was to assess durability of treatment response and incidence of rebound (for example, increase in PASI score to 125 % of baseline value or above, or onset of new pustular erythrodermic psoriasis within 3 months) following cessation of dosing. Patients in Part B were assessed during follow- up visits at weeks 24 and 28. Only patients who had achieved a PASI- 50 or greater at week 16 were also evaluated at week 40. Patients were not permitted to start other psoriasis treatments or trials during Part B. In February 2022, we announced data from Part B of the Phase 2 trial in psoriasis, which included durable and deeper clinical responses. Eighty- three patients who had received EDP1815 in Part A entered Part B. Thirty of these 83 patients had achieved a PASI- 50 or greater reduction at week 16 of Part A. Eighteen of the 30 patients remained at PASI- 50 or greater at the end of Part B. Ten of the 30 patients had achieved a PASI- 75 or greater at the end of Part A and 5 remained at PASI- 75 or greater at the end of Part B. These durable results were achieved without any new psoriasis medication being used during this time. Nineteen of the 83 patients had achieved clear skin (PGA 0) or nearly clear skin (PGA 1) at the end of Part A and of these, 9 remained at PGA 0 / 1 at the end of Part B. Of the 30 patients who had reached a PASI- 50 at the end of Part A and entered Part B, 10 had already achieved a PASI- 75 response at week 16 in Part A. Of the remaining 20 patients, 9 achieved a PASI- 75 or greater response during the post- treatment period. These data, combined with the durability data, suggest that longer dosing could lead to further deepening of the responses in some patients. There were no drug related adverse events in Part B of the Phase 2 trial, with the additional finding of no flare or rebound following cessation of dosing (which are often seen with other therapies for psoriasis). In February 2022, we also announced the results of immunological biomarker analyses from Part A of the Phase 2 trial in psoriasis. We had previously reported reductions in inflammatory cytokines in a Phase 1b trial of EDP1815 in mild and moderate psoriasis, and these data were replicated in the Phase 2 psoriasis trial, with high statistical significance. Blood samples were taken from 96 patients at baseline and after 16 weeks of dosing with EDP1815 or placebo. The figures below show the changes in pro- inflammatory cytokines interleukin 6 (IL- 6), interleukin 8 (IL- 8) and tumor necrosis factor (TNF). Each vertical bar represents the fold change up or down from 0 in ex vivo stimulated cytokine production between the baseline and week 16 samples from a patient. Three different stimuli were used on each sample and the results from all three stimuli are presented together in the figures, giving the aggregate N (sample) numbers shown in the figures. Treatment with EDP1815 led to a statistically significant reduction in the release of cytokines compared to placebo: IL- 6 ($p = 0. 0003$), IL- 8 ($p = 0. 0007$), and TNF ($p = 0. 0037$). The effect observed for EDP1815 may be clearly seen by the deep tail of reduced cytokine production on the left of the distribution for each cytokine, which was absent in the placebo groups. There was no worsening compared to placebo on the right of the distributions, resulting in the overall significant difference between EDP1815 and placebo. In addition, skin biopsies of active lesions were taken from a subset of patients in the trial. Six of the patients who received EDP1815 and achieved at least a PASI- 50 response from baseline at week 16 had paired biopsies. RNAseq analysis of the biopsies showed reductions in transcript levels for psoriasis- relevant cytokines interleukin 23 (IL- 23), interleukin 12b (IL- 12b), and interleukin 17 (IL- 17) in these lesions between baseline and week 16. The box plot below shows the median and interquartile ranges, as well as individual values of the cytokine expression levels in the skin, at baseline and week 16. These data suggest that EDP1815 reduced inflammation in the skin by modulating multiple proinflammatory cytokines. We believe these data support the biology of the SINTAX and the development of a new potential class of medicine that is designed to act locally in the small intestine to affect inflammation throughout the body. In the Phase 2 trial, there was no observed distribution of EDP1815 outside the gut. Based on these data, we currently intend to move EDP1815 towards registration trials in psoriasis, following the completion of meetings with health authorities. Pediatric Investigation Plan for EDP1815 in Psoriasis In February 2022, the European Medicines Agency (" EMA") agreed to our Pediatric Investigation Plan (" PIP") for EDP1815 in psoriasis, in accordance with

Regulation (EC) No 1901 / 2006 of the European Parliament and of the Council. The EMA agreement allows Evelo to include patients 12 – 17 years old in Phase 3 trials, conduct a single clinical trial in patients 2 – 5 years old and 6 – 11 years old after the adult Marketing Authorization Application (" MAA") has been submitted, and develop a pediatric formulation suitable for administration to patients 2 – 11 years old. Furthermore, the EMA confirmed that juvenile toxicity studies are not required for EDP1815 and granted us a waiver from studying EDP1815 in patients less than 2 years old. Phase 1b and Phase 2 clinical trials in atopic dermatitis In 2021, we reported preliminary clinical data from two cohorts of patients with mild and moderate atopic dermatitis in a Phase 1b randomized, placebo- controlled, dose- escalating safety and tolerability trial of EDP1815. The primary endpoint was safety and tolerability. In the first readout, we reported positive clinical data in a cohort of patients with mild and moderate atopic dermatitis (n = 24), randomized 2: 1 to receive EDP1815 in capsules (8. 0 x 1011 total cells) or placebo for 56 days. This was the same concentration of EDP1815 that was used as one of the doses in our Phase 2 trial in psoriasis. In the first Phase 1b trial cohort of patients with atopic dermatitis, EDP1815 was well- tolerated with no treatment- related adverse events of moderate or severe intensity, and no serious adverse events. Secondary endpoints included a range of established markers of clinical efficacy in atopic dermatitis, such as Eczema Area and Severity Index (" EASI "), the Investigator' s Global Assessment times body surface area (" IGA * BSA "), and the SCORing Atopic Dermatitis (" SCORAD ") scores. Table 1Clinical MeasureTreatment Difference between EDP1815 and Placebo Percentage Change at Day 56 * EASI52 % (p = 0. 062) IGA * BSA65 % (p = 0. 022) SCORAD35 % (p = 0. 068) * Least Squares Mean Percentage Change From Baseline. Note that the Phase 1b trial was not powered to detect statistically significant outcomes on efficacy endpoints: p- values presented are nominal values presented for illustrative purposes only. The preliminary data showed consistent improvements in percentage change from baseline compared to placebo for all three clinical scores: EASI, IGA * BSA, and SCORAD. In January 2022, in connection with locking the database for the Phase 1b trial, we further analyzed these preliminary data and methodology used to report the SCORAD results from the first cohort of atopic dermatitis patients in the Phase 1b trial described above. In the course of such review, we determined that the initial calculation of the SCORAD values was incorrect and we recalculated the SCORAD values. The correct SCORAD values are shown in Table 1 above. The p- value change in SCORAD does not alter our prior belief that the SCORAD secondary endpoint showed consistent improvement in percentage change from baseline compared to placebo. In addition, 7 out of 16 (44 %) patients treated with EDP1815 achieved an outcome of a 50 % improvement from baseline in EASI score (an" EASI- 50 " response) by day 70, compared with 0 % in the placebo group, showing sustained improvement in those patients responding to EDP1815. In addition to physician- reported clinical outcomes, patient- reported outcomes were also assessed. Treatment with EDP1815 resulted in clinically meaningful improvement in DLQI and Patient- Oriented Eczema Measure (" POEM "). These patient- reported outcomes capture the important impact of the disease on patients, including the domains of itch and sleep, both of which saw improvements in patients receiving EDP1815 in the trial. All five measures of itch within the Pruritus- Numerical Rating Scale (" Pruritus- NRS "), SCORAD, POEM, and DLQI showed greater improvements in the treated group at day 56 compared with placebo. We believe these results provide further evidence that modulating SINTAX has the potential to drive significant clinical benefit without the need for systemic exposure. We reported data from a second cohort in the Phase 1b trial of 24 patients with moderate atopic dermatitis who were randomized in a 2: 1 ratio, with 16 receiving a higher per capsule concentration formulation of EDP1815 (6. 4 x 1011 total cells) and 8 receiving a matching placebo once daily for eight weeks. The primary objective was to assess the safety and tolerability of the higher per capsule concentration formulation of EDP1815 after eight weeks of dosing. The secondary objective was to assess the clinical improvement in patients with moderate atopic dermatitis. All the patients used an emollient twice daily for at least seven consecutive days immediately prior to day 1 and continued to use the background emollient treatment twice daily throughout the trial. In this second cohort, EDP1815 was shown to be well- tolerated with no treatment- related adverse events of moderate or severe intensity and no serious adverse events through eight weeks of dosing. An initial improvement in mean percent change in EASI was observed at day 15 compared to placebo; however, the population mean change decreased over the remainder of the dosing period, and there was no overall difference from placebo at the end of the dosing period. Given the difference in clinical effects observed between the two cohorts in the Phase 1b trial, which were dosed with EDP1815 produced using different manufacturing processes, we are evaluating drug substance produced using both manufacturing processes in our Phase 2 atopic dermatitis trial. In February 2022, we began dosing patients in a Phase 2 trial of EDP1815 in atopic dermatitis. The primary objective of this multicenter, randomized, double- blind, placebo- controlled Phase 2 trial is to show superiority of EDP1815, dosed for 16 weeks, over placebo. The trial will enroll patients with mild, moderate, and severe atopic dermatitis and will evaluate EDP1815 drug substance produced using two different manufacturing processes. The primary endpoint will be the percent of patients who achieve an EASI- 50 response at week 16. Secondary endpoints will include several physician- reported outcomes, such as IGA and BSA, along with patient- reported outcomes such as DLQI, itch using the daily Pruritus- NRS, and POEM. Patients will be randomized into one of three cohorts. Each cohort will include approximately 100 patients randomized in a 3: 1 ratio (75 to EDP1815 and 25 to placebo) for a total of 300 patients. Cohort 1 will explore a daily dose of 1. 6 x 1011 total cells of EDP1815 or matching placebo administered as two capsules once daily. Cohorts 2 and 3 will explore a daily dose of 6. 4 x 1011 total cells of EDP1815 or matching placebo administered as two capsules once daily or one capsule twice daily, respectively. The different dosages of drug (1. 6 x 1011 total cells and 6. 4 x 1011 total cells) are prepared from two different manufacturing processes. All patients will have the opportunity to join an open label extension trial once they complete 16 weeks of dosing. Patients in the open label extension trial will receive EDP1815 for a further 36 weeks. Topline results from 16 weeks of dosing are anticipated in the first half of 2023. In March 2022, the Independent Data Monitoring Committee for the TACTIC- E clinical trial of EDP1815 for the treatment of hospitalized COVID- 19 patients met for a scheduled review of data. No adverse signal was noted in the EDP1815 arm. However, we have concluded that the progressive mildness of the COVID- 19 pandemic makes yielding an outcome for EDP1815 unlikely. No further patients will be recruited. The trial will report once all the data are complete. The TACTIC- E clinical trial was a Phase 2 / 3 randomized trial, sponsored by Cambridge University

Hospitals NHS Foundation Trust. The trial was investigating the safety and efficacy of certain experimental therapies in the prevention and treatment of life- threatening complications associated with COVID- 19 in hospitalized individuals at early stages of the disease. Previously in 2021, due to recruitment issues, we closed a smaller US phase 2 trial evaluating the safety and efficacy of EDP1815 for the treatment of hospitalized patients with newly diagnosed COVID- 19. Scintigraphy Studies We continue to evaluate EDP1815 to ensure optimum delivery of the drug substance in the small intestine. As part of the delivery optimization process, we are utilizing gamma scintigraphy imaging to assess delivery characteristics. An on- going Phase 1 single center clinical trial in healthy human volunteers is assessing the release characteristics of capsules of EDP1815 by gamma scintigraphy. In March 2022, results from the Phase 1 trial showed that a capsule with an improved release profile was able to deliver EDP1815 higher up in the small intestine. In 17 of the human volunteers studied, 15 (or 88 %) showed that EDP1815 released in the jejunum, the upper part of the small intestine. Preclinical data, meanwhile, have shown that the higher that EDP1815 is released in the small intestine, the greater the observed effect. We currently intend to evaluate this capsule in patients in one or more suitable upcoming clinical trials. We currently intend to evaluate EDP1815 in additional inflammatory disease indications. Potential indications include psoriatic arthritis, asthma, allergy, axial spondylarthritis and rheumatoid arthritis. EDP1867 is an investigational, non- live pharmaceutical preparation of a single strain of Veillonella parvula, isolated from the ileum of a human donor. It is made non- live by gamma- irradiation in the manufacturing process, which we believe makes it unable to colonize or persist in the gut, a central design feature of SINTAX medicines. EDP1867 is currently in clinical development, and we believe it has the potential to treat a wide range of inflammatory and neuroinflammatory diseases. In preclinical studies, EDP1867 resolved multiple pathways of inflammation. This observed activity suggests a number of possible indications for the development of EDP1867, including Th2- dependent inflammation which underlies atopic diseases such as atopic dermatitis, asthma and perennial rhinitis. Additionally, in October 2021, we presented further preclinical data for EDP1867 at the European Committee for Treatment and Research in Multiple Sclerosis (" ECTRIMS "). In the relevant preclinical study, EDP1867 was tested in a relapsing- remitting autoimmune encephalomyelitis (" EAE ") mouse model of neuroinflammation. Oral daily treatment with EDP1867 administered prophylactically or therapeutically reduced the severity of disease as demonstrated by a decreased mean maximum score and a decreased incidence of relapse compared to placebo. Treatment with EDP1867 reduced inflammation and demyelination in the spinal cord as shown in histopathological analysis. Transcriptional profiling of small intestine tissue confirmed that EDP1867 upregulated genes in lymphocyte pathways that resolve inflammation, as well as genes associated with intestinal homeostasis. We believe these data support the development of EDP1867 for the treatment of neuroinflammatory diseases. We initiated our first Phase 1b clinical trial of EDP1867 in healthy volunteers and patients with moderate atopic dermatitis in February 2021 and expect to report interim data in the second quarter of 2022. EDP2939 is an investigational oral EV biologic being developed for the treatment of inflammatory diseases. In May 2021, we presented preclinical data for EDP2939 at the American Association of Immunologists Meeting. In the preclinical mechanism of action study, mice undergoing a delayed- type hypersensitivity (DTH) reaction against keyhole limpet hemagglutinin (KLH) were treated with EDP2939, EDP2939 in combination with different blocking antibodies, or with placebo. These data suggest that the pharmacological activity of EDP2939 may require the stimulation of both the TLR2 receptor and IL- 10 receptor signaling, in addition to lymphocyte homing from the systemic circulation to the intestinal lymphoid tissue. In- vitro, EDP2939 induced TLR2- dependent release of IL- 10. Fluorescent biodistribution analysis showed that EDP2939 was not detected outside the gastrointestinal tract. We also did not observe any apparent adverse safety or tolerability issues in these preclinical studies. We believe these data suggest that treatment with EDP2939 could result in broad- based resolution of inflammation and the establishment of immune homeostasis. EDP2939 is the first EV product candidate we have nominated in our inflammation program. We anticipate initiation of clinical development in 2022, and expect data from a cohort of patients with psoriasis will be available in the second half of 2023. Inflammation Preclinical and Clinical Data Each of the product candidates in our inflammation program has demonstrated the potential to simultaneously impact multiple pathways and associated cytokines in preclinical assays, suggesting that they may have broader applicability than individual cytokine- directed therapies. Specifically, the product candidates demonstrate efficacy in Th1, Th2 and Th17 preclinical models of inflammation. The clinical and biomarker data from the EDP1815 trials suggest this preclinical activity translates to humans, with the biomarker data suggesting activity in Th1 driven inflammation, atopic dermatitis (Th2 driven inflammation), and psoriasis (Th17 driven inflammation). Importantly, pre- clinical experiments and human biomarker data from the EDP1815 Phase 1b and Phase 2 clinical trials in patients with psoriasis suggest that SINTAX medicines are inflammation resolving and are not immunosuppressive. Inflammation Development Strategy We selected psoriasis and atopic dermatitis, the most common type of eczema, as indications for first- in- human studies based upon our preclinical data, unmet need in large patient populations, the ease of access to patient tissue for biomarker analysis and the speed of clinical data readout. Patients with mild and moderate disease represent between 80 % and 90 % of the patient population, which is estimated to represent more than 25 million people in the United States. We believe these patients are underserved by current treatments, including topical steroids, which either inadequately control the inflammation, are not safe for long- term use, or are inconvenient and burdensome in application, leading to poor adherence and reduced efficacy in a real- world setting. The majority of novel therapies, including next generation biologics for psoriasis targeting IL- 17, IL- 23 or IL4RA, two pro- inflammatory cytokines and a cytokine receptor, are only approved for patients with moderate- to- severe disease. Even in the moderate and severe settings, a large majority of eligible patients do not receive biologics. Many patients are uncomfortable with high- cost, injectable antibody therapies or with the toxicity concerns and monitoring requirements of systemic immunosuppressants. There is a large need across the spectrum of disease severity, and especially for midline, pre- biologic patients, for a safe and well- tolerated oral medicine that resolves the systemic inflammation that drives psoriasis and atopic dermatitis. If our product candidates demonstrate placebo- like safety and tolerability and limited adverse events in clinical trials, they could open up a larger market than the one currently treated by biologics. We also intend to broaden our studies to treat patients with moderate and severe inflammation, potentially expanding

this market opportunity further. In preclinical mouse models, our inflammatory disease product candidates reduced systemic inflammation with equal or better activity than current standard of care therapies. We believe that this observation may translate to broad activity across a variety of inflammatory diseases. We have produced preclinical data in distinct mouse models that are driven by different immune mechanisms, suggesting that single SINTAX medicines may impact multiple immune pathways. Th1- and Th17- driven inflammation are implicated in psoriasis, joint inflammatory diseases and neuroinflammation, while Th2- driven inflammation plays a larger role in atopic and allergic diseases. With current cytokine- directed therapies, agents are targeted towards a specific cytokine to influence one or more of these pathways. For instance, Th1- driven inflammation can be controlled by TNFa or IL- 6 inhibition, Th17- driven inflammation can be controlled by IL- 17 or IL- 23 inhibition, and Th- 2 driven inflammation can be controlled by IL- 4 or IL- 13 inhibition. In preclinical studies, EDP1815 simultaneously modulated each of these inflammatory pathways. Oncology Portfolio We are developing SINTAX medicines for the treatment of multiple cancer types. In December 2020, we announced EDP1908 as our lead product candidate in oncology following presentation of preclinical data at the Society for Immunotherapy for Cancer meeting in November 2020. Preclinical data showed that orally administered EDP1908, an EV, resulted in superior tumor growth control versus either the parent microbe or anti- PD- 1 therapy, with an observed dose- dependent reduction in tumor growth. Preclinical data suggest that EDP1908 is active through different immune mechanisms beyond those targeted by checkpoint inhibitors, such as PD- 1 / PD- L1, or cytotoxic T- lymphocyte associated protein 4 (CTLA4) inhibitors. Research suggests that checkpoint inhibition prevents the downregulation of the immune system induced by tumors. In preclinical models, we observed that EDP1908 stimulated upregulation of the immune response to tumors. Oral administration of EDP1908 in preclinical mouse models resulted in robust, dose- dependent anti- tumor activity superior to that of anti- PD- 1 using different immune mechanisms. The effects were at least comparable to those reported in the literature for intratumorally administered immune stimulators. We believe that EDP1908, and possibly additional EV product candidates, have the potential to broaden the base of cancer immunotherapy and augment current standard- of- care therapies. Treatment with EDP1908 in syngeneic mice suggested a variety of potential effects on innate and adaptive immunity, including activated IFNg- positive cytolytic and helper lymphocytes, dendritic cells, and interferon gamma- induced protein 10 (IP- 10) levels in the tumor microenvironment. Fluorescent biodistribution analysis showed that EDP1908 was not detected outside the gastrointestinal tract. These data suggest that EDP1908 activated immunity locally on host immune cells in the gut and triggered distal immune responses within the tumor microenvironment, with no apparent adverse safety or tolerability issues. We believe that oral administration of EDP1908 has the potential to offer an improved safety profile compared to systemically- or intratumorally- administered immunotherapy agents, as well as broader potential for combination regimens with existing therapies. We have developed proprietary methods for the manufacture of pharmacologically active whole microbes and EVs that are scalable and transferable to GMP manufacturing facilities. Microbes are isolated, developed and purified in a manner analogous to the manufacture of pharmaceutical drugs. The whole microbe and EV manufacturing process produces drug substance in a powder form that makes our product candidates suitable for oral administration, for instance in the form of a capsule, tablet or powder. Additionally, we believe we have established robust analytical methods to assess the identity, strength and purity of our product candidates. We expect that these controlled manufacturing processes and analytical methods will allow us to produce and release GMP- compliant batches of drug substance with consistent quality. Our internal manufacturing capabilities include production of non- GMP materials for in vitro and in vivo preclinical assessment of product candidates. We currently use third- party contract manufacturing organizations (" CMOs ") for the production of drug substance and drug product for clinical studies. Our internal personnel have GMP manufacturing experience to ensure efficient technology transfer and oversee the development and manufacturing activities conducted by our CMOs. We currently have a contractual arrangement in place with one of our CMOs that will require us to spend an aggregate minimum amount of 1. 5 million Euros annually during each of 2022, 2023, and 2024. Our agreements with CMOs include confidentiality and intellectual property provisions to protect our proprietary rights to our SINTAX medicine candidates. We expect our CMOs to meet manufacturing requirements and drug supply demands required by our clinical studies. In some instances, we have reserved resources from CMOs for the development and manufacture of our product candidates for near- term clinical programs. We believe that these relationships are integral to ensuring reliable, high- quality drug supply for clinical development. While we do not have a current need for commercial manufacturing capacity, we intend to evaluate both building internal capabilities and contracting with CMOs at the appropriate time. In anticipation of a need for commercial supplies of EDP1815, we have established relationships with CMOs who have the capacity to rapidly scale the manufacturing of EDP1815. Process development and manufacturing are critical for the development of whole microbe and EV product candidates. We believe our internal expertise and external partnerships have allowed us to address unique challenges associated with whole microbe and EV manufacturing. Some of these major challenges include limited prior know- how in the field for novel microbes, strict anaerobic growth conditions required by many commensal microbes and temperature and oxygen sensitivities that affect downstream processing. Our proprietary methods for the manufacture of pharmacologically active SINTAX medicines address these three challenges. Many human commensals are strict anaerobes with no development precedent. Process development of commensal microbes requires strong technical expertise in microbiology and anaerobic fermentation. We are pioneering strict anaerobic bioprocessing technologies that can allow for rapid development of robust manufacturing processes. We continue to optimize processes across a wide range of parameters in fermentation and formulation. Our manufacturing processes consist of drug substance and drug product manufacturing. We have established expertise across all aspects of drug substance manufacturing operations including cell banking, fermentation, cell separation and lyophilization. We have also advanced knowledge related to drug product manufacturing and our drug product has demonstrated stability under long- term storage conditions. We will continue to advance novel formulation technologies for enhanced delivery and activity in future trials. Sales and Marketing Given the current developmental stage of our product candidates and platform, we have not yet established a robust commercial organization. We intend to commercialize our products globally and in multiple disease areas. We intend to do this both through

selectively building our own sales and marketing team and partnering or collaborating with third parties. In 2021, we hired a full- time chief commercial officer and have begun pre- commercial activities. Intellectual Property We strive to protect the proprietary technology that we believe is important to our business, including seeking and maintaining patents intended to cover both our broad platform and individual product candidates. We seek to obtain domestic and international patent protection, and endeavor to promptly file patent applications for new commercially valuable inventions. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We plan to continue to expand our intellectual property estate by filing patent applications directed to pharmaceutical compositions, methods of treatment, methods of manufacture, methods of analysis, and methods for patient selection created or identified from our ongoing development of our product candidates, as well as discoveries based on our proprietary platforms. Our success will depend 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 any patents that we may obtain, preserve the confidentiality of our trade secrets, and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know- how and continuing technological innovation to develop and maintain our proprietary position and, in the future, may rely on or leverage in- licensing opportunities. 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 may be challenged in courts after issuance. Moreover, many jurisdictions permit third parties to challenge issued patents in administrative proceedings, which may result in narrowing or even cancellation of patent claims. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or at all, whether the claims of any patent applications, should they issue, will cover our product candidates, or whether the claims of any issued patents will provide sufficient protection from competitors or otherwise provide any competitive advantage, or, if challenged in courts or administrative proceedings, be determined to be invalid or unenforceable. Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months or potentially even longer, and because publication of discoveries in the scientific or patent literature often lags behind actual discoveries and patent application filings, we cannot be certain of the priority of inventions covered by pending patent applications. Accordingly, we may not have been the first to invent the subject matter disclosed in some of our patent applications or the first to file patent applications covering such subject matter, and we may have to participate in interference proceedings or derivation proceedings declared by the United States Patent and Trademark Office (the" USPTO") to determine priority of invention. Patent Portfolio Our patent portfolio includes patent applications in varying stages of prosecution in the United States and selected jurisdictions outside of the United States. As of March 16, 2022, our patent portfolio consisted of sixteen issued U. S. patents, one European patent, one Singaporean patent, one South African patent, and 67 patent families, which include composition, method of use, formulation, analytical method, and manufacturing process claims, and three design patent families. Of the U. S. patents in our portfolio, 11 are owned by us, and five are exclusively licensed from the Mayo Clinic Foundation for Medical Education and Research, an affiliate of Mayo Clinic (the" Mayo Clinic"). The European patent is owned by us, and the Singaporean and South African patents are exclusively licensed from the University of Chicago. Of the patent families in our portfolio, 65 are owned by us, one is exclusively licensed to us from the University of Chicago and one is exclusively licensed to us from the Mayo Clinic. The patent portfolio includes patents and applications covering the following: • Formulation platforms in which applications that issue as a patent are expected to expire in 2038 to 2042. • Manufacturing platforms in which applications that issue as a patent are expected to expire in 2041. • Modality platforms in which applications that issue as a patent are expected to expire in 2038 to 2042. • Analytical methods in which applications that issue as a patent are expected to expire in 2042. • Inflammation portfolio: ▪ EDP1815, consisting of five issued U. S. patents in- licensed from the Mayo Clinic, covering compositions and methods of use (the patents from the Mayo Clinic are expected to expire in 2030) and twelve patent families we own directed to compositions, methods of use, formulations and manufacturing processes. Any applications claiming priority to these applications we own that issue as patents are expected to expire in 2040 to 2043; ▪ EDP1867, consisting of seven patent families we own directed to compositions, methods of use and formulations. Any applications claiming priority to these applications that issue as patents are expected to expire in 2039, 2041 and 2042; and ▪ EDP2939, consisting of four patent families we own directed to compositions and methods of use. Any applications claiming priority to these applications that issue as patents are expected to expire in 2038, 2042 and 2043. • Oncology portfolio: ▪ EDP1908, consisting of three patent families we own directed to compositions and methods of use. Any applications claiming priority to these applications that issue as patents are expected to expire in 2041 and 2042. ▪ An oral oncology platform exclusively licensed from the University of Chicago, consisting of 23 pending applications, one issued patent in Singapore, and one issued patent in South Africa. Patents in this family are expected to expire in 2036. Patent Term The base term of a U. S. patent is 20 years from the filing date of the earliest- filed non- provisional patent application from which the patent claims priority. The term of a U. S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the USPTO. In some cases, the term of a U. S. patent is shortened by terminal disclaimer that reduces its term to that of an earlier- expiring patent. The term of a U. S. patent may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch- Waxman Act, to account for at least some of the time the drug is under development and regulatory review after the patent is granted. With regard to a drug for which FDA approval is the first permitted marketing of the active ingredient, the Hatch- Waxman Act allows for extension of the term of one U. S. patent that includes at least one claim covering the composition of matter of such an FDA- approved drug, an FDA- approved method of treatment using the drug and / or a method of manufacturing the FDA- approved drug. The extended patent term cannot exceed the shorter of five years beyond the non-extended expiration of the patent or fourteen years from the date of the FDA approval of the drug, and a patent cannot be extended more than once or for more than a single product. During the period of extension, if granted, the scope of exclusivity is limited to the approved product for approved uses. Some foreign jurisdictions, including Europe and Japan, have analogous

patent term extension provisions, which allow for extension of the term of a patent that covers a drug approved by the applicable foreign regulatory agency. In the future, if and when our product candidates receive FDA approval, we expect to apply, if appropriate, for patent term extension on patents covering those product candidates, their methods of use and / or methods of manufacture. Trade Secrets In addition to patents, we rely on trade secrets and know- how to develop and maintain our competitive position. We typically rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. We protect trade secrets and know- how by establishing confidentiality agreements and intellectual property assignment agreements with our employees, consultants, scientific advisors, contractors and collaborators. These agreements provide that all confidential information developed or made known during the course of an individual or entities' relationship with us must be kept confidential during and after the relationship. These agreements also provide that all inventions resulting from work performed for us or relating to our business and conceived or completed during the period of employment or assignment, as applicable, shall be our exclusive property. In addition, we take other appropriate precautions, such as physical and technological security measures, to guard against misappropriation of our proprietary information by third parties. License and Manufacturing Agreements We are a party to several license agreements under which we license patents, patent applications and other intellectual property. The licensed intellectual property includes composition of matter and methods of using monoclonal microbials. In some cases, licenses cover physical material in the form of microbial strains. Certain diligence and financial obligations are tied to these agreements. Additionally, we are a party to manufacturing agreements for committed resources and exclusivity. We consider the following agreements to be material to our business. University of Chicago License Agreement In March 2016, we entered into an exclusive license agreement with the University of Chicago. This agreement gives us an exclusive, worldwide, sublicensable license to patent rights related to administration of microbes to treat cancer. Under this agreement, we may make, have made, use, import, have sold, offer to sell, and sell microbial products to treat cancer in combination with checkpoint inhibitors. Many microbial genera are covered by these patent rights. In addition, we have a non- exclusive, worldwide license to use technical information disclosed to us by the University of Chicago for the development and commercialization of microbial products to treat cancer in combination with checkpoint inhibitors. Under this agreement, we must use commercially reasonable efforts to develop and market licensed products. Commercially reasonable efforts can be demonstrated by achieving specific milestones by specific dates. Pursuant to the terms of the license agreement, we paid the University of Chicago an upfront fee of an amount less than $ 0. 5 million and are required to make low five- digit license maintenance fees on an annual basis, creditable against royalties owed in that given year. In addition, we may owe the University of Chicago future milestone payments totaling an aggregate of approximately $ 60. 9 million upon achievement of specific milestones, the vast majority of which are associated with specific regulatory and commercial milestones. The University of Chicago is entitled to receive low single- digit percentage royalties on annual net sales of products that fall under the licensed patent rights on a country- by- country and product- by- product basis. The royalty percentage depends on the amount of annual net sales and whether the product is covered by valid patent claims, un- published technical information, or published technical information. Our valid claims royalty obligations to the University of Chicago will expire upon the later of (a) expiration of the last- to- expire valid claim covering the product, or (b) the expiration of regulatory exclusivity of a product covered by the patent rights. Technical information royalty obligations will expire upon the earlier of (a) fifteen years from first commercial sale of the applicable product, or (b) when a substantially similar product comes onto the market. Under the license agreement, we have the right to sublicense licensed rights to third parties, provided that the sublicense agreement is consistent with the terms of the original license and that we hold any sublicensees compliant. Should we enter a sublicense under these patent rights, we are required to pay the University of Chicago a percentage of our sublicense revenue. The University of Chicago is entitled to percentages of sublicense revenue in the low- to mid- teens depending on the stage of development of licensed products at the time the sublicense is entered. The University of Chicago maintains control of patent prosecution, defense and maintenance on their patent rights. We are responsible for reimbursing the University of Chicago for patent costs incurred. If we cease payment for patent prosecution, our patent rights will terminate and revert to the University of Chicago. We have the first right, but not obligation, to control any post grant proceedings and to take action in the prosecution or prevention of any infringement by a third party to patent rights. The license granted by the University of Chicago is subject to any retained rights of the U. S. government in the patent rights and to retained rights of the University of Chicago to use the patent rights for non- commercial research purposes. The license agreement will expire on a country- by- country and product- by- product basis on the later of (a) expiration date of the last to expire licensed patents, or (b) a set number of years in the mid- teens from first commercial sale of a licensed product. Prior to the expiration date, we may terminate the license with written notification to the University of Chicago. Prior to the expiration date, the University of Chicago may terminate the agreement in whole or in part if we fail to make payments within thirty days of receiving a written notice of missed payment, if we breach any material obligation of the agreement and do not cure such breach within thirty days, if we become bankrupt or insolvent, or if we are dissolved or liquidated. The University of Chicago may also terminate the license if we fail to show commercially reasonable efforts in meeting diligence milestones. License Agreement with the Mayo Clinic In August 2017, we entered into an agreement with the Mayo Clinic to license intellectual property and a microbial strain. This agreement, as amended, gives us an exclusive, worldwide, sublicensable license to patent rights related to compositions of matter and methods of using microbes from specific species to treat autoimmune and inflammatory diseases. In addition to patent rights, this agreement, as amended, also includes an exclusive, worldwide, sublicensable license to an immuno- modulatory microbial strain isolated from a human small intestinal sample by the Mayo Clinic. Under the licensed patent rights and / or using the licensed microbial strains, we may make, have made, use, offer for sale, sell, and import products containing microbes of specific species to treat autoimmune and inflammatory diseases. In addition, we have a non- exclusive, worldwide license to use know- how disclosed to us by the Mayo Clinic related to the development and commercialization of products containing microbes of specific species to treat autoimmune and inflammatory diseases. The licensed patents include multiple issued U. S. patents. Issued claims cover

compositions containing microbes from specified species and methods of using these compositions to treat autoimmune and inflammatory diseases. EDP1815, one of our lead candidates in the inflammation program, contains a microbial strain licensed from the Mayo Clinic and is covered by these patent rights. Under this agreement, we must use commercially reasonable efforts to bring licensed products to the market. In consideration for the licenses, we paid the Mayo Clinic upfront payments totaling under $ 0. 3 million. Beginning on the second anniversary of the effective date, we owe the Mayo Clinic escalating annual license maintenance fees in the low- to mid- five digits. Annual license maintenance fees count towards milestones and royalties owed in a given year. The Mayo Clinic is entitled to future clinical, approval and sales milestones. In addition, we have agreed to pay the Mayo Clinic future milestone payments upon achievement of specific developmental, regulatory and commercial milestones totaling a maximum of $ 59. 1 million. The Mayo Clinic is entitled to receive low single- digit percentage royalties on annual net sales of products that fall under the licensed patent rights or contain the licensed microbial strains on a country- by- country and product- by- product basis. The royalty percentage depends on the amount of annual net sales and whether the product is covered by valid patent claims or contains the licensed microbial strains. Royalties on products containing the licensed microbial strains will only be due in countries where licensed products are not covered by valid claims. Our valid claims royalty obligations to the Mayo Clinic will terminate on expiration of the last to expire valid claim covering the product. Royalty obligations on products containing the licensed microbial strains will expire 15 years from the first commercial sale of the licensed product. Under the license agreement, we have the right to sublicense licensed patent rights and the licensed microbial strains to third parties through multiple tiers, provided that the sublicense agreement is on substantially the same terms as the original license and that we are responsible for the performance of sublicensees. We must obtain the Mayo Clinic' s permission to grant any fully paid- up, royalty- free or exclusive sublicenses. We have no financial obligations to the Mayo Clinic related to sublicenses. The Mayo Clinic has the responsibility to prepare, file, prosecute or abandon its patent rights. We may provide prior comment and advice to the Mayo Clinic and we are responsible for reimbursing the Mayo Clinic for past and future patent costs. If we cease payment for patent preparation, filing or prosecution, our patent rights will terminate and revert to the Mayo Clinic. We have the first right, but not obligation, to control any post grant proceedings and to take action in the prosecution or prevention of any infringement by a third party to patent rights. The license granted by Mayo Clinic is subject to any retained rights of the US government in the patent rights and to retained rights of Mayo Clinic to use the patent rights and licensed microbial strains for non- commercial research purposes, which excludes human use. The license to patent rights will expire on a country- by- country and product- by- product basis upon the expiration date of the last to expire licensed patents. The license to Mayo Clinic' s microbial strains will expire 15 years from first commercial sale of a product containing the licensed microbial strain. Prior to the expiration date, Mayo Clinic may terminate the license if we fail to make payments within thirty days of receiving a written notice of missed payment, if we breach any material obligation of the agreement and do not cure such breach within thirty days, if we become bankrupt or insolvent, or if we or any sublicensee directly or indirectly brings suit against Mayo Clinic. Upon early termination of our license, any sublicensee that is not in material breach of the agreement will have the right to retain its sublicense to the patent rights and microbial strains. We do not have the right to terminate the agreement prior to the expiration date. Sacco Collaboration Agreement In July 2019, we entered into a collaboration agreement with Sacco S. r. l. (" Sacco"), an affiliate of one of our contract manufacturing organizations. Pursuant to the agreement, Sacco has agreed that it and its affiliates will, on an exclusive and worldwide basis for and on behalf of us, manufacture and supply single strain, non- genetically modified microbes intended for oral delivery or oral use in pharmaceutical products for a period of five years. Sacco and its affiliates may not manufacture and supply single strain, non- genetically modified microbes for oral delivery or oral use in pharmaceutical products for itself or other parties, with the exception of pre- existing products for pre- existing customers. Under the terms of the agreement, we have agreed to pay annual fees in the mid six- digits to Sacco during the exclusivity period. The agreement will remain in effect during the exclusivity period and may be terminated by (i) us upon written notice to Sacco if an independent third- party representative concludes following an audit that Sacco or its affiliates are not in compliance with the exclusivity provisions of the agreement, (ii) Sacco upon written notice to us if the manufacturing relationship has been inactive for a period of six consecutive months and there are no services scheduled to be performed or products scheduled to be supplied within the next six months, or (iii) either party in the event of a material breach of the agreement by the other party that remains uncured for 20 business days or the insolvency of the other party. Cambrex Master Services Agreement In December 2020, we entered into a development and clinical master services agreement with Halo Pharmaceutical, Inc. d / b / a Cambrex Whippany (" Cambrex "). Pursuant to the agreement, Cambrex has agreed that it will perform manufacturing process development, manufacturing, packaging, related analytical and storage services for us, as mutually agreed by the parties from time to time in work orders. Under the terms of the agreement, we have agreed to pay service fees to Cambrex and to reimburse Cambrex for purchasing excipients, components, consumables, raw materials, packaging and other items necessary for Cambrex to perform the services, as mutually agreed in a work order. We will supply active pharmaceutical ingredients to Cambrex to enable it to perform the services. At our request or upon expiration or termination of the agreement, Cambrex has agreed to provide technical assistance to us, at our cost, to implement the technology transfer of the manufacturing processes developed by Cambrex under the agreement to us and of related analytical testing methodologies to us or a third party designated by us. Unless earlier terminated, the agreement will expire on the later of (i) five years from the effective date or (ii) six months after the expiration or termination of all work orders. We may terminate the agreement or any work order at any time upon 60 days or 5 business days, respectively, prior written notice to Cambrex. In addition, either party may terminate for an uncured material default or if the other party becomes bankrupt or insolvent. The agreement contains customary representations, warranties and covenants by Evelo, indemnification obligations of Evelo and Cambrex, and other obligations of the parties. In February 2022, we amended the agreement to specify that affiliates of Cambrex may perform services under the terms of the agreement. Meddist Company Limited In March 2021, we announced a strategic collaboration to develop and commercialize our lead inflammation product candidate, EDP1815, in the Middle East,

Turkey, and Africa with Meddist Company Limited (" ALJ"), a company focused on accelerating access to affordable modern medical care while addressing unmet medical needs in developing markets around the world. Together, we and ALJ will work to address the significant disparity in access to medical care in the fastest- growing populations and growth economies of the developing world. Africa' s population is projected to reach 1. 7 billion by 2030 and 2. 5 billion by 2050. Under the terms of the agreement, we received an upfront payment from ALJ. We will be primarily responsible for the development and manufacturing of EDP1815 worldwide, whilst ALJ will be primarily responsible for development, regulatory submissions and commercialization activities in the agreed- upon regions. ALJ and we will participate in a 50: 50 profit share arrangement. See the notes, including Note 3, to our consolidated financial statements in this Annual Report on Form 10- K for additional information regarding the commercialization and license agreement with ALJ. The biotechnology and pharmaceutical industries are characterized by rapid growth and a dynamic landscape of proprietary therapeutic candidates. While we believe that our monoclonal microbial platform and candidates, coupled with our resources and industry expertise, give us a competitive advantage in the field, we face competition from a variety of institutions, including larger pharmaceutical companies with more resources. Specialty biotechnology companies, academic research institutions, governmental agencies, as well as public and private institutions are also potential sources of competitive products and technologies. In both inflammatory diseases and oncology, we anticipate intensifying competition as new therapies are approved and advanced technologies become available. Many of our competitors, either alone or with strategic partners, have considerably greater financial, technical, and human resources than we do. Competitors may also have more experience developing, obtaining approval for, and marketing novel treatments in the indications we are pursuing. These factors could give our competitors an advantage over us in recruiting and retaining qualified personnel, completing clinical development, and commercializing their products. Competitors that are able to obtain FDA or other regulatory approval for their products more rapidly than we can for our products may also establish a stronger market position, diminishing our commercial opportunity. Key considerations that would impact our capacity to effectively compete include the efficacy, safety, ease of use, as well as pricing and reimbursement, of our products. In autoimmune or inflammatory diseases, we may be challenged by a wide range of competitors. In later, more severe stages of disease, the majority of competition will stem from companies marketing or developing injectable biologics and novel small molecule therapies, such as AbbVie Inc., Johnson & Johnson, Pfizer Inc, Novartis International A. G., Regeneron Pharmaceuticals, Inc. Sanofi S. A., Bristol Myers Squibb, and Amgen Inc. Potentially competing mechanisms of action include TNF, IL- 4, IL- 17, IL- 23, JAK, TYK2, and PDE4 inhibitors. Novel delivery of biologics, particularly via oral administration, and the entry of biosimilars will also add to competition within the therapeutic area. In more mild disease segments, we may face competition from companies marketing or developing topical formulations of small molecules for inflammatory skin diseases, including Pfizer Inc., Arcutis Biotherapeutics Inc., and Roivant Sciences Ltd. Significant competition exists in the immuno- oncology field, where we are developing product candidates. Although our SINTAX medicine approach is unique from most other existing or investigational therapies in immuno- oncology, we will need to compete with all currently or imminently available therapies within the indications where our development is focused. Although there is a wide range of potentially competitive mechanisms, possible synergies between these and SINTAX medicines will also be evaluated. The main classes of immunotherapy that are available or are being evaluated by our competitors include: • Checkpoint inhibitors: Agenus Inc., AstraZeneca plc, Bristol Myers Squibb, F. Hoffmann- La Roche A. G., Merck, Pfizer Inc., Regeneron Pharmaceuticals Inc.; and • Cell therapy: Bristol Myers Squibb, Gilead Sciences, Inc., and Novartis International A. G. Government Regulation Government Regulation in the United States The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post- approval monitoring and post- approval reporting of drugs and biologics such as those we are developing. We, along with our contract manufacturers, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval for our product candidates. The process of obtaining regulatory approvals and ensuring subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. In the United States, the FDA regulates drug and biologic products under the Federal Food, Drug and Cosmetic Act, its implementing regulations and other laws, including, in the case of biologics, the Public Health Service Act. Our product candidates are subject to regulation by the FDA as biologics. Biologics require the submission of a biologics license application (" BLA") and licensure, which constitutes approval, by the FDA before being marketed in the United States. The process required by the FDA before our biologic product candidates may be marketed in the United States generally involves the following: • completion of preclinical laboratory tests and animal studies performed in accordance with the FDA' s good laboratory practice (" GLP") requirements; • submission to the FDA of an investigational new drug application (" IND") which must become effective before clinical trials in the United States may begin; • approval by an institutional review board (" IRB "), or ethics committee at each clinical site before the clinical trial is commenced; • performance of adequate and well- controlled human clinical trials to establish the safety, purity and potency of the product candidate for each proposed indication, conducted in accordance with the FDA' s good clinical practice (" GCP") requirements; • preparation and submission to the FDA of a BLA after completion of all pivotal trials; • satisfactory completion of an FDA Advisory Committee review, 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 inspection of the manufacturing facility or facilities at which the product candidate is produced to assess compliance with cGMP regulations, and to assure that the facilities, methods and controls are adequate to preserve the biological product' s continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with GCP; and • FDA review and approval of the BLA prior to any commercial marketing, sale or shipment of the product. Preclinical and Clinical Trials Once a product candidate is identified for development, it enters the preclinical testing stage.

Preclinical studies include laboratory evaluations of drug chemistry, formulation and stability, as well as studies to evaluate toxicity in animals, which must be conducted in accordance with GLP requirements, when applicable. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational new drug to humans. The central focus of an IND submission is on the general investigational plan and the protocol (s) for clinical trials. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30- day time period, raises concerns or questions about the conduct of the clinical trial, including concerns that human research subjects will be exposed to unreasonable health risks, and imposes a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Submission of an IND may result in the FDA not allowing clinical trials to commence or not allowing clinical trials to commence on the terms originally specified in the IND. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development, and the FDA must grant permission, either explicitly or implicitly by not objecting, before each clinical trial can begin. Progress reports detailing the results of the clinical trials, among other information, must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected suspected adverse events, findings from other clinical trials or animal or in vitro testing that suggest a significant risk for human subjects and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Clinical trials involve the administration of the product candidate 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 clinical trial and the parameters and criteria to be used in monitoring safety and evaluating effectiveness. Each protocol must be submitted to the FDA as part of the IND. An independent IRB for each investigator site proposing to participate in a clinical trial must also review and approve the clinical trial and its informed consent form before it can begin at that site, and the IRB must monitor the clinical trial until it is completed. The FDA, the IRB, or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some clinical trials also include oversight by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board, which provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries. For purposes of BLA approval, clinical trials are typically conducted in three sequential phases, which may overlap or be combined. • Phase 1- the investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These trials are typically designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence of effectiveness. • Phase 2- the investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials. • Phase 3- the investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk / benefit ratio of the investigational product and to provide an adequate basis for product approval and physician labeling. In some cases, the FDA may condition approval of a BLA on the sponsor' s agreement to conduct additional clinical trials to further assess the biologic' s safety and effectiveness after BLA approval. Such post- approval clinical trials are typically referred to as Phase 4 clinical trials. Concurrent with clinical trials, biotechnology companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the biologic and finalize a process for manufacturing the biologic in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and manufacturers must develop, among other things, methods for testing the identity, strength, quality and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life. BLA Submission and FDA Review Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of preclinical studies and clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the biologic, are submitted to the FDA in the form of a BLA requesting approval to market the biologic for one or more specified indications. The BLA must include all relevant data available from preclinical and clinical studies, 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. Data can come from company- sponsored clinical studies intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by investigators. The submission of a BLA requires payment of a substantial user fee unless a waiver is granted, and the sponsor of an approved BLA is also subject to an annual program fee. Each BLA submitted to the FDA is reviewed for administrative completeness and reviewability within 60 days of the FDA' s receipt of the application. If the BLA is found to be complete, the FDA will file the BLA, triggering a full substantive review of the application. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission. Once a BLA has been accepted for filing, under the Prescription Drug User Fee Act, the FDA has a goal of reviewing BLAs within ten months of the 60- day filing date for standard review or within six months for BLAs designated for priority review, but the overall time frame may be extended

by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether the biological product is safe, pure and potent and whether the facility or facilities in which it is manufactured meet standards designed to assure the product' s continued safety, purity and potency. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving a BLA, the FDA will inspect the facility or the facilities at which the biologic product is manufactured, and will not license the product unless cGMP compliance is satisfactory. The FDA may also inspect the sites at which the clinical trials were conducted to assess their compliance with GCP requirements, and will not license the biologic unless compliance with such requirements is satisfactory. After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and / or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response Letter (" CRL "). An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A CRL will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the CRL without first conducting required inspections, testing submitted product lots, and / or reviewing proposed labeling. In issuing the CRL, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and / or require post- marketing testing and surveillance to monitor safety or efficacy of a product. If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy (" REMS "), to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy implemented to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and 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 also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post- marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post- market studies and surveillance to further assess and monitor the product' s safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post- marketing studies. Expedited Development and Review Programs The FDA maintains several programs intended to facilitate and expedite development and review of new drugs and biologics to address unmet medical needs in the treatment of serious or life- threatening diseases or conditions. For example, a product candidate is eligible for Fast Track designation if it is intended to treat a serious or life- threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast Track designation applies to the combination of the product candidate and the specific indication for which it is being studied. Fast Track designation provides increased opportunities for sponsor meetings with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the FDA may review portions of the marketing application before the sponsor submits the complete application, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA. In addition, a product candidate may be eligible for Breakthrough Therapy designation if it is intended to treat a serious or life- threatening disease or condition and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough Therapy designation provides all the features of Fast Track designation in addition to intensive guidance on an efficient development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross- disciplinary review, where appropriate. Any product candidate submitted to the FDA for approval, including a product candidate with Fast Track or Breakthrough Therapy designation, may also be eligible for additional FDA programs intended to expedite the review process, including Priority Review designation and Accelerated Approval. A BLA is eligible for Priority Review if the product candidate is designed to treat a serious or life- threatening disease or condition, and if approved, would provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. Additionally, product candidates studied for their safety and effectiveness in treating serious or life- threatening diseases or conditions may receive Accelerated Approval if they can be shown to have an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality which is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well- controlled post- marketing clinical trials to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post- marketing clinical trials or if such trials fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre- approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast Track designation, Breakthrough Therapy designation, Priority Review designation and Accelerated Approval do not change the standards for approval but may expedite the development or review process. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for

FDA review or approval will not be shortened. Orphan Drug Designation and Exclusivity Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200, 000 individuals in the United States, or a patient population greater than 200, 000 individuals in the United States and when there is no reasonable expectation that the cost of developing and making available the drug or biologic in the United States will be recovered from sales in the United States for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. If a product that has orphan drug designation subsequently receives the first FDA approval for a particular active ingredient for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or if the FDA finds that the holder of the orphan drug exclusivity has not shown that it can assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee. A designated orphan drug many not receive orphan drug exclusivity if it is approved for a use that is broader than the disease or condition for which it received orphan designation. In addition, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or, as noted above, if a second applicant demonstrates that its product is clinically superior to the approved product with orphan exclusivity or the manufacturer of the approved product is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Post- Approval Requirements Licensed biologics that are manufactured or distributed in the United States are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record keeping, periodic reporting, product distribution, advertising and promotion and reporting of adverse experiences with the product. There is also a continuing, annual prescription drug product program user fee. Any biologics manufactured or distributed pursuant to FDA approvals remain subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the product. Manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP, which impose certain procedural and documentation requirements upon BLA sponsors and their contract manufacturers. Failure to comply with statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, product seizures, injunctions, civil penalties or criminal prosecution. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, requirements for post- market studies or clinical trials to assess new safety risks, or imposition of distribution or other restrictions under a REMS. Other potential consequences include, among other things: • restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls; • fines, warning letters, untitled letters or holds on post- approval clinical trials; • refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of product approvals; • product seizure or detention, or refusal to permit the import or export of products; • mandated modification of promotional materials and labeling and the issuance of corrective information; • the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or • injunctions or the imposition of civil or criminal penalties. The FDA closely regulates the post- approval marketing and promotion of biologics, including standards and regulations for direct- to- consumer advertising, off- label promotion, industry- sponsored scientific and educational activities, and promotional activities involving the internet and social media. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Physicians may prescribe legally available biologics for uses that are not described in the product' s labeling and that differ from those tested by us and approved by the FDA. Such off- label uses are common across medical specialties. Physicians may believe that such off- label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off- label use. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Biosimilars and Regulatory Exclusivity As part of the Patient Protection and Affordable Care Act enacted in 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively the" ACA"), the Biologics Price Competition and Innovation Act (the" BPCIA") established an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The abbreviated regulatory pathway provides legal authority for the FDA to review and approve biosimilar biologics based on their similarity to an existing brand product, referred to as a reference product, including the possible designation of a biosimilar as interchangeable with a brand product. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. Under the BPCIA the approval of a biosimilar product may not be made effective by the

FDA until 12 years from the date on which the reference product was first licensed. Moreover, the extent to which a biosimilar, once approved, will be substituted for a reference product in a way that is similar to traditional generic substitution for non-biological drug products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. In addition, the period of exclusivity provided by the BPCIA only operates against third parties seeking approval via the abbreviated pathway, but would not prevent third parties from pursuing approval via the traditional approval pathway. In addition, a biological product can also obtain pediatric market exclusivity in the United States. Pediatric exclusivity, if granted, adds six- months to existing exclusivity periods and patent terms. This six- month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric clinical trial in accordance with an FDA- issued " Written Request " for such a trial. Government Regulation Outside of the United States To market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries governing, among other things, clinical trials, marketing authorization, manufacturing, commercial sales and distribution of drugs and biologics. Whether or not we obtain FDA approval for a product candidate, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product candidates in those countries. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Failure to comply with applicable foreign regulatory requirements may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution. Non- clinical Studies and Clinical Trials Similar to the United States, the various phases of non- clinical and clinical research in the European Union (" EU ") are subject to significant regulatory controls. Non- clinical studies are performed to demonstrate the health or environmental safety of new chemical or biological substances. Non- clinical studies must be conducted in compliance with the principles of good laboratory practice (" GLP ") as set forth in EU Directive 2004 / 10 / EC. In particular, non- clinical studies, both in vitro and in vivo, must be planned, performed, monitored, recorded, reported and archived in accordance with the GLP principles, which define a set of rules and criteria for a quality system for the organizational process and the conditions for non- clinical studies. These GLP standards reflect the Organization for Economic Co- operation and Development requirements. Clinical trials of medicinal products in the EU must be conducted in accordance with EU and national regulations and the International Conference on Harmonization (" ICH ") guidelines on Good Clinical Practices (" GCP "), as well as the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki. If the sponsor of the clinical trial is not established within the EU, it must appoint an EU entity to act as its legal representative. The sponsor must take out a clinical trial insurance policy and, in most EU countries, the sponsor is liable to provide ' no fault' compensation to any study subject injured in the clinical trial. The regulatory landscape related to clinical trials in the EU has been subject to recent changes. The EU Clinical Trials Regulation (" CTR "), which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. Unlike directives, the CTR is directly applicable in all EU member states without the need for member states to further implement it into national law. The CTR notably harmonizes the assessment and supervision processes for clinical trials throughout the EU via a Clinical Trials Information System, which contains a centralized EU portal and database. While the Clinical Trials Directive required a separate clinical trial application (" CTA ") to be submitted in each member state to both the competent national health authority and an independent ethics committee, much like the FDA and IRB respectively, the CTR introduces a centralized process and only requires the submission of a single application to all member states concerned. The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The CTA must include, among other things, a copy of the trial protocol and an investigational medicinal product dossier containing information about the manufacture and quality of the medicinal product under investigation. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state' s decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR contains a three- year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. For clinical trials whose CTA was made under the Clinical Trials Directive before January 31, 2022, the Clinical Trials Directive will continue to apply on a transitional basis for three years. Additionally, sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be governed by the Clinical Trials Directive until January 31, 2025. By that date, all ongoing trials will become subject to the provisions of the CTR. Medicines used in clinical trials must be manufactured in accordance with GMP. Other national and EU- wide regulatory requirements may also apply. In order to market our future product candidates in the EU, and in many other foreign jurisdictions, we must obtain separate regulatory approvals. More concretely, in the EU, medicinal product candidates can only be commercialized after obtaining a marketing authorization (" MA"). To obtain regulatory approval of a product candidate (including an investigational biological product) under EU regulatory systems, we must submit a MAA. The process for doing this depends, among other things, on the nature of the medicinal product. There are two types of MAs: •" Centralized MAs " are issued by the European Commission, through the centralized procedure, based on the EMA' s Committee for Medicinal Products for Human Use (" CHMP"), and are valid throughout the EU. The centralized procedure is compulsory for certain types of medicinal product candidates such as: (i) medicinal products derived from biotechnology processes; (ii) advanced therapy medicinal products (" ATMPs ") such as gene therapy, somatic cell therapy and tissue engineered products; (iii) medicinal products that contain a new active substance indicated for the treatment of certain diseases, such as HIV / AIDS, cancer, neurodegenerative diseases, diabetes, autoimmune diseases and other immune dysfunctions and viral diseases; and (iv) designated orphan medicines. For medicines that do not fall within these categories, an applicant has the option of submitting an application via the centralized procedure, as long as the medicine concerned contains a new active substance not yet authorized in the EU, is a significant therapeutic, scientific or

technical innovation, or if its authorization would be in the interest of public health in the EU. Under the centralized procedure the maximum timeframe for the evaluation of a MAA by the EMA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of an MAA under the accelerated assessment procedure is 150 days, excluding clock stops. Innovative products that target an unmet medical need and are expected to be of major public health interest may be eligible for a number of expedited development and review programs, such as the PRIME scheme, which provides incentives similar to the breakthrough therapy designation in the U. S. PRIME is a voluntary scheme aimed at enhancing the EMA' s support for the development of medicines that target unmet medical needs. It is based on increased interaction and early dialogue with companies developing promising medicines, to optimize their product development plans and speed up their evaluation to help them reach patients earlier. Many benefits accrue to sponsors of product candidates with PRIME designation including, but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated MAA assessment once a dossier has been submitted. Importantly, a dedicated contact and rapporteur from the CHMP is appointed early in the PRIME scheme facilitating increased understanding of the product at EMA' s committee level. An initial meeting initiates these relationships and includes a team of multidisciplinary experts at the EMA to provide guidance on the overall development and regulatory strategies. •" National MAs", which are issued by the competent authorities of the EU member states and only cover their respective territory, are available for product candidates not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU member state, this national MA can be recognized in another member state through the mutual recognition procedure. If the product has not received a national MA in any member state at the time of application, it can be approved simultaneously in various member states through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the member states in which the MA is sought, one of which is selected by the applicant as the reference member state. MAs have an initial duration of five years. After these five years, the authorization may be renewed for an unlimited period on the basis of a reevaluation of the risk- benefit balance. Data and Marketing Exclusivity In the EU, new products authorized for marketing (i. e., reference products) generally receive eight years of data exclusivity and an additional two years of market exclusivity upon receiving MA. If granted, the data exclusivity period prevents generic or biosimilar applicants from relying on the preclinical and clinical trial data contained in the dossier of the reference product when applying for a generic or biosimilar MA in the EU during a period of eight years from the date on which the reference product was first authorized in the EU. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until ten years have elapsed from the initial MA of the reference product in the EU. The overall ten- year market exclusivity period can be extended to a maximum of eleven years if, during the first eight years of those ten years, the MA holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU' s regulatory authorities to be a new chemical entity, and products may not qualify for data exclusivity. Also in the EU, there is a special regime for biosimilars, or biological medicinal products that are similar to a reference medicinal product but that do not meet the definition of a generic medicinal product, for example because of differences in raw materials or manufacturing processes. For such products, the results of appropriate preclinical or clinical trials must be provided, and guidelines from the EMA detail the type of quantity of supplementary data to be provided for different types of biological product. There are no such guidelines for complex biological products, such as gene or cell therapy medicinal products, and so it is unlikely that biosimilars of those products will currently be approved in the EU. However, guidance from the EMA states that they will be considered in the future in light of the scientific knowledge and regulatory experience gained at the time. Orphan Medicinal Products The criteria for designating an" orphan medicinal product" in the EU are similar in principle to those in the United States. In the EU, a medicinal product may be designated as orphan if: (1) it is intended for the diagnosis, prevention or treatment of a life- threatening or chronically debilitating condition; (2) either (a) such condition affects no more than five in 10, 000 persons in the EU when the application is made, or (b) the product, without the benefits derived from orphan status, would not generate sufficient return in the EU to justify investment; and (3) there exists no satisfactory method of diagnosis, prevention or treatment of such condition authorized for marketing in the EU, or if such a method exists, the product will be of significant benefit to those affected by the condition. In the EU, an application for designation as an orphan product can be made any time prior to the filing of the application for MA. Medicinal products designated as an orphan entitle a party to financial incentives such as reduction of fees or fee waivers and access to the centralized procedure. Once authorized, orphan medicinal products are entitled to ten years of market exclusivity for the approved therapeutic indication. During this ten- year orphan market exclusivity period, no MAA shall be accepted and no MA shall be granted for a similar medicinal product for the same indication. The period of market exclusivity is extended by two years for orphan medicinal products that have also complied with an agreed pediatric investigation plan. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The ten year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation, for example if the product is sufficiently profitable not to justify maintenance of market exclusivity or where the prevalence of the condition has increased above the threshold. Additionally, MA may be granted to a similar product for the same indication at any time if (i) the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; (ii) the applicant consents to a second orphan medicinal product application; or (iii) the applicant cannot supply enough orphan medicinal product. Pediatric Development In the EU, MAAs for new medicinal products have to

include the results of trials conducted in the pediatric population, in compliance with a PIP agreed with the EMA' s Pediatric Committee (" PDCO "). The PIP sets out the timing and measures proposed to generate data to support a pediatric indication of the drug for which an MA is being sought. The PDCO can grant a deferral of the obligation to implement some or all of the measures of the PIP until there are sufficient data to demonstrate the efficacy and safety of the product in adults. Further, the obligation to provide pediatric clinical trial data can be waived by the PDCO when these data are not needed or appropriate because the product is likely to be ineffective or unsafe in children, the disease or condition for which the product is intended occurs only in adult populations, or when the product does not represent a significant therapeutic benefit over existing treatments for pediatric patients. Once the MA is obtained in all member states and study results are included in the product information, even when negative, the product is eligible for a six- months supplementary protection certificate extension (if any is in effect at the time of approval) or, in the case of orphan pharmaceutical products, a two year extension of the orphan market exclusivity is granted. Similar to the United States, both MA holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA, the European Commission and / or the competent regulatory authorities of the member states. The holder of a MA must establish and maintain a pharmacovigilance system and appoint an individual qualified person for pharmacovigilance who is responsible for oversight of that system. Key obligations include expedited reporting of suspected serious adverse reactions and submission of periodic safety update reports (" PSURs "). All new MAA must include a risk management plan (" RMP ") describing the risk management system that we will put in place and documenting measures to prevent or minimize the risks associated with the product. The regulatory authorities may also impose specific obligations as a condition of the MA. Such risk- minimization measures or post- authorization obligations may include additional safety monitoring, more frequent submission of PSURs, or the conduct of additional clinical trials or post- authorization safety studies. The advertising and promotion of medicinal products is also subject to laws concerning promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. All advertising and promotional activities for the product must be consistent with the approved summary of product characteristics, and therefore all off- label promotion is prohibited. Direct- to- consumer advertising of prescription medicines is also prohibited in the EU. Although general requirements for advertising and promotion of medicinal products are established under EU directives, the details are governed by regulations in each member state and can differ from one country to another. The aforementioned EU rules are generally applicable in the European Economic Area (" EEA "), which consists of the 27 EU member states plus Norway, Liechtenstein and Iceland. Failure to comply with EU and member state laws that apply to the conduct of clinical trials, manufacturing approval, MA of medicinal products and marketing of such products, both before and after grant of the MA, manufacturing of pharmaceutical products, statutory health insurance, bribery and anti- corruption or with other applicable regulatory requirements may result in administrative, civil or criminal penalties. These penalties could include delays or refusal to authorize the conduct of clinical trials or to grant MA, product withdrawals and recalls, product seizures, suspension, withdrawal or variation of the MA, total or partial suspension of production, distribution, manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, fines and criminal penalties, any of which could be detrimental to our business. Brexit and the Regulatory Framework in the United Kingdom The United Kingdom (" UK ") left the EU on January 31, 2020, following which existing EU medicinal product legislation continued to apply in the UK during the transition period under the terms of the EU- UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to the global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement (" TCA ") and became effective on the January 1, 2021. The TCA includes specific provisions concerning pharmaceuticals, which include the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, but does not foresee wholesale mutual recognition of UK and EU pharmaceutical regulations. EU laws which have been transposed into UK law through secondary legislation continue to be applicable as " retained EU law ". However, new legislation such as the EU CTR will not be applicable. The UK government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an ' appropriate authority' to amend or supplement existing regulations in the area of medicinal products and medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps and future changes in the fields of human medicines, clinical trials and medical devices. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency (" MHRA ") is the UK' s standalone medicines and medical devices regulator. As a result of the Northern Ireland protocol, different rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain, (" GB "). Broadly, Northern Ireland will continue to follow the EU regulatory regime, but its national competent authority will remain the MHRA. The MHRA has published a guidance on how various aspects of the UK regulatory regime for medicines will operate in GB and in Northern Ireland following the expiry of the Brexit transition period on December 31, 2020. The guidance includes clinical trials, importing, exporting, and pharmacovigilance and is relevant to any business involved in the research, development, or commercialization of medicines in the UK. The new guidance was given effect via the Human Medicines Regulations (Amendment etc.) (EU Exit) Regulations 2019 (the " Exit Regulations "). The MHRA has introduced changes to national licensing procedures, such as procedures to prioritize access to new medicines that will benefit patients, including a 150- day assessment and a rolling review procedure. All existing EU MAs for centrally authorized products were automatically converted or grandfathered into UK MAs, effective in GB (only), free of charge on January 1, 2021, unless the MA holder chooses to opt- out. In order to use the centralized procedure to obtain a MA that will be valid throughout the EEA, companies must be established in the EEA. Therefore after Brexit, companies established in the UK can no longer use the EU centralized procedure and instead an EEA entity must hold any centralized MAs. In order to obtain a UK MA to commercialize products in the UK, an applicant must be established in the UK and must follow one of the UK national authorization procedures or one of the remaining post- Brexit international

cooperation procedures. The MHRA may rely on a decision taken by the European Commission on the approval of a new (centralized procedure) MA when determining an application for a GB authorization; or use the MHRA' s decentralized or mutual recognition procedures which enable MAs approved in EU member states (or Iceland, Liechtenstein and Norway) to be granted in GB. Other Healthcare Laws Pharmaceutical manufacturers are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation, the U. S. federal anti- kickback, fraud and abuse, false claims, consumer fraud, pricing reporting, and transparency laws and regulations related to payments and other transfer of value made to physicians and other healthcare providers, as well as similar state and foreign laws in the jurisdictions outside the U. S. Violation of any such laws or any other governmental regulations that apply may result in penalties, including, without limitation, significant administrative, civil and criminal penalties, damages, fines, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non- compliance with these laws, the curtailment or restructuring of operations, exclusion from participation in governmental healthcare programs and imprisonment. Coverage and Reimbursement Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third- party payors and governments provide coverage, and establish adequate reimbursement levels for such products. In the United States, third- party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. The process for determining whether a third- party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Third- party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA- approved products for a particular indication. Third- party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost- effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. We may need to conduct expensive pharmaco- economic studies in order to demonstrate the medical necessity and cost- effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost- effective. A payor' s decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Furthermore, one payor' s determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third- party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Different pricing and reimbursement schemes exist in other countries. In the EU, 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 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 has become very intense. As a result, increasingly high 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 product candidates 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, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on healthcare 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. Healthcare Reform In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system. The ACA substantially changed the way healthcare is financed by both governmental and private insurers in the United States. By way of example, the ACA increased the minimum level of Medicaid rebates payable by manufacturers of brand name drugs from 15. 1 % to 23. 1 %; required collection of rebates for drugs paid by Medicaid managed care organizations; imposed a non- deductible annual fee on pharmaceutical manufacturers or importers who sell certain " branded prescription drugs " to specified federal government programs; implemented a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted, or injected; expanded eligibility criteria for Medicaid programs; created a new Patient- Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the United States Supreme Court dismissed a judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA. Prior to the United States Supreme Court' s decision, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through August 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers of 2 % per fiscal year, which will remain in effect through 2030 with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 and a 1 % reduction from April 1, 2022 through June 30, 2022, absent additional congressional action. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to

~~providers from three to five years. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted legislation designed, among other things, to bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for pharmaceutical products. In addition, individual states in the United States have also become increasingly active in implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, mechanisms to encourage importation from other countries and bulk purchasing. Furthermore, there has been increased interest by third party payors and governmental authorities in reference pricing systems and publication of discounts and list prices. Data Privacy and Security Laws Numerous state, federal and foreign laws, regulations and standards govern the collection, use, access to, confidentiality and security of health- related and other personal information, and could apply now or in the future to our operations or the operations of our partners. In the United States, numerous federal and state laws and regulations, including data breach notification laws, health information privacy and security laws and consumer protection laws and regulations govern the collection, use, disclosure, and protection of health- related and other personal information. In addition, certain foreign laws govern the privacy and security of personal data, including health- related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and / or criminal penalties and restrictions on data processing. Research and Development We have dedicated a significant portion of our resources to our efforts to develop our product candidates. We incurred research and development expenses of $ 83. 6 million and $ 69. 6 million for the years ended December 31, 2021 and 2020 respectively. We anticipate that a significant portion of our operating expenses will continue to be related to research and development in 2022 as we continue to advance our product candidates through clinical development. Employees As of March 14, 2022, we had 122 full- time employees, including 43 with M. D. or Ph. D. degrees. Of those full- time employees, 86 were engaged in research and development. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationships with our employees to be good. Corporate and Other Information We were incorporated in Delaware in May 2014. Our principal executive offices are located at 620 Memorial Drive, Cambridge, Massachusetts 02139 and our telephone number is (617) 577- 0300. Our website address is www. evelobio. com. Information contained on or accessible through our website is not a part of this Annual Report on Form 10- K, and the inclusion of our website address in this Annual Report on Form 10- K is an inactive textual reference only. We file or furnish electronically with the U. S. Securities and Exchange Commission (the" SEC") our annual reports on Form 10- K, quarterly reports on Form 10- Q, current reports on Form 8- K, proxy statements and other information. Our SEC filings are available to the public over the Internet at the SEC' s website at http: / / www. sec. gov. We make available on our website at www. evelobio. com, under" Investors," free of charge, copies of these reports as soon as reasonably practicable after filing or furnishing these reports with the SEC. Item 1A. Risk Factors. Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, as well as the other information in this Annual Report on Form 10- K, including our consolidated financial statements and the related notes and " Management' s Discussion and Analysis of Results of Operations and Financial Condition, " before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Risks Related to Our Financial Position and Need for Additional Capital Since inception, we have incurred significant operating losses. Our net loss was $ 122. 2 million and $ 93. 7 million for the years ended December 31, 2021 and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of $ 414. 7 million. As noted below, we have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.~~ Through December 31, ~~2021~~ **2022** , we have financed our operations through proceeds from equity offerings of our common stock, private placements of our **since redeemed** preferred stock and borrowings under loan and security agreements. We have devoted substantially all of our financial resources and efforts to developing our platform, identifying potential product candidates and conducting preclinical **studies** and clinical trials. We are in the early stages of developing our product candidates, and we have not completed the development of any product candidate. We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we **, without limitation** : • seek to initiate additional and larger clinical trials of our product candidates; • seek to enhance our platform and discover and develop additional product candidates; • seek regulatory approvals for any product candidates that successfully complete clinical trials; • seek to establish a sales, marketing and distribution infrastructure and scale- up manufacturing capabilities to commercialize any products for which we may obtain regulatory approval; • maintain, expand and protect our intellectual property portfolio; and • add clinical, scientific, operational, financial and management information systems and personnel, including personnel to support our product development and potential future commercialization efforts **,** and to support our operations as a public company. In addition, we anticipate that our expenses will increase substantially if we experience any delays or encounter any issues with any of the above, including but not limited to failed studies **or trials** , complex results, safety issues or other regulatory challenges. To become and remain profitable, we must succeed in developing and eventually commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical ~~testing~~ **studies** and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of most of these activities. We may never succeed in these activities and, even if we do, **we** may never generate revenue that is significant enough to achieve profitability. Because of the numerous risks and uncertainties associated with pharmaceutical product and biological product development, we are unable

to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. If we are required by the FDA or other regulatory authorities to perform preclinical studies or clinical trials in addition to those currently expected, or if there are any delays in completing our preclinical studies or clinical trials or the development of any of our product candidates, our expenses could increase and revenue could be further delayed. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress our value and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product offerings or even continue our operations. We will need additional funding in order to complete development of our product candidates and commercialize our products, if approved. If we are unable to raise capital when needed, we could be forced to delay, reduce or discontinue our product development programs or commercialization efforts. We expect our expenses to increase in connection with our ongoing activities, particularly as we conduct clinical trials, **scale or** build manufacturing capacity and expand into additional therapeutic areas. ~~We~~ **Based on our current operating plans, we** expect that our existing cash and cash equivalents as of December 31, ~~2021~~ **2022** will **be sufficient to** enable us to fund ~~our planned~~ operating expenses and capital expenditure requirements into the third quarter of ~~2022~~ **2023** . We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including: • the progress and results of any ongoing and future clinical trials; • the cost of manufacturing clinical supplies of our product candidates, including EDP1815 **and** ~~, EDP1867,~~ EDP2939 ~~and EDP1908~~ ; • the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for any other future product candidates; • the costs, timing and outcome of regulatory review of our product candidates; • **our ability to repay and / or refinance our existing debt and to do so on acceptable terms, if at all; •** the costs and timing of future commercialization activities, including manufacturing, marketing, sales and distribution ~~,~~ for any of our product candidates for which we receive marketing approval; • the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval; • 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; • the effect of competing technological and market developments; and • the extent to which we acquire or invest in businesses, products and technologies, including entering into licensing or collaboration arrangements for product candidates. Any additional 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. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Additionally, market volatility resulting from the COVID- 19 pandemic ~~or other~~ **and global economic** factors **, including rising interest and inflation rates,** could also adversely impact our ability to access capital as and when needed. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities **by us** , whether equity or debt ~~, by us~~ , or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity, including any shares subject to warrants that we have previously issued or may in the future issue, or of convertible securities, would dilute all of our stockholders. The occurrence of additional indebtedness could result in increased fixed payment obligations **,** and we may be required to agree to certain restrictive covenants ~~,~~ such as limitations on our ability to incur additional 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. We could also be required to seek funds through arrangements with collaborators or others at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects. **In addition, we maintain our cash and cash equivalents at financial institutions, and our deposits at these institutions exceed federally insured limits. Market conditions can impact the viability of these institutions and, in the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we will be able to access uninsured funds in a timely manner or at all.** 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 product development programs or the commercialization of any product candidates or cease our operations. In addition, we may be unable to make milestone and royalty payments due under our intellectual property license agreements or other payments under our agreements with ~~contract~~ **Contract** ~~research~~ **Research** ~~organizations~~ **Organizations** (" CROs") and academic research collaborators, or expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations. Our limited operating history may make it difficult to evaluate the success of our business to date and to assess our future viability. Since our inception in 2014, we have devoted substantially all of our resources to identifying and developing our product candidates, building our intellectual property portfolio, process development and manufacturing function, planning our business, raising capital and providing general and administrative support for these operations. All of our product candidates are in clinical or preclinical development. We have not yet demonstrated our ability to successfully complete a Phase 3 or other pivotal clinical trial, obtain regulatory approvals to commercialize a product, manufacture a commercial scale product ~~,~~ or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Additionally, we expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history. We ~~will be forced to delay or reduce the scope of our development programs, reduce our research and development costs and / or limit or cease our operations if we are unable to obtain additional funding to support our current operating plan. We~~ have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. **We will be forced to delay or reduce the scope of our development programs, reduce our research and development costs and / or limit or cease our operations if we are**

unable to obtain additional funding to support our current operating plan. We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. As of December 31, ~~2021~~ **2022** , we had $ ~~68~~ **47** . ~~4~~ **9** million in cash and cash equivalents. Based on our available cash resources, we believe we do not have sufficient cash and cash equivalents on hand to support current operations for at least one year from the date of issuance of the financial statements appearing within this Annual Report on Form 10- K. This condition raises substantial doubt about our ability to continue as a going concern for at least one year from the date that our financial statements for the ~~year~~ **quarter** ended December 31, ~~2021~~ **2022** were issued. Nevertheless, our financial statements do not include any adjustments that might result from the outcome of this uncertainty. We will need to raise additional capital to fund our future operations and remain as a going concern. There can be no assurance that we will be able to obtain additional funding on acceptable terms, if at all. To the extent that we raise additional capital through future equity offerings, the ownership interest of common stockholders will be diluted, which ~~dilution~~ may be significant. However, we cannot guarantee that we will be able to obtain any or sufficient additional funding or that such funding, if available, will be obtainable on terms satisfactory to us. In the event that we are unable to obtain any or sufficient additional funding, there can be no assurance that we will be able to continue as a going concern, and we will be forced to delay, reduce or discontinue our product development programs or commercialization efforts. The terms of our loan and security agreements place restrictions on our operating and financial flexibility. If we raise additional capital through debt financing, the terms of any new debt could further restrict our ability to operate our business. ~~Our~~ **On December 15, 2022 (the " ~~loan~~ Loan Closing Date "), we entered into a Loan** and ~~security~~ **Security** ~~agreement~~ **Agreement (the " Loan Agreement ") with Horizon Technology Finance Corporation, as lender and collateral agent (" Horizon" or the " Lender "), pursuant to which the Lender agreed to make term loans, in an aggregate principal amount of up to $ 45. 0 million, available to us on the Loan Closing Date, and we borrowed $ 45. 0 million. Borrowings under the Loan Agreement are collateralized by substantially all of our personal property, excluding intellectual property, and we pledged our equity interests in our subsidiaries, subject to certain limitations with respect to certain our domestic and foreign subsidiaries. The loans carry a 3- year interest only period and begin to amortize in February 2026. In connection with the entry into the Loan Agreement, on the Loan Closing Date, we repaid in full all outstanding indebtedness under our previous Loan and Security Agreement with K2 HealthVentures LLC (together with its affiliates," K2HV" or the" Prior Lender")** dated July 19, 2019 ~~(~~**,** as amended **(the " ~~prior~~ Prior Loan Agreement "** ~~to June 16, 2021, the" 2019 Credit Facility")~~ ~~with K2 Health Ventures (" K2HV") for~~ **and the Prior Lender terminated all of its interests thereunder. The aggregate principal amount of the loan outstanding under the Prior Loan Agreement at the time of repayment was** $ 45. 0 million **in principal** ~~was secured by a lien covering substantially all of our personal property, excluding intellectual property~~ . ~~Contemporaneous~~ **The Prior Lender' s security interest in our assets under the Prior Loan Agreement were terminated in connection** with ~~the closing of the first tranche of funding under the facility, we repaid the entire $ 15. 0 million loan balance outstanding under our prior loan and security agreement with Pacific Western Bank. On June 16, 2021 (the" Amended Credit Facility Effective Date"), we further amended the 2019 Credit Facility (as so amended, the " Amended Credit Facility "), pursuant to which (i) the existing $ 15. 0 million third tranche commitment was replaced and superseded with a new $ 15. 0 million fourth tranche commitment, which we drew down on June 16, 2021, (ii) K2HV may convert up to $ 5. 0 million of outstanding principal of the Loans (as defined in the Amended Credit Facility) into shares of our common stock, (iii) the interest- only period is extended through February 28, 2023, with the first amortization payment on March 1, 2023, (iv) includes an election to adjust the amortization schedule to be based on a 30- month repayment period, and upon final payment or~~ **our** ~~prepayment~~ **discharge** of ~~the loans and we must pay a final payment equal to 4. 8 % of the aggregate original principal amount of the loans borrowed which we elected on December 22, 2021, and (v) at our election, we may prepay the loans, subject to a prepayment fee of 2 % of the amount prepaid if such prepayment occurs no later than the 18- month anniversary of the Amended Credit Facility Effective Date, or~~ **our indebtedness thereunder** ~~if the prepayment occurs after the 18- month anniversary of the Amended Credit Facility Effective Date but prior to the maturity date, 1 % of the amount prepaid. All of the other terms and conditions of the Amended Credit Facility remain unchanged and in full force and effect~~ . As of December 31, ~~2021~~ **2022** , the outstanding principal balance under the **Loan Agreement** ~~Amended Credit Facility~~ was $ 45. 0 million. The **Loan Agreement** ~~Amended Credit Facility~~ contains customary representations, warranties, affirmative and negative covenants and events of default applicable to us and our subsidiaries. ~~If we~~ **Upon our** default under the **Loan Agreement** ~~Amended Credit Facility~~ , ~~K2HV~~ **the Lender** may accelerate all of our repayment obligations and **/ or** exercise all of their **other** rights and remedies under the **Loan Agreement** ~~Amended Credit Facility~~ and applicable law, potentially requiring us to renegotiate our agreement on terms less favorable to us or to immediately cease operations. **During the third quarter of 2022, we identified instances of noncompliance with provisions of the Prior Loan Agreement, which resulted in events of default that were not identified on a timely basis. There is no certainty that future defaults under the current Loan Agreement will not occur or that the Lender (or any then applicable lender) would agree to similar corrective actions as those accepted by the Prior Lender to waive these events of default, not assert their right to accelerate any outstanding loans in full and not charge penalty interest. Future defaults could result in, among other things, immediate acceleration of principal payment under the loan and penalty interest being assessed.** Further, if we are liquidated, **the** ~~lenders~~ **Lender** ' **s** ~~right~~ **rights** to repayment would be senior to the rights of the holders of our common stock to receive any proceeds from the liquidation. ~~K2HV~~ **The Lender** could declare a default upon the occurrence of any event, among others, that they interpret as a material adverse effect **(including potentially with respect to our declining cash position or negative data results)** or a change of control as delineated under the **Loan Agreement** ~~Amended Credit Facility~~ , payment defaults, or breaches of covenants thereby requiring us to repay the loan immediately **, which we would be unable to do given our current cash position,** or to attempt to reverse the declaration of default through negotiation or litigation. Any declaration by ~~K2HV~~ **the Lender** of an event of default would significantly harm our business and prospects and could cause the price of our common stock to decline **or force us to discontinue our**

operations immediately . If we raise any additional debt financing, the terms of such additional debt could further restrict our operating and financial flexibility. **With our current cash resources, we do not expect to be able to meet our future debt repayment obligation to our current Lender. In order to meet this obligation, we will need to raise additional capital and / or restructure our existing debt, which may be on unfavorable terms, if available at all. Pursuant to the terms of the Loan Agreement, we are required to make interest- only payments on the loans on the stub period date (January 1, 2023) and for the first thirty- six monthly payment dates prior to when the loans are scheduled to begin amortizing on February 1, 2026. Beginning on February 1, 2026, we must pay twenty- four equal consecutive monthly installment payments repaying $ 35. 0 million of the principal, plus interest on all outstanding balances until the loans mature on January 1, 2028 (the " Maturity Date "). The remaining $ 10. 0 million of principal is due and payable on the Maturity Date. See Note 8- Loan and Security Agreement. As our current cash resources are insufficient to meet these principal and interest obligations, we will need to raise additional capital and / or restructure the existing debt obligation on new terms which may be less favorable than the existing terms, if available at all. Such new terms, if available, may include additional encumbrances placed on our assets, incremental dilutive conversion features, the imposition of more restrictive covenants or other onerous conditions. We have in the past and may continue to seek to establish collaboration agreements in the future, and we may not be successful or we may not be able to establish them on commercially reasonable terms and may have to alter our development and commercialization plans. We have in the past and may continue to seek to form collaborations to fund our operations, potentially accelerate research and development activities, expand our capabilities, and provide for commercialization activities by third parties. These relationships have and may in the future require us to incur up- front expenses, increase our near and long- term expenditures, commit to substantial future milestone and royalty payments, issue securities that dilute our existing stockholders, and divert attention of our management. If and when we seek to enter into future collaborations, we may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of a product candidate, reduce or delay development programs, delay potential commercialization, or reduce the scope of any sales or marketing activities.** Risks Related to the Discovery, Development and Regulatory Approval of Our Product Candidates We are early in our development efforts and may not be successful in our efforts to use our platform to build a pipeline of product candidates and develop marketable drugs. We are using our technology platform to harness **SINTAX, or** the small intestinal axis, with an initial focus on developing therapies in immunology, specifically inflammatory diseases ~~, and also oncology~~ . While we believe our preclinical studies and clinical trials to date have validated our platform to a degree, we are at an early stage of development and our platform has not yet, and may never lead to, approvable or marketable products. We are developing ~~these~~ product candidates and **possible** additional product candidates that we intend to use to **potentially** treat **other** ~~broader immunological~~ diseases ~~, respiratory diseases, neuro- inflammation and degeneration, liver diseases, type I diabetes, food allergy, neurobehavior, cardiovascular disease and diseases of metabolism~~ . We may have problems applying our technologies to these other areas, and our new product candidates may not demonstrate a comparable ability in treating disease as our initial product candidates. Even if we are successful in identifying additional product candidates, they may not be suitable for clinical development as a result of our inability to manufacture more complex oral biologics, limited efficacy, unacceptable safety profiles or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. The success of our product candidates will depend on several factors, including the following: • completion of preclinical studies and clinical trials with positive results; • receipt of marketing approvals from applicable regulatory authorities; • obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates; • making arrangements with CMOs, or establishing our own ~~,~~ commercial manufacturing capabilities; • launching commercial sales of our products, if and when approved, whether alone or in collaboration with others; • entering into new collaborations throughout the development process as appropriate, from preclinical studies through to commercialization; • acceptance of our products, if and when approved, by patients, the medical community and third- party payors; • effectively competing with other therapies; • obtaining and maintaining coverage and adequate reimbursement by third- party payors, including government payors, for our products, if approved; • protecting our rights in our intellectual property portfolio; • operating without infringing or violating the valid and enforceable patents or other intellectual property of third parties; • maintaining an acceptable safety profile of the products following approval; and • maintaining and growing an organization of scientists and business people who can develop and commercialize our products and technology. If we do not successfully develop and commercialize product candidates based upon our ~~technological~~ ---- **technical** approach, we will not be able to obtain product revenue in future periods, which likely would result in significant harm to our financial position and adversely affect **our stock price. In February 2023, for example, we announced that the first three patient cohorts in a Phase 2 trial of EDP1815 in atopic dermatitis trial failed to meet the primary endpoint, which adversely affected** our stock price. Our product candidates are designed to act on cells in the small intestine to produce systemic therapeutic effects with limited systemic exposure. This biological interaction between the small intestine and the rest of the body may not function in humans the way we have observed in mice and our drugs may not reproduce the systemic effects we have seen in preclinical **and early clinical** data. We believe our product candidates, including EDP1815 **and** ~~, EDP1867,~~ EDP2939 **,** ~~and EDP1908~~ have the potential to work by modulating systemic responses via interactions with cells in the small intestine. Dosing to achieve sufficient exposure may require an inconvenient dosing regimen. Even with a successful formulation and appropriate delivery profile to achieve proper exposure of our microbes **or extracellular vesicles** to the small intestine, we may not get sufficient or even any activity at the site of disease. This may be because our understanding of the mechanisms of the small intestine do not work in humans the way we believe they do. Despite there being strong academic literature to support the concept and our observations in preclinical studies in mice **and early clinical trials in human patients with psoriasis** , these principles and the ability to use pharmaceutical preparations derived from single strains of microbes to

modulate the immune system and other systems ~~has~~ **have** not yet been proven in humans. Our product candidates are an unproven approach to therapeutic intervention. All of our product candidates are based on targeting SINTAX. We have not, nor to our knowledge has any other company, received regulatory approval for an oral therapeutic based on this approach. We cannot be certain that our approach will lead to the development of approvable or marketable products. In addition, our product candidates may have different safety profiles and efficacy in various indications. Finally, the FDA or other regulatory agencies may lack experience in evaluating the safety and efficacy of products based on singe strains of microbes **or extracellular vesicles** , which could result in a longer than expected regulatory review process, increase our expected development costs and delay or prevent commercialization of our product candidates. Our platform relies on third parties for biological materials to expand our microbial library. Our platform relies on third parties for biological materials, including human samples containing bacteria, to expand our microbial library. Some biological materials have not always met our expectations or requirements, and any disruption in the supply of these biological materials could materially adversely affect our business and ability to build our pipeline of product candidates. For example, if any supplied biological materials are contaminated, we would not be able to use such biological materials. Although we have quality control processes and screening procedures, biological materials are susceptible to damage and contamination. Improper storage of these materials, by us or any third- party ~~suppliers~~ **supplier** , may require us to destroy some or all of our raw materials or products. Even if our product candidates do not cause off **-** target adverse events, there may be immunotoxicity associated with the fundamental pharmacology of our product candidates. Our product candidates, including EDP1815 **and** ~~, EDP1867,~~ EDP2939 **,** ~~and EDP1908~~ are designed to work by modulating the immune system. While we have observed limited systemic exposure in preclinical **studies** and **early** clinical ~~studies~~ **trials** , the pharmacological immune effects we aim to induce are systemic. Systemic immunomodulation from taking our product candidates could lead to immunotoxicity in patients, which may cause us or regulatory authorities to delay, limit or suspend clinical development. Other immunomodulatory agents have shown immunotoxicity. This includes immune suppressive agents, such as HUMIRA or REMICADE, which have shown an increased risk of infection or **,** in rare instances **,** certain types of blood cancer. In the case of immune activating agents, such as YERVOY, induction of adverse auto- immune events has been observed in some patients. Immunotoxicity in one program could cause regulators to view these adverse events as a class effect of our product candidates which may impact the timing of the development of our pipeline of potential product candidates. Even if the adverse events are manageable, the profile of the drug may be such that it limits or diminishes the possible number of patients who could receive our therapy. Our 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. Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. For example, some of our product candidates may consist of live biological material that may remain viable in humans, which carries a risk of causing infections in patients. Some infections may require treatment with antibiotics to eliminate the bacteria. All **of** our product candidates are screened for antibiotic sensitivity **,** but it is possible that if antibiotic therapy does not eliminate the live biological material, a resistant version of our strain could emerge. These events, while unlikely, could cause a delay in our clinical development and / or could increase the regulatory standards for the entire class of our product candidates. In an instance where the infection risk of taking our product candidates is high, this may cause the benefit risk profile of therapy to be non-competitive in the market and may lead to discontinuation of development of the product candidate. In addition, it is possible that infections from our product candidates could be rare and not frequently observed in our clinical trials. In larger post marketing authorization trials, however, data could show that the infection risk, while small, does exist. If unacceptable side effects arise in the development of our product candidates, we, the FDA or comparable foreign regulatory authorities, the IRBs at the institutions in which our clinical trials are conducted, or the data safety monitors could suspend or terminate our clinical trials, or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment- related side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or **could** result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly. If any of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including: • regulatory authorities may withdraw their approval of the product; • we may be required to recall a product or change the way such product is administered to patients; • additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof; • we may be required to conduct post- marketing studies or clinical trials; • regulatory authorities may require the addition of labeling statements, such as a **"** ~~‘ ‘~~ black box **"** ~~’ ’~~ warning or a contraindication; • we may be required to implement a risk evaluation and mitigation strategy or create a medication guide outlining the risks of such side effects for distribution to patients or similar risk management measures; • we could be sued and held liable for harm caused to patients; • the product may become less competitive; and • our reputation may suffer. Any of the foregoing events could prevent us from achieving or maintaining market acceptance of ~~the~~ **a** particular product candidate, if approved, and result in the loss of significant revenues to us, which would materially and adversely affect our results of operations and business. Companies with microbiome products or differing microbial products may produce negative clinical data which will adversely affect public perception of our product candidates, and may negatively impact regulatory approval of,

or demand for, our potential products. Our product candidates are pharmaceutical compositions of commensal microbes **or derivatives thereof** . While we believe our approach is distinct from microbiome therapies, negative data from clinical trials using microbiome- based therapies (e. g., fecal transplant) and other microbial therapies could negatively impact the perception of the therapeutic use of microbial- based products. This could negatively impact our ability to enroll patients in clinical trials. The clinical and commercial success of our potential products will depend in part on the public and clinical communities' acceptance of the use of therapeutic microbes **and derivatives thereof** . Moreover, our success depends upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of product candidates we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which greater clinical data may be available. Adverse events in our preclinical studies or clinical trials **,** or those of our competitors or of academic researchers utilizing therapeutic microbes, even if not ultimately attributable to our product candidates, and the resulting publicity **,** could result in increased governmental regulation, unfavorable public perception, increased volatility in our stock price, potential regulatory delays in the testing or approval of our potential product candidates, stricter labeling requirements for our product candidates that are approved, if any, and a decrease in demand for any such products. Catastrophic loss of our master cell banks could significantly impair our ability to manufacture our product candidates. Our product candidates require that we manufacture **our microbial strains** from master cell banks (" MCBs") ~~our microbial strains~~ . There is a possibility of a catastrophic failure or destruction of our MCBs. This could make it impossible for us to continue to manufacture a specific product candidate or product. Recreating and **re-** ~~recertifying~~ -- **certifying** our MCBs is possible but not certain and could put at risk the supply of our product candidates for preclinical studies or clinical trials or any products, if approved, to our customers. Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates. All of our product candidates are currently in clinical or preclinical development. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval, and the risk of failure through the product development process is high. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failed clinical trial can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, in certain of our clinical trials, investigational drug products are being delivered in a capsule for targeted release in the small intestine. This formulation has not previously been clinically tested, nor are we able to dose mice with a capsule for targeted release in the small intestine. Our ongoing clinical trials will be the first time this formulation is tested, and we cannot assure you that the results of this formulation will be consistent with the observations from our preclinical studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in advanced clinical trials due to adverse safety profiles or lack of efficacy, notwithstanding promising results in earlier trials, and we cannot be certain that we will not face similar setbacks. The results from earlier clinical trials of product candidates may not predict the results that will be obtained in subsequent subjects or in subsequent human clinical trials of that product candidate. There can be no assurance that any trial will ultimately be successful or support further clinical advancement of any given product candidate. In addition, we cannot be certain as to the type and number of clinical trials the FDA or similar foreign regulatory authorities will require us to conduct before we may successfully gain approval, referred to as licensure with respect to biological products in the United States, to market any of our product candidates. Requirements for us to conduct more **or more complex** clinical trials than we anticipate for a given product candidate could cause us to incur significant development costs, delay or prevent the commercialization of our products or otherwise adversely affect our business. We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including: • regulators, IRBs or ethics committees may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site; • we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites; • clinical trials of our product candidates may demonstrate undesirable side effects or produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs; • the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be lower or slower than we anticipate, or patients may drop out of these clinical trials at a higher rate than we anticipate; • our CROs, CMOs and other third- party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all; • we may have to, or regulators or IRBs may require ~~,~~ that we or our investigators **,** suspend or terminate clinical trials of our product candidates for various reasons, including noncompliance with regulatory requirements or a finding that ~~the~~ patients are being exposed to unacceptable health risks; • the cost of clinical trials of our product candidates may be greater than we anticipate; • the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; • regulators may revise the requirements for approving our product candidates, or such requirements may not be as we anticipate; and • regarding trials managed by any future collaborators, our collaborators may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but potentially suboptimal for us. If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our product candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive, or if there are safety concerns, we may: • be delayed in obtaining marketing approval for our product candidates; • lose the support of any future collaborators, requiring us to bear more of the burden of developing certain microbial strains **or derivatives thereof** ; • not obtain marketing

approval at all; • obtain marketing approval in some countries and not in others; • obtain approval for indications or patient populations that are not as broad as we intend or desire; • obtain approval with labeling that includes significant use or distribution restrictions or safety warnings; • be subject to additional post- marketing testing requirements; or • have the product removed from the market after obtaining marketing approval. In addition, disruptions caused by the COVID- 19 pandemic may increase the likelihood that we encounter such difficulties or delays in initiating, enrolling, conducting or completing our planned and ongoing clinical trials. We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by a data safety monitoring board or ethics committee for such trial or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, or changes in governmental regulations or administrative actions. For example, in September 2021 the FDA placed the IND for ~~a~~ **our** Phase 2 atopic dermatitis trial of EDP1815 on clinical hold and requested that we amend our protocol to account for risks to patients that require their current atopic dermatitis medications be discontinued, the manner in which safety data is collected, and defined study halting criteria. The FDA subsequently lifted the clinical hold. Further, conducting clinical trials in foreign countries, as we have ~~in the past~~ and may continue to do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to the clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries. Our product development costs will increase if we experience delays in clinical testing or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical **study** or clinical trial delays also could 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, potentially impairing our ability to successfully commercialize our product candidates **, if approved,** and harming our business and results of operations. In addition, the FDA' s and other regulatory authorities' policies with respect to clinical trials may change and additional government regulations may be enacted. For instance, the regulatory landscape related to clinical trials in the EU recently evolved. The ~~EU~~ CTR ~~"~~ **,** which was adopted in April 2014 and repeals the EU Clinical Trials Directive, became applicable on January 31, 2022. While the Clinical Trials Directive required a separate Clinical Trial Application (" CTA ") to be submitted in each member state ~~,~~ **in which the clinical trial takes place** to both the competent national health authority and an independent ethics committee, the CTR introduces a centralized process and only requires the submission of a single application ~~to all member states concerned~~ **for multi- center trials** . The CTR allows sponsors to make a single submission to both the competent authority and an ethics committee in each member state, leading to a single decision per member state. The assessment procedure of the CTA has been harmonized as well, including a joint assessment by all member states concerned, and a separate assessment by each member state with respect to specific requirements related to its own territory, including ethics rules. Each member state' s decision is communicated to the sponsor via the centralized EU portal. Once the CTA is approved, clinical study development may proceed. The CTR entails a three- year transition period. The extent to which ongoing and new clinical trials will be governed by the CTR varies. ~~For clinical~~ **Clinical** trials ~~whose CTA~~ **for which an application** was ~~made~~ **submitted: (i) prior to January 31, 2022** under the Clinical Trials Directive ~~before~~ **, or (ii) between** January 31, 2022 **and January 31** , **2023 and for which** the **sponsor has opted for the application of the EU** Clinical Trials Directive ~~will continue to apply on a transitional basis for three years. Additionally~~ , **remain** ~~sponsors may still choose to submit a CTA under either the Clinical Trials Directive or the CTR until January 31, 2023 and, if authorized, those will be~~ governed by **said** ~~the Clinical Trials~~ Directive until January 31, 2025. ~~By that~~ **After this** date, all **clinical trials (including those which are** ongoing ~~trials~~ **)** will become subject to the provisions of the CTR. Compliance with the CTR requirements by us and our third- party service providers, such as CROs, may impact our development plans. It is currently unclear to what extent the UK will seek to align its regulations with the EU. The UK regulatory framework in relation to clinical trials is derived from existing EU legislation (as implemented into UK law, through secondary legislation). On January 17, 2022, the MHRA ~~,~~ launched an eight- week consultation on reframing the UK legislation for clinical trials. The consultation closed on March 14, 2022 and aims to streamline clinical trial approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality ~~,~~ and promote patient and public involvement in clinical trials. The outcome of the consultation ~~will be~~ **is being** closely watched and will determine whether the UK chooses to align with the ~~regulation~~ **(EU) CTR** or diverge from it to maintain regulatory flexibility. **Under the terms of the Protocol on Ireland / Northern Ireland, provisions of the (EU) CTR which relate to the manufacture and import of investigational medicinal products and auxiliary medicinal products apply in Northern Ireland. On February 27, 2023, the UK Government and the European Commission reached a political agreement on the " Windsor Agreement " which will revise the Protocol on Ireland / Northern Ireland in order to address some of the perceived shortcomings. Once implemented, this may have further impact on the application of the (EU) CTR in Northern Ireland.** A decision by the UK **Government** not to closely align its regulations with the new approach that will be adopted in the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries ~~and / or make it harder to seek a marketing authorization in the EU for our product candidates on the basis of clinical trials conducted in the UK~~ . If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies governing clinical trials, our development plans may be impacted. If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented. We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar

regulatory authorities outside the United States. For example, we are developing certain product candidates, such as EDP1815 ~~and EDP1867~~, to treat inflammatory diseases including psoriasis and atopic dermatitis. There are a limited number of patients from which to draw for clinical trials concerning any given indication. Patient enrollment is also affected by other factors including: • the severity of the disease under investigation; • the patient eligibility criteria for the trial in question; • the perceived risks and benefits of the product candidate under study; • the availability of other treatments for the disease under investigation; • the existence of competing clinical trials; • the efforts to facilitate timely enrollment in clinical trials; • our payments for conducting clinical trials; • the patient referral practices of physicians; • the ability to monitor patients adequately during and after treatment; and • the proximity and availability of clinical trial sites for prospective patients. Our inability to enroll a sufficient number of patients or volunteers for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. The COVID- 19 pandemic has adversely impacted and may continue to adversely impact our business, including our preclinical studies and clinical trials, and finances. **The pandemic caused by the** ~~In 2020, a strain of~~ novel coronavirus disease, COVID- 19, ~~was declared a pandemic and spread across the world, including throughout the United States, Europe and Asia. The pandemic~~ and government measures taken in response **, had and continues to** have ~~had and~~ **an** ~~continue to have a significant~~ impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, supply chains have been disrupted, **and some** facilities and production have been suspended ~~, and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen~~ . **Due** ~~In response to the spread of COVID- 19, we have adopted and continue to employ several flexible business practices, including telecommuting and staggered work shifts in our laboratories, to protect our employees while continuing business operations. In addition, due~~ to the COVID- 19 pandemic, enrollment of new patients into, and the retention of existing patients in, our ~~on- going~~ clinical trials **was** ~~have been and continue to be~~ impacted ~~,~~ due primarily to lower patient participation ~~. As a result of the COVID- 19 pandemic, we may continue to experience disruptions and face new disruptions that could severely impact our business, preclinical studies and clinical trials, and finances, including: • delays in receiving approval from local regulatory authorities to initiate our planned clinical trials; • delays or difficulties in enrolling patients in our clinical trials; • delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff; • delays in clinical sites receiving the supplies and materials needed to conduct our clinical trials, including interruptions in global shipping that may affect the transport of clinical trial materials; • changes in local regulations as part of a response to the COVID- 19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs, or to discontinue such clinical trials altogether; • diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials; • interruptions of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by governments, employers and others or interruption of clinical trial subject visits and study procedures (such as skin biopsies that are deemed non- essential activities), which may impact the integrity of subject data and clinical trials endpoints; • risk that patients enrolled in our clinical trials will contract COVID- 19 while the clinical trial is ongoing, which could impact the results of the clinical trial, including by increasing the number of observed adverse events; • interruptions or delays in the operations of the FDA and similar regulatory authorities, which may impact review and approval timelines; • interruptions of, or delays in receiving, supplies of our product candidates from our CMOs due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems; • limitations on employee resources that would otherwise be focused on the conduct of our preclinical studies and clinical trials, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; • refusal of the FDA or similar foreign regulatory authorities to accept data from clinical trials in affected geographies; • impacts from prolonged remote work arrangements, such as increased cybersecurity risks and strains on our business continuity plans; and • delays or difficulties with securities offerings due to disruptions and uncertainties in securities markets. The COVID- 19 pandemic continues to evolve~~ . The extent to which the outbreak impacts our business, preclinical studies and clinical trials will depend on future developments ~~,~~ which are highly uncertain and cannot be predicted with confidence, such as the ~~ultimate geographic spread and~~ severity of the disease and its variants, the duration of the pandemic, ~~travel restrictions~~ and **related impacts to** ~~social distancing in the United States and other countries, business closures or~~ **our** ~~business disruptions~~ **supply chain** and **available labor pool** ~~the effectiveness of actions taken in the United States and other countries to contain and treat the disease~~ . While the **continued** potential economic impact brought by and the duration of the COVID- 19 pandemic may be difficult to assess or predict, the widespread pandemic has resulted in, and may continue to result in, significant disruption of global financial markets ~~,~~ reducing our ability to access capital, which **has and** could in the future negatively affect our liquidity. In addition, ~~a recession~~ **recessions** ~~or~~ **and** market ~~correction~~ **corrections** resulting from the COVID- 19 pandemic **have and** could ~~materially affect~~ **continue to detrimentally impact** our business **and stock price** . We have conducted and may continue to conduct clinical trials for our product candidates in sites outside the United States, and the FDA may not accept data from trials conducted in foreign locations. We have conducted and may continue to conduct clinical trials outside the ~~United States~~ **U. S.** for our product candidates. The acceptance of study data from clinical trials conducted outside the U. S. or another jurisdiction by the FDA or comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. In cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U. S., the FDA will generally not approve the application on the basis of foreign data alone, unless: (i) the data are applicable to the U. S. population and U. S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on- site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on- site inspection or other

appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well- designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection, if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. There can be no assurance that the FDA or any comparable foreign regulatory authority will accept data from trials conducted outside of the U. S. or the applicable jurisdiction. If the FDA or any comparable foreign regulatory authority does not accept such data, it would result in the need for additional trials, which could be costly and time- consuming, and which may result in current or future product candidates that we may develop not receiving approval for commercialization in the applicable jurisdiction **in a timely manner** or at all. Interim," topline" 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 topline data from our preclinical studies and clinical trials, which is 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 topline or preliminary results that we report may differ from future results of the same trials, or different conclusions or considerations may qualify such results ~~,~~ once additional data have been received and fully evaluated. Topline 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. For example, we previously disclosed certain SCORAD figures from a Phase 1b clinical trial that, upon further review and analysis, required modification in subsequent disclosure. As a result, topline and other preliminary data should be viewed with caution until the final data are available and have been fully analyzed. From time to time, we may also disclose interim data from our preclinical studies and clinical trials. 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 topline, 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 the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular **preclinical** 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. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize our product candidates or will not be able to do so as soon as anticipated, and our ability to generate revenue will be materially impaired. Our product candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation and requirements by the FDA and other regulatory agencies in the United States, **EU and UK,** by legislative bodies in the EU and EU member states ~~,~~ and by other regulatory authorities outside ~~the~~ **these jurisdictions** ~~United States~~ . Failure to obtain marketing approval for a product candidate in any jurisdiction will prevent us from commercializing the product candidate in that jurisdiction ~~,~~ and may affect our plans for commercialization in other jurisdictions as well. We have not received approval to market any of our product candidates from regulatory authorities in any jurisdiction. We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and **we** expect to rely on third parties to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate' s safety and efficacy to such regulatory authorities' satisfaction. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, ~~the~~ regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. The process of obtaining marketing approvals, both in the United States and abroad, is expensive and may take many years. The scope and amount of clinical data required to obtain marketing approvals can vary substantially from jurisdiction to jurisdiction, and it may be difficult to predict whether a particular regulatory body will require additional or different clinical trials than those conducted by a sponsor, especially for novel product candidates such as our product candidates. The FDA or other foreign regulatory authorities may delay, limit, or deny the approval of our product candidates for many reasons, including: • our inability to demonstrate that the clinical benefits of our product candidates outweigh any safety or other perceived risks; • the regulatory authority' s disagreement with the interpretation of data from nonclinical or clinical studies **or trials** ; • the regulatory agency' s requirement that we conduct additional preclinical studies and clinical trials; • changes in marketing approval policies during the development period; • changes in or the enactment of additional statutes or regulations, or changes in regulatory review process for each submitted product application; or • the regulatory authority' s failure to approve the manufacturing processes or third- party manufacturers with which we contract. Regulatory authorities have substantial discretion in the approval process and may refuse to accept a marketing application as deficient. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post- approval commitments that render the approved product not commercially viable. Of the large number of drugs in development, only a small percentage successfully

complete the FDA or other regulatory approval processes and are commercialized. Furthermore, our product candidates may not receive marketing approval even if they achieve their specified endpoints in clinical trials. Clinical data are often susceptible to varying interpretations **,** and many companies that have believed that their products performed satisfactorily in clinical trials have nonetheless failed to obtain FDA or ~~the~~ applicable foreign regulatory agency approval for their products. The FDA or foreign regulatory authorities may disagree with our trial design and our interpretation of data from nonclinical and clinical studies **and trials** . Upon the review of data from any pivotal trial, the FDA or applicable foreign regulatory agency may request that the sponsor conduct additional analyses of the data and, if it believes the data are not satisfactory, could advise the sponsor to delay filing a marketing application. Even if we eventually complete clinical testing and receive approval of a BLA or foreign marketing authorization for one of our product candidates, the FDA or applicable foreign regulatory agency may grant approval contingent on the performance of costly additional clinical trials which may be required after approval. The FDA or the applicable foreign regulatory agency may also approve our products for a more limited indication and / or a narrower patient population than we originally request, and the FDA or applicable foreign regulatory agency may not approve the labeling that we believe is necessary or desirable for the successful commercialization of our products. Any delay in obtaining, or inability to obtain, applicable regulatory approval would delay or prevent commercialization of our product candidates and would materially adversely impact our business and prospects. The development of SINTAX medicines and their interactions with cells in the small intestine is an emerging field, and it is possible that the FDA or other regulatory authorities or bodies could issue regulations or new policies in the future affecting our product candidates. If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be materially impaired. We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we intend to focus on developing product candidates for multiple initial indications that we identify as most likely to succeed ~~,~~ in terms of both regulatory approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and product development programs and product candidates for specific indications may not yield 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 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. A fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process. We may seek fast track designation for some of our product candidates. If a drug or biologic is intended for the treatment of a serious or life- threatening condition and nonclinical or clinical data demonstrate the potential to address unmet medical needs for this condition, the drug or biologic sponsor may apply for FDA fast track designation. Fast track designation provides increased opportunities for sponsor meetings with the FDA during preclinical and clinical development ~~,~~ in addition to the potential for rolling review ~~once~~ **of** a marketing application ~~is filed~~ **, if the relevant criteria are met** . The FDA has broad discretion whether or not to grant this designation, and even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. Fast track designation does not assure ultimate approval by the FDA. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from ~~our~~ **the** product development program. Additionally, similar considerations and concerns exist with respect to the pursuit of expedited regulatory approval pathways in jurisdictions outside of the U. S. A breakthrough therapy designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval. We may seek a breakthrough therapy designation for our product candidates. A breakthrough therapy is defined as a drug or biologic that is intended to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor can help to identify the most efficient path for clinical development. Drugs designated as breakthrough therapies by the FDA receive all the Fast Track program features, including eligibility for rolling review of BLA submissions. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification and rescind the designation. Additionally, similar considerations and concerns exist with respect to the pursuit of expedited regulatory approval pathways in jurisdictions outside of the U. S. Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved or commercialized in a timely manner or at all, which could negatively impact our business. The ability of the FDA and comparable foreign regulatory authorities to review and **/** or approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, the FDA' s and comparable foreign regulatory authorities' ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA' s and comparable foreign regulatory authorities' ability to perform routine

functions. Average review times at the FDA and comparable foreign regulatory authorities 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, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies such as the EMA, following its relocation to Amsterdam and resulting staff changes, may also slow the time necessary for new drugs and biologics 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. Separately, in response to the COVID- 19 pandemic, ~~in March 2020,~~ the FDA ~~announced its intention to postpone~~ **postponed** most inspections of **domestic and** foreign manufacturing facilities **at various points. Even though** ~~, and on March 18, 2020,~~ the FDA **has since** ~~temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Subsequently, in July 2020, the FDA resumed certain on- site inspections of domestic manufacturing facilities subject to a risk- based prioritization system. The FDA utilized this risk- based assessment system to assist in determining when and where it was safest to conduct prioritized domestic inspections. Additionally, on April 15, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary remote interactive evaluations of certain drug manufacturing facilities and clinical research sites, among other facilities. According to the guidance, the FDA may request such remote interactive evaluations where the FDA determines that remote evaluation would be appropriate based on mission needs and travel limitations. In May 2021, the FDA outlined a detailed plan to move toward a more consistent state of inspectional operations, and in July 2021, the FDA~~ resumed standard ~~inspectional~~ -- **inspection** operations of domestic facilities **where feasible** ~~and was continuing to maintain this level of operation as of September 2021. More recently~~ , the FDA has continued to monitor and implement changes to its inspectional activities to ensure the safety of its employees and those of the firms it regulates ~~,~~ as it adapts to the evolving COVID- 19 pandemic **, and any resurgence of the virus or emergence of new variants may lead to further inspectional delays** . Regulatory authorities outside the United States have adopted similar restrictions or other policy measures in response to the COVID- 19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews ~~,~~ or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Risks Related to our Dependence on Third Parties and Manufacturing We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials. We rely, and expect to continue to rely, on third parties, such as CROs, clinical data management organizations, medical institutions, clinical investigators and potential pharmaceutical partners, to conduct and manage our clinical trials. Our reliance on these third parties for research and development activities will reduce our control over these activities but does not relieve us of our responsibilities. For example, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulatory standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, safety and welfare of patients are protected. Other countries' regulatory agencies also have requirements for clinical trials with which we must comply. We also may be required in certain instances to register ongoing clinical trials and post the results of completed clinical trials on government- sponsored databases ~~,~~ such as ClinicalTrials. gov ~~,~~ or similar foreign databases within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, do not meet expected deadlines, experience work stoppages, terminate their agreements with us or need to be replaced, or do not conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may need to enter into new arrangements with alternative third parties, which could be difficult, costly or impossible, and our clinical trials may be extended, delayed ~~,~~ or terminated or may need to be repeated. If any of the foregoing occur, we may not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and may not be able ~~to~~ , or may be delayed in our efforts ~~to~~ , **to** successfully commercialize our product candidates. We also expect to rely on other third parties to store and distribute drug product required by our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, **thereby** producing additional losses and depriving us of potential product revenue. We rely on third parties for the manufacture of our product candidates for preclinical and clinical testing and expect to continue to do so for the foreseeable future. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or that such quantities may not be available at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts. We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for **the** commercial manufacture **,** if any **,** of our product candidates **that may** receive marketing approval. Reliance on third parties for the manufacture of our product candidates increases the risk that we will not have sufficient quantities of our product candidates on a timely basis or at all, or that such quantities will be available at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts. We may be unable to establish agreements with third- party manufacturers on acceptable terms or at all. Even if we are able to establish agreements with third- party manufacturers, reliance on third- party manufacturers entails additional risks, including: • failure of third- party manufacturers to comply with regulatory requirements and maintain quality assurance; • breach of manufacturing agreements by the third- party manufacturers; • failure to manufacture our product according to our specifications; • failure to manufacture our product according to our schedule or at all; • misappropriation or disclosure of our proprietary information, including our trade secrets and know- how; and • termination or non- renewal of agreements by third- party manufacturers at times that are costly or

inconvenient for us. Third- party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third- party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocations, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. Some of the contract manufacturers we rely on to produce our product candidates have never produced ~~a~~ **an** FDA- approved therapeutic. If our contract manufacturers are unable to comply with cGMP or similar foreign regulations or if the FDA or foreign regulatory authorities do not approve their facility upon a pre- approval inspection, our product candidates may not be approved or may be delayed in obtaining approval. In addition, there are a limited number of manufacturers that operate under cGMP or similar foreign regulations ~~and~~ that might be capable of manufacturing our products. Therefore, our product candidates and any future product candidates that we may develop may compete with other products for access to manufacturing facilities. Any failure to gain access to these limited manufacturing facilities could severely impact the clinical development, marketing approval and commercialization of our product candidates. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We ~~do~~ **may** not ~~currently~~ **, and may not be able to,** have arrangements in place for redundant sources of **all** clinical supplies for both drug substance and drug product. If our current contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers and we may be unable to replace them on a timely basis or at all. Our current and anticipated future dependence upon others for the manufacture of our product candidates or products could delay, prevent or impair our development and commercialization efforts. Moreover, as a result of the COVID- 19 pandemic, third- party manufacturers may be affected, which could disrupt their activities and, as a result, we could face difficulties and delays in the manufacture of our product candidates, which may negatively affect our preclinical and clinical development activities. We have no experience manufacturing our product candidates at commercial scale, and if we decide to establish our own manufacturing facility, we cannot assure you that we can manufacture our product candidates in compliance with regulations at a cost or in quantities necessary to make them commercially viable. We may establish ~~a~~ **one or more** manufacturing ~~facility~~ **facilities** for our product candidates for production at a commercial scale. We have no experience in commercial- scale manufacturing of our product candidates. We **may** ~~currently intend to~~ develop our manufacturing capacity in part by expanding our current facility or building additional facilities. ~~This~~ **These** ~~activity~~ **activities** ~~will~~ **would** require substantial additional funds and we would need to hire and train a significant number of qualified employees to staff these facilities. We may not be able to develop commercial- scale manufacturing facilities that are adequate to produce materials for additional later- stage clinical trials or commercial use. The equipment and facilities employed in the manufacture of pharmaceuticals are subject to stringent qualification requirements by regulatory agencies, including validation of facility, equipment, systems, processes and analytics. We may be subject to lengthy delays and expense in conducting validation clinical trials, if we can meet the requirements at all. Risks Related to Commercialization of Our Product Candidates and Other Legal Compliance Matters Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, hospitals, third- party payors and others in the medical community necessary for commercial success. If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third- party payors and others in the medical community. For example, current psoriasis treatment involves the use of steroids and biologics that are well established in the medical community, and physicians may continue to rely on these treatments. If our product candidates receive approval but do not achieve an adequate level of acceptance, we may not generate significant product revenue and we may not become profitable. The degree of market acceptance of our approved product candidates, if any, will depend on a number of factors, including: • their efficacy, safety and other potential advantages compared to alternative treatments; • the clinical indications for which our products are approved; • our ability to offer them for sale at competitive prices; • their convenience and ease of administration compared to alternative treatments; • the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies; • the strength of marketing and distribution support; • the availability of third- party coverage and adequate reimbursement for our product candidates; • the prevalence and severity of their side effects and their overall safety profiles; • any restrictions on the use of our products together with other medications; • interactions of our products with other medicines patients are taking; and • the inability of certain types of patients to take our product. We currently have no sales organization. If we are unable to establish effective sales, marketing and distribution capabilities or **we** enter into agreements with third parties with such capabilities, we may not be successful in commercializing our product candidates if and when they are approved. We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of our product candidates. To achieve commercial success for any product **candidate** for which we **may** obtain marketing approval, we will need to establish a sales and marketing organization or make arrangements with third parties to perform sales and marketing functions **,** and we may not be successful in doing so. In the future, we expect to build a focused sales and marketing infrastructure to market or promote our product candidates in the United States and potentially elsewhere, if and when they are approved. There are risks involved with establishing our own sales, marketing and distribution capabilities. 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. Factors that may inhibit our efforts to commercialize our products on our own include: • our inability to recruit, train and retain an adequate number of effective sales and marketing personnel; • the inability of sales personnel to obtain access to or educate physicians on the benefits of our products; • the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; • unforeseen costs and expenses associated with creating an

independent sales and marketing organization; and • the inability to obtain sufficient coverage and reimbursement from third-party payors and governmental agencies. Outside the United States, we may rely on third parties to sell, market and distribute our product candidates. We may not be successful in entering into arrangements with such third parties or may be unable to do so on terms that are favorable to us. In addition, our product revenue and our profitability, if any, may be lower if we rely on third parties for these functions than if we were to market, sell and distribute any products that we develop ourselves. 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 products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates. We face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than we do. The development and commercialization of new drug and biologic products is highly competitive and is characterized by rapid and substantial technological development and product innovations. We face competition with respect to our current product candidates and will face competition with respect to product candidates that we may seek to develop or commercialize in the future, including from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. We are aware of a number of large pharmaceutical and biotechnology companies, including **:** AbbVie Inc., ~~Agenus~~ **Amgen** Inc., ~~AstraZeneca plc~~ **Arcutis Biotherapeutics Inc.** , Bristol Myers Squibb **Company** ~~, F. Hoffmann- La Roche A. G., Gilead Sciences, Inc., Incyte Corporation~~ , Johnson & Johnson, ~~Merck~~ **Incyte Corporation** , Novartis International A. G., Pfizer Inc. ~~and~~ **,** Regeneron Pharmaceuticals ~~,~~ Inc **., Roivant Sciences Ltd., and Sanofi S. A** ., as well as smaller, early- stage companies, that are pursuing the development of products, including microbial- based therapeutics **,** in some instances, for disease indications **that** we are targeting. Some of these competitive products and therapies are **or may be** based on scientific approaches that are the same as or similar to our approach, and others **are or** may be based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations. Many of the companies and organizations against which we are competing or against which we may compete in the future have significantly greater financial resources, established presence in the market and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and reimbursement and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. These **and other** third parties **also** compete with us in recruiting and retaining qualified scientific, sales and marketing and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could delay us from obtaining FDA or other regulatory approval to market our product candidates and result in our competitors establishing a strong market position before we are able to enter the market, especially for any competitor developing a microbial- based therapeutic which will likely share our same regulatory approval requirements. For more information, please see" Risk Factors- Our product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated, which may delay us from marketing our product candidates." In addition, our ability to compete may be affected in many cases by insurers or other third- party payors seeking to encourage the use of generic or biosimilar products. Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations or third- party coverage and reimbursement policies, any of which could harm our business. Our ability to commercialize any product candidates successfully will depend, in part, on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third- party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and impact reimbursement levels. Obtaining and maintaining adequate reimbursement for our products may be difficult. We cannot be certain if and when we will obtain coverage and an adequate level of reimbursement for our products by third- party payors. A primary trend in the U. S. healthcare industry and elsewhere is cost containment. Government authorities and third- party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third- party payors require that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. In addition, reimbursement rates from private health insurance companies vary depending on the insurance company, the insurance plan and other factors. We may also be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval, and the royalties resulting from the sales of those products may also be adversely impacted. There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside the United States. Moreover, eligibility for reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly

obtain coverage and adequate reimbursement rates from both government- funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition. The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be reimbursed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription drug pricing remains subject to continuing governmental control, including possible price reductions ~~,~~ even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country ~~,~~ but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, ~~and~~ **thereby** negatively ~~impact~~ **impacting** the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval. There can be no assurance that our product candidates, if they are approved for sale in the United States or in other countries, will be considered medically necessary or cost- effective for a specific indication, or that **reimbursement** coverage or an adequate level of reimbursement will be available. Product liability lawsuits against us could cause us to incur substantial liabilities and limit commercialization of any products that we may develop. We face an inherent risk of product liability exposure related to the testing of our product candidates in clinical trials and will face an even greater risk if we commercially sell any products that we develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in: • regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions; • decreased demand for any product candidates or products that we may develop; • injury to our reputation and significant negative media attention; • withdrawal of clinical trial patients; • significant costs to defend the related litigation; • substantial monetary awards to trial participants or patients; • loss of revenue; • reduced resources of our management to pursue our business strategy; and • the inability to commercialize any products that we may develop. Our current product liability insurance coverage and any product liability insurance coverage that we acquire in the future may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to **acquire or** maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars. The Biologics Price Competition and Innovation Act (“ BPCIA ”) created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA- licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12- year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor’ s own preclinical data and data from adequate and well- controlled clinical trials to demonstrate the safety, purity and potency of their product. We believe that any of our product candidates approved as a biological product under a BLA should qualify for the 12- year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non- biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. In the EU, the European Commission has granted marketing authorizations for biosimilars pursuant to a set of general and product class- specific guidelines for biosimilar approvals issued over the past few years. In the EU, upon receiving marketing authorization, new innovative products generally receive eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the EU from referencing the innovator' s data to assess a biosimilar application. During the additional two- year period of market exclusivity, a biosimilar marketing authorization can be submitted, and the innovator' s data may be referenced, but no biosimilar product can be marketed until 10 years have elapsed from the initial authorization of the reference product in the EU. The overall 10- year of market exclusivity period may be extended to a maximum of 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our products. If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences. Failure to obtain marketing approval in international jurisdictions would prevent our product candidates from being marketed abroad. In order to market and sell our product candidates in the EU and many other jurisdictions, we or our collaborators must obtain separate marketing ~~approvals~~ **authorizations** and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval in foreign countries may differ substantially from that required to obtain FDA or other applicable regulatory approval. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the

product can be approved for sale in that country. We or our collaborators may not obtain approvals for our product candidates from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market. Additionally, the EU pharmaceutical legislation is currently undergoing a complete review process in the context of the Pharmaceutical Strategy for Europe initiative, launched by the European Commission in November 2020. ~~A~~ **The European Commission' s** proposal for revision of several legislative instruments related to medicinal products (potentially revising the duration of regulatory exclusivity, eligibility for expedited pathways, etc.) is **currently** expected **during** ~~to be adopted by~~ the **first quarter** ~~European Commission by the end~~ of ~~2022~~ **2023** . The proposed revisions, once they are agreed and adopted by the European Parliament and European Council (**which is** not expected before the end of 2024 **or early 2025**), may have a significant impact on the pharmaceutical industry in the long term. Any product candidate for which we obtain marketing approval could be subject to post- marketing restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved. Any product candidate for which we **may** obtain marketing approval, along with the manufacturing processes, post- approval clinical data, labeling, advertising and promotional activities for such product, will be subject to the continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post- marketing information and reports, registration and listing requirements, cGMP and similar requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. We and our contract manufacturers will also be subject to continual review and periodic inspections to assess compliance with cGMP and similar requirements. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production and quality control. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to specific conditions of approval, including a requirement to implement a risk evaluation and mitigation strategy, which could include requirements for a medication guide, communication plan ~~,~~ or restricted distribution system. If any of our product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product. The FDA and foreign regulatory authorities may also impose requirements for costly post- marketing studies or clinical trials and surveillance to monitor the safety or efficacy of our approved products. The FDA and foreign regulatory authorities closely regulate the post-approval marketing and promotion of drugs and biologics to ensure they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and foreign regulatory authorities impose stringent restrictions on manufacturers' communications regarding off- label use, and if we market our products outside of their approved indications, we may be subject to enforcement action for off- label marketing. Violations of the FDA' s or foreign regulatory authorities' restrictions relating to the promotion of prescription drugs may also lead to investigations alleging violations of federal, state, local or foreign health care fraud and abuse laws, as well as consumer protection laws. In addition, if a regulatory agency or we later discover previously unknown problems with our products, such as adverse events of unanticipated severity or frequency, problems with manufacturers or manufacturing processes, or failure to comply with regulatory requirements, the regulatory agency may impose restrictions on the products or us, including requiring withdrawal of the product from the market. Any failure to comply with applicable regulatory requirements may yield various problematic results, including: • litigation involving patients taking our products; • restrictions on such products, manufacturers or manufacturing processes; • restrictions on the labeling or marketing of a product; • restrictions on product distribution or use; • requirements to conduct post- marketing studies or clinical trials; • warning letters; • withdrawal of products from the market; • suspension or termination of ongoing clinical trials; • refusal to approve pending applications or supplements to approved applications that we submit; • recall of products; • fines, restitution or disgorgement of profits or revenues; • suspension or withdrawal of marketing approvals; • damage to relationships with potential collaborators; • unfavorable press coverage and damage to our reputation; • refusal to permit the import or export of our products; • product seizure or detention; • injunctions; or • imposition of civil or criminal penalties. Noncompliance with similar EU requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties. ~~Similarly~~ **Furthermore** , failure to comply with U. S. and foreign regulatory requirements regarding the development of products for pediatric populations and the protection of personal health information can also lead to significant penalties and sanctions. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. In addition, the FDA' s and foreign regulatory authorities' regulations, policies or guidance may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our product candidates or further restrict or regulate post- approval activities. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues. If regulatory sanctions are applied or if regulatory approval is withheld or withdrawn, the value of our company and our operating results will be adversely affected. Our relationships with customers, physicians and third- party payors will be subject to applicable anti- kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from governmental healthcare programs, contractual damages, reputational harm and diminished profits and future earnings. Healthcare providers, physicians and third- party payors will play a primary role in the recommendation and prescription of any product candidates for which we may obtain marketing approval. Our future arrangements with third- party payors, physicians and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may restrict the business or financial arrangements and relationships

through which we market, sell and distribute any products for which we obtain marketing approval. Restrictions under applicable federal, state **, local** and foreign healthcare laws and regulations include the following: • the federal Anti- Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program, such as Medicare and Medicaid; a person or entity does not need to have actual knowledge of the statute or specific intent to violate the statute to have committed a violation; • the false claims and civil monetary penalties laws, including the federal False Claims Act, which, among other things, impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment 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 or 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 or services resulting from a violation of the federal Anti- Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act; • the federal Health Insurance Portability and Accountability Act of 1996 imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters; similar to the federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them to have committed a violation; • the federal Physician Payment Sunshine Act requires applicable manufacturers of covered drugs to report payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain non- physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, anesthesiologist assistants and certified nurse midwives) ~~and~~ **,** teaching hospitals ~~,~~ and ownership and investment interests held by physicians and their immediate family members. Manufacturers are required to submit reports to the government by the 90th day of each calendar year; and • analogous state **, local** and foreign laws and regulations, such as state anti- kickback and false claims laws, may apply to our business practices, including but not limited to: research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third- party payors, including private insurers. State **and foreign** laws **may** require pharmaceutical companies to comply with the pharmaceutical industry' s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to ~~:~~ payments and other transfers of value to physicians and other healthcare providers, pricing information or marketing expenditures. The risk of our being found in violation of these laws and regulations is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws and regulations, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management' s attention from the operation of our business. The shifting compliance environment and the need to build and maintain a robust system to comply with multiple jurisdictions with different compliance and reporting requirements increases the possibility that a healthcare company may violate one or more of the requirements. Efforts to ensure that our business arrangements with third parties **do and** will comply with applicable healthcare laws and regulations ~~will involve~~ **involves** substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs ~~,~~ such as Medicare and Medicaid ~~,~~ and the curtailment or restructuring of our operations. Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval for and commercialize our product candidates and affect the prices we may obtain. In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post- approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In the United States, the Patient Protection and Affordable Care Act (" ACA") was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Among the provisions of the ACA that are of importance to our potential product candidates are the following: • establishment of a new pathway for approval of lower cost biosimilars to compete with biologic products, such as those we are developing; • an annual, nondeductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents; • an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program; • a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70 % point- of- sale discounts off negotiated prices; • extension of manufacturers' Medicaid rebate liability; • expansion of eligibility criteria for Medicaid programs; • expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; • a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and • a new Patient- Centered Outcomes Research Institute to oversee, identify priorities ~~in~~ and conduct comparative clinical effectiveness research, along with funding for such research. Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. On June 17, 2021, the U. S. Supreme Court dismissed the most recent judicial challenge to the ACA brought by several states without specifically ruling on the constitutionality of the ACA. Prior to the Supreme Court' s decision, President Biden issued an executive order initiating a special enrollment period from February 15, 2021 through August 15, 2021 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. ~~It is unclear how healthcare reform measures enacted by Congress or implemented by the Biden administration, if any, will impact our business.~~ In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers ~~of 2 % per fiscal year~~, which went into effect on April 1, 2013 and, due to subsequent legislative amendments, will remain in effect through ~~2030~~ **2032**, with the exception of a temporary suspension from May 1, 2020 through March 31 ~~, 2022 and a 1 % reduction from April 1, 2022 through June 30~~, 2022, unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, including hospitals, and ~~an increase~~ **increased** ~~in~~ the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, in March 2021, the American Rescue Plan Act of 2021 was signed into law, which, among other things, eliminated the statutory cap on drug manufacturers' Medicaid Drug Rebate Program rebate liability ~~,~~ effective January 1, 2024. Under current law enacted as part of the ACA, drug manufacturers' Medicaid Drug Rebate Program rebate liability is capped at 100 % of the average manufacturer price for a covered outpatient drug. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain **for our products**. We expect that other healthcare reform measures that may be adopted in the future ~~,~~ may result in additional reductions in Medicare and other healthcare funding, **in** more rigorous coverage criteria, **in** new payment methodologies and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates, if approved. Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products **. Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or IRA, was signed into law. Among other things, the IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (first due in 2023); and replaces the Part D coverage gap discount program with a new discounting program (beginning in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. For that and other reasons, it is currently unclear how the IRA will be effectuated, and the impact of the IRA on our business and the pharmaceutical industry cannot yet be fully determined**. Individual states in the United States have become increasingly active in implementing regulations designed to contain pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures. Legally mandated price controls on payment amounts by third- party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects. Legislative and regulatory proposals have been made to expand post- approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by Congress of the FDA' s approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post- marketing testing and other requirements. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action and we may not achieve or sustain profitability. We may be subject to the **UK** ~~U. K.~~ Bribery Act 2010 (the" Bribery Act"), the U. S. Foreign Corrupt Practices Act of 1977, as amended (the" FCPA"), and other anti- corruption laws, as well as export control laws, import and customs laws, trade and economic sanctions laws and other laws governing our operations. Our operations may be subject to anti- corruption laws, including the Bribery Act, the FCPA, the U. S. domestic bribery statute contained in 18 U. S. C. § 201, the U. S. Travel Act ~~,~~ and other anti- corruption laws that apply in countries where we do business. The Bribery Act, the FCPA and these other laws generally prohibit us, our employees and our intermediaries from authorizing, promising, offering ~~,~~ or providing, directly or indirectly, improper or prohibited payments ~~,~~ or anything else of value ~~,~~ to government officials or other persons to obtain or retain business or gain some other business advantage. Under the Bribery Act, we may also be liable for failing to prevent a person associated with us from committing a bribery offense. We and our partners may operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose corrupt or illegal activities could potentially subject us to liability under the Bribery Act, FCPA or local anti- corruption laws, even if we do not explicitly authorize or have actual knowledge of such activities. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted. We may also be subject to other laws and regulations from time to time governing our international operations, including regulations administered by the governments of the United States, the United Kingdom or elsewhere ~~,~~ and authorities in the European Union or elsewhere, including applicable export control regulations, economic sanctions and embargoes on certain countries and persons, anti- money laundering laws, import and customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws. There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti- corruption laws, including the Bribery Act, the FCPA or other

legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures ~~,~~ and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. Likewise, any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by the United Kingdom, United States or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition. We may be subject to various laws relating to foreign investment and the export of certain technologies, and our failure to comply with these laws or adequately monitor the compliance of our suppliers and others **with which** we do business with could subject us to substantial fines, penalties and injunctions, the imposition of which on us could have a material adverse effect on the success of our business. We may be subject to U. S. laws that regulate foreign investments in U. S. businesses and access by foreign persons to technology developed and produced in the United States. These laws include section 721 of the Defense Production Act of 1950, as amended by the Foreign Investment Risk Review Modernization Act of 2018, and the regulations at 31 C. F. R. Parts 800 and 801, as amended, administered by the Committee on Foreign Investment in the United States, and the Export Control Reform Act of 2018, which is being implemented in part through Commerce Department rule- making to impose new export control restrictions on " emerging and foundational technologies " yet to be fully identified. Application of these laws, including as they are implemented through regulations being developed, may negatively impact our business in various ways, including by: • restricting our access to capital and markets; • limiting the collaborations we may pursue; • regulating the export **of** our products, services, and technology from the United States and abroad; • increasing our costs and the time necessary to obtain required authorizations and to ensure compliance; and ~~threatening~~ **• threat of** monetary fines and other penalties for non-compliance. Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any. In some countries, particularly the EU member states, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various EU member states, and parallel distribution or arbitrage between low- priced and high- priced member states, can further reduce prices. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost- effectiveness of our product candidate to other available therapies. If coverage and reimbursement of our products are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially. 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 harm 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 for failure to comply with such laws and regulations. Although we maintain workers' compensation insurance to cover us for costs and expenses that we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against all potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. 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. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions. Risks Related to Our Intellectual Property If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents which are sufficient to protect our product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects. Our success depends in large part on our ability to obtain and maintain patent and other intellectual property protection in the United States and other countries with respect to our proprietary technology and ~~products~~ **product candidates**. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection. The patent prosecution 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, in a timely manner ~~,~~ or in all jurisdictions. 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. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist ~~,~~ or may arise in the future, such as ~~,~~ with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business, financial condition and operating results. Pursuant to our current and future license agreements with third parties, in some circumstances we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. We may also require the

cooperation of our licensors to enforce any licensed patent rights, and such cooperation may not be provided or may be deficient. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Although we have numerous patent applications pending, we cannot provide any assurances that any of our pending patent applications will mature into issued patents and, if they do, that such patents or our current patents will include claims with a scope sufficient to protect our product candidates or otherwise provide any competitive advantage. For example, we are pursuing claims to compositions of certain bacterial populations. Any claims that are issued may provide coverage for such compositions and / or their use. However, such claims would not prevent a third party from commercializing alternative compositions that do not include the bacterial populations claimed in pending applications, potential applications or patents that have issued or may issue. There can be no assurance that any such alternative composition will not be equally effective. These and other factors may provide opportunities for our competitors to design around our patents, should they issue. Moreover, other parties **may** have developed or may develop technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming similar methods or by claiming subject matter that could dominate our patent position. In addition, the standards that the United States Patent and Trademark Office (" USPTO") and other jurisdictions use to grant patents are not always applied predictably or uniformly and can change. Similarly, the ultimate degree of protection that will be afforded to biotechnology inventions, including ours, in the United States and other jurisdictions ~~,~~ remains uncertain and is dependent upon the scope of the protection decided upon by patent offices, courts ~~,~~ and lawmakers. Publications of discoveries in the scientific literature often lag behind actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until ~~18~~ **eighteen** months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in any issued patents or pending patent applications, or that we were the first to file for patent protection of such inventions, nor can we know whether those from whom we may license patents were the first to make the inventions claimed or were the first to file. For these and other reasons, the issuance, scope, validity, enforceability and commercial value of our patent rights are subject to a level of uncertainty. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in the patent laws and / or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. We may be subject to a third- party pre- issuance submission of prior art to the USPTO or become involved in derivation, reexamination, inter partes review, ex partes reexamination, post- grant review or ~~interference~~ **other** proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us ~~,~~ without payment to us, or result in our inability to manufacture or commercialize products without infringing third- party patent rights. For example, in February 2021, the European Patent Office informed us of a ~~notice~~ **Notice** of ~~opposition~~ **Opposition** by a third party for a patent issued to us. ~~In July~~ **Oral proceedings were held in September** ~~2021~~ **2022** , **and the Opposition Board maintained claims that** we **presented in an auxiliary request. No appeal from the Opposition Board' s decision was** filed ~~a reply to the notice of opposition~~ . The patent at issue does not relate to **any of** our current product candidates. Any limitation on the protection of the subject technology could hinder our ability to develop and commercialize applicable product candidates. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Furthermore, an adverse decision in **a** ~~an interference~~ proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize our product candidates. The issuance, scope, validity, enforceability and commercial value of our patents are subject to a level of uncertainty. The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. Due to legal standards relating to patentability, validity, enforceability and claim scope of patents covering biotechnological and pharmaceutical inventions, our ability to obtain, maintain and enforce patents is uncertain and involves complex legal and factual questions. Even if issued, a patent' s validity, inventorship, ownership or enforceability is not conclusive. Accordingly, rights under any existing patent or any patents we might obtain or license may not cover our product candidates, or may not provide us with sufficient protection for our product candidates to afford a commercial advantage against competitive products or processes, including those from branded and generic pharmaceutical companies. The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that: • any of our pending patent applications, if issued, will include claims having a scope sufficient to protect our product candidates or any other products or product candidates; • any of our pending patent applications will issue as patents; • we will be able to successfully commercialize our product candidates, if approved, before our relevant patents expire; • we were the first to make the inventions covered by any existing patent and pending patent applications; • we were the first to file patent applications for these inventions; • others will not develop similar or alternative technologies that do not infringe or design around our patents; • others will not use pre- existing technology to effectively compete against us; • any of our patents, if issued, will be found to ultimately be valid and enforceable; • third parties will not compete with us in jurisdictions where we do not pursue and obtain patent protection; • we will be able to obtain and / or maintain necessary or useful licenses on reasonable terms or at all; • any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties; • we will develop additional proprietary technologies or product candidates that are separately patentable; or • our commercial activities or products will not infringe upon the patents or proprietary rights of others. Any litigation to enforce or defend our patent rights, even if we were to prevail, could be costly and time- consuming and would divert the attention of our management and key personnel from our business operations. We may not prevail in any lawsuits that

we initiate, and the damages or other remedies awarded even if we were to prevail may not be commercially meaningful. Even if we are successful, domestic or foreign litigation, or USPTO or foreign patent office proceedings, may result in substantial costs and distraction to our management. We may not be able, alone or with our licensors or potential collaborators, to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other proceedings, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. In addition, during the course of this kind of litigation or proceedings, there could be public announcements of the results of hearings, motions or other interim proceedings or developments or public access to related documents. If investors perceive these results to be negative, the market price for our common stock could be significantly harmed. If we fail to comply with our obligations in the agreements under which we may license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose rights that are important to our business. We have entered into, and may be required to enter into in the future, intellectual property license agreements that are important to our business. These license agreements may impose various diligence, milestone payment, royalty and other obligations on us. For example, we have entered into **an** exclusive license ~~agreements~~ **agreement** with the ~~University of Chicago and~~ Mayo Clinic pursuant to which we are required to use efforts to engage in various development and commercialization activities with respect to licensed products **,** and **we** are required to satisfy specified milestone and royalty payment obligations. If we fail to comply with any obligations under our agreements with licensors, we may be subject to termination of the license agreement in whole or in part or increased financial obligations to our licensors, in which case our ability to develop or commercialize products covered by the license agreement will be impaired. Further, we may need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our products covered under our current and future license agreements. Delay or failure by these third parties could adversely affect the continuation of our license agreements with our licensors. In addition, 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 intellectual property of the licensor that is not subject to the licensing agreement; and • our diligence obligations under the license agreement and what activities satisfy those obligations. 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. The intellectual property which we have licensed from the ~~University of Chicago and~~ Mayo Clinic was discovered through government funded programs and thus may be subject to federal regulations such as" march- in" rights, certain reporting requirements ~~,~~ and a preference for U. S. industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements ~~,~~ and limit our ability to contract with non- U. S. manufacturers. We have licensed certain intellectual property from the ~~University of Chicago and~~ Mayo Clinic. ~~These~~ -- **The** ~~agreements~~ **agreement** ~~indicate~~ **indicates** that the rights licensed to us are subject to the obligations to and the rights of the U. S. government, including those set forth in the Bayh- Dole Act of 1980. As a result, the U. S. government may have certain rights to intellectual property embodied in our current or future therapeutics based on the licensed intellectual property. These U. S. government rights in certain inventions developed under a government- funded program include a non- exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U. S. government has the right to require us to grant exclusive, partially exclusive ~~,~~ or nonexclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as" march- in rights." While the U. S. government has sparingly used, and to our knowledge never successfully exercised, such march- in rights, any exercise of the march- in rights by the U. S. government could harm our competitive position, business, financial condition, results of operations and prospects. If the U. S. government exercises such march- in rights, we may receive compensation that is deemed reasonable by the U. S. government in its sole discretion, which may be less than what we might be able to obtain in the open market. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U. S. government requires that any therapeutics embodying any invention generated through the use of U. S. government funding be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. **Absent a waiver,** ~~This~~ **this** preference for U. S. manufacturers ~~may~~ **could** limit our ability to ~~contract with non- U. S. therapeutic~~ **sell our product candidates in the United States, since our product candidates currently are** ~~manufacturers~~ **manufactured** ~~for therapeutics covered by such intellectual property~~ **in part outside of the United States** . If we are unable to protect the confidentiality of our trade secrets and know-how, our business and competitive position would be harmed. In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know- how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non- disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also seek to enter into confidentiality and invention or patent assignment agreements with our employees, **contractors, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants,** advisors and ~~consultants~~ **other third parties** . Despite these efforts, 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. Our trade secrets may also be obtained by third

parties by other means, such as breaches of our physical or computer security systems. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time- consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. Moreover, if any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them ~~,~~ or those to whom they communicate ~~,~~ from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed. Changes in patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products. As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involves both technological and legal complexity, and is therefore costly, time- consuming and inherently uncertain. Patent reform legislation in the United States, including the Leahy- Smith America Invents Act (the" Leahy- Smith Act") ~~,~~ signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy- Smith Act included a number of significant changes to U. S. patent law. These changes included provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost- effective avenues for competitors to challenge the validity of patents. In addition, the Leahy- Smith Act transformed the U. S. patent system into a " first to file " system. The first- to- file provisions became effective on March 16, 2013. The Leahy- Smith Act and its implementation could make it more difficult to obtain patent protection for our inventions and 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 harm our business, results of operations and financial condition. In addition, ~~recent United States~~ **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. From time to time, the U. S. Supreme Court, other federal courts, the United States Congress ~~,~~ or the USPTO, may change the standards of patentability and any such changes could have a negative impact on our business. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. The U. S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. For example, in Association for Molecular Pathology v. Myriad Genetics, Inc., the Supreme Court held that claims to isolated genomic DNA are not patentable, but claims to complementary DNA, or cDNA, molecules, which are not genomic sequences, may be patent eligible because they are not a natural product. The effect of the decision on patents for other isolated natural products is uncertain. Our current product candidates include natural products. Therefore, this decision and its interpretation by the courts and the USPTO may impact prosecution, defense and enforcement of our patent portfolio. Depending on future actions by the U. S. Congress, the U. S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future. **.** In addition to increasing uncertainty with regard to our ability to obtain future patents,this combination of events has created uncertainty with respect to the value of patents,once obtained.Depending on these and other decisions by ~~the U.S.~~ Congress,the federal courts and the USPTO,the laws and regulations governing patents could change or be interpreted in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that may issue to us in the future.In addition,these events may adversely affect our ability to defend any patents that may issue in procedures in the **USPTO or in courts** Europe' s planned Unified Patent Court may in particular present uncertainties for our ability to protect and enforce our patent rights against competitors in Europe. While that new court is being implemented to provide more certainty and efficiency to patent enforcement throughout Europe, it will also provide our competitors with a new forum to use to centrally revoke our European patents. It will be several years before we will understand the scope of patent rights that will be recognized and the strength of patent remedies that will be provided by that court. We will have the right to opt our patents out of that system over the first seven years of the court, but doing so may preclude us from realizing the benefits of the new unified court . In addition to increasing uncertainty with..... procedures in the USPTO or in courts . Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. While no such litigation has been brought against us and we have not been held by any court to have infringed a third party' s intellectual property rights, we cannot guarantee that our technology, products or use of our products do not infringe third- party patents. Numerous patents and pending applications are owned by third parties in the fields in which we are developing product candidates, both in the United States and elsewhere. It is also possible that we have failed to identify relevant third- party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Moreover, it is difficult for industry participants, including us, to identify all third- party patent rights that may be relevant to our product candidates and technologies because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. We may fail to identify relevant patents or patent applications or may identify pending patent applications of potential interest but incorrectly predict the likelihood that such patent applications may issue with claims of relevance to our technology. In addition, we may be unaware of one or more issued patents that would be infringed by the manufacture, sale or use of a current or future product candidate, or we may incorrectly conclude that a third-party patent is invalid, unenforceable or not infringed by our activities. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our technologies, our ~~products~~ -

product candidates or the use of our ~~products~~ **product candidates** . We are aware of several pending patent applications containing one or more claims that could be construed to cover some of our product candidates or technology, should those claims issue in their original form or in the form presently being pursued. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Other parties may allege that our product candidates or the use of our technologies infringe patent claims or other intellectual property rights held by them **,** or that we are employing their proprietary technology without authorization. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our products and technology, including ~~interference or derivation~~ proceedings before the USPTO and similar bodies in other countries. Third parties may assert infringement claims against us based on existing intellectual property rights and intellectual property rights that may be granted in the future. If we were to challenge the validity of an issued U. S. patent in court, such as an issued U. S. patent of potential relevance to some of our product candidates or methods of use, we would need to overcome a statutory presumption of validity that attaches to every U. S. patent. This means that in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent' s claims. There is no assurance that a court would find in our favor on questions of infringement or validity. Patent and other types of intellectual property litigation can involve complex factual and legal questions, and their outcome is uncertain. If we are found **,** or believe there is a risk we may be found, to infringe a third party' s intellectual property rights, we could be required or may choose to obtain a license from such third party to continue developing and marketing our products and technology. However, we may not be able to obtain any such license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non- exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees **,** if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business. Even if we are successful in proceedings defending our intellectual property, we may incur substantial costs and divert management time and attention in pursuing these proceedings, which could have a material adverse effect on us. If we are unable to avoid infringing the patent rights of others, we may be required to seek a license, defend an infringement action or challenge the validity of the patents in court, or redesign our products. Patent litigation is costly and time-consuming. We may not have sufficient resources to bring these actions to a successful conclusion. In addition, intellectual property litigation or claims could force us to do one or more of the following: • cease developing, selling or otherwise commercializing our product candidates; • pay substantial damages for past use of the asserted intellectual property; • obtain a license from the holder of the asserted intellectual property, which license may not be available on reasonable terms, if at all; and • in the case of trademark claims, redesign or rename some or all of our product candidates or other brands to avoid infringing the intellectual property rights of third parties, which may not be possible and, even if possible, could be costly and time- consuming. Any of these risks coming to fruition could have a material adverse effect on our business, results of operations, financial condition and prospects. Issued patents covering our product candidates could be found invalid or unenforceable or could be interpreted narrowly if challenged in court. Competitors may infringe our intellectual property, including our patents or the patents of our licensors. As a result, we may be required to file infringement claims to stop third-party infringement or unauthorized use. This can be expensive, particularly for a company of our size, and time- consuming. If we initiated legal proceedings against a third party to enforce a patent, if and when issued, covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid and / or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and / or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non- enablement, or failure to claim patent eligible subject matter. Grounds for unenforceability assertions include allegations 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, such as opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, 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 and / or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Moreover, even if not found invalid or unenforceable, the claims of our patents could be construed narrowly or in a manner that does not cover the allegedly infringing technology in question. Such a loss of patent protection would have a material adverse impact on our business. 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 noncompliance with these requirements. Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and, in some jurisdictions, during the pendency of a patent application. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include,

but are not limited to, failure to respond to official actions within prescribed time limits, non- payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business. We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property. It is our policy to enter into confidentiality and intellectual property assignment agreements, including with our employees, **contractors, corporate collaborators, outside scientific collaborators, contract manufacturers,** consultants, ~~contractors and~~ advisors **and other third parties** . These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign all such intellectual property to his or her employing institution. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. 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. We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property. Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We may also engage advisors and consultants who are concurrently employed at universities or other organizations or who perform services for other entities. Although we try to ensure that our employees, **contractors, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants,** advisors and ~~consultants~~ **other third parties engaged by us** 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 **they** ~~our employees, advisors or consultants~~ have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such party' s former or current employer or in violation of an agreement with another party. Although we have no knowledge of any such claims being alleged to date, if such claims were to arise, litigation may be necessary to defend against any such claims. In addition, while it is our policy to require our employees, **contractors, corporate collaborators, outside scientific collaborators, contract manufacturers,** consultants, advisors and ~~contractors~~ **other third parties engaged by us** who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self- executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Similarly, we may be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person' s obligations to a third party, such as an employer, and thus ~~, that~~ the third party has an ownership interest in the intellectual property arising out of work performed for us. ~~Litigation may be necessary to defend against these claims.~~ Although we have no knowledge of any such claims being alleged to date, if such claims were to arise, litigation may be necessary to defend against any such claims. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management. If our trademarks and trade names are not adequately protected, ~~then~~ we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing other marks. We may not be able to protect our rights to these trademarks and trade names ~~,~~ which we need to build name recognition among potential collaborators or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade names, domain names or other intellectual property may be ineffective and could result in substantial costs and diversion of resources **,** and could adversely impact our financial condition or results of operations. We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection. Filing, prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than in the United States, assuming that rights are obtained in the United States and assuming that rights are pursued outside the United States. The statutory deadlines for pursuing patent protection in individual foreign jurisdictions are based on the priority date of each of our patent applications. For some of the patent families in our portfolio, including the families that may provide coverage for our lead product candidates, the relevant statutory deadlines have not yet expired. Therefore, for each of the patent families that we believe provide coverage for our lead product candidates, we will need to decide whether and where to pursue protection outside 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, even if we do elect to pursue patent rights outside the United States, we may not be able to obtain relevant claims and / or 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..... as the laws of the United States . Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country- by- country basis, which is an expensive and time- consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries. ~~.~~Competitors may use our technologies in jurisdictions where we do not pursue and obtain 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.Even if we pursue and obtain issued patents in particular jurisdictions,our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing **.** If our ability to obtain and, if obtained, enforce our patents to stop infringing activities is inadequate, third parties may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Accordingly, our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property we develop or license. Risks Related to Employee Matters and Managing Growth and Other Risks Related to Our Business Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel. We are highly dependent on ~~Balkrishan (Simba) Gill, our President and Chief Executive Officer, as well as the other~~ -- **the** principal members of our management, scientific and clinical teams. Although we have entered into agreements with our executive officers, each of them may terminate their employment with us at any time. We do not maintain" key person" insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will ~~also~~ be critical to our success. The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives **,** and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time due to the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. **In January 2023, our Board approved the reduction of our workforce by 48 employees, or approximately 45 % of our headcount as of such date, in order to preserve cash and prioritize investment in our core clinical programs. This reduction may negatively impact our ability to attract candidates to the Company in the future.** Competition to hire from ~~this~~ **the** limited pool **referred to above** is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. If we are unable to ~~continue to~~ attract and retain high quality personnel, our ability to pursue our ~~growth~~ **business** strategy will be limited **and our business will be harmed. Our reduction in force undertaken to extend our cash runway and focus more of our capital resources on our prioritized research and development programs may not achieve our intended outcome. In January 2023, our board approved a reduction in force affecting approximately 45 % of our workforce, in order to preserve cash and prioritize investment in our core clinical programs. The reduction in force may result in unintended consequences and costs, such as the loss of institutional knowledge and expertise, attrition beyond the intended number of employees, decreased morale among our remaining employees, and the risk that we may not achieve the anticipated benefits of the reduction in force. In addition, while positions have been eliminated, certain functions necessary to our operations remain, and we may be unsuccessful in distributing the duties and obligations of departed employees among our remaining employees. The reduction in workforce could also make it difficult for us to pursue, or prevent us from pursuing, new opportunities and initiatives due to insufficient personnel, or require us to incur additional and unanticipated costs to hire new personnel to pursue such opportunities or initiatives. If we are unable to realize the anticipated benefits from the reduction in force, or if we experience significant adverse consequences from the reduction in force, our business, financial condition, and results of operations may be materially adversely affected** . We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. ~~We~~ **In the future, we** expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of product development, regulatory affairs, clinical affairs and manufacturing and, if any of our product candidates receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business

plans or disrupt our operations. A variety of risks associated with operating internationally could materially adversely affect our business. We currently have limited international operations, but our business strategy incorporates potentially expanding internationally if any of our product candidates receive regulatory approval. Doing business internationally involves a number of risks, including but not limited to: • multiple, conflicting and changing laws and regulations, such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements and other governmental approvals, permits and licenses; • failure by us to obtain and maintain regulatory approvals for the use of our products in various countries; • additional potentially relevant third- party patent rights; • complexities and difficulties in obtaining protection and enforcing our intellectual property; • difficulties in staffing and managing foreign operations; • complexities associated with managing multiple payor reimbursement regimes, government payors or patient self- pay systems; • limits in our ability to penetrate international markets; • financial risks, such as longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products and exposure to foreign currency exchange rate fluctuations; • natural disasters, political and economic instability ~~,~~ including wars, terrorism and political unrest (**for example,** ~~e. g.~~ the ~~developing~~ **ongoing** conflict between Russia and Ukraine), outbreak of disease (**for example,** ~~e. g.~~ the COVID- 19 pandemic), boycotts, curtailment of trade and other business restrictions; • certain expenses including, among others, expenses for travel, translation and insurance; and • regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U. S. Foreign Corrupt Practices Act, its books and records provisions, ~~or~~ its anti- bribery provisions ~~,~~ or other anti- bribery and anti- corruption laws. Any of these factors could significantly harm our future international expansion and operations and, consequently, our results of operations. The United Kingdom' s withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business. **Since** ~~The UK left~~ the **end of** ~~EU on January 31, 2020, following which existing EU legislation continued to apply in~~ the **Brexit** ~~UK during a~~ transition period ~~under the terms of the EU- UK Withdrawal Agreement. The transition period, which ended on December 31, 2020, maintained access to the EU single market and to global trade deals negotiated by the EU on behalf of its members. The transition period provided time for the UK and EU to negotiate a framework for partnership for the future, which was then crystallized in the Trade and Cooperation Agreement (" TCA ") which became effective~~ on January 1, 2021 ~~. These developments~~ , **Great Britain (England** ~~or the perception that any related developments could occur~~ , **Scotland** ~~have had~~ and ~~may continue~~ **Wales) has not been directly subject** to ~~have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Any of these factors could depress economic activity and restrict our access to capital, which could have a material adverse effect on our business, financial condition and results of operations and reduce the price of common stock. The long term effects of Brexit will depend on the implementation and application of the TCA and any other relevant agreements between the UK and the EU.~~ EU laws **. However, under the terms of the Ireland / Northern Ireland Protocol, EU laws have generally applied to Northern Ireland. On February 27, 2023 the UK Government and the European Commission reached a political agreement on the " Windsor Agreement "** which **will revise the Protocol on Ireland / Northern Ireland in order to address some of the perceived shortcomings in its operation. Under the proposed changes, Northern Ireland would be reintegrated under the regulatory authority of the MHRA with respect to medicinal products. These proposed changes need to be codified and agreed by the respective parliaments of the UK and EU before taking effect. There could be additional uncertainty and risk around what these changes will mean to our business. More generally, it is currently unclear to what extent the UK Government will seek to align its regulations with the EU. The EU laws that** have been transposed into UK law through secondary legislation **remain** ~~continue to be~~ applicable ~~as "~~ **in Great Britain. However, under the Retained EU Law (Revocation and Reform) Bill 2022, which is currently before the UK parliament, any** retained EU law **not expressly preserved and " assimilated "** into **domestic law or extended by ministerial regulations (to no later than June 23, 2026) will automatically expire and be revoked by December 31, 2023** . ~~However~~ **In addition** , new legislation **such as the (EU) CTR is not applicable in Great Britain. Whilst the EU- UK Trade and Cooperation Agreement (" TCA ") includes the mutual recognition of GMP inspections of manufacturing facilities for medicinal products and GMP documents issued, it does not contain wholesale mutual recognition of UK and EU pharmaceutical regulations and product standards. There may be divergent local requirements in Great Britain from the EU in the future, which may impact clinical and development activities that occur in the UK in the future. Similarly, clinical trial submissions in the UK** will not be ~~applicable. The~~ **able to be bundled with those of EU countries within the EMA Clinical Trial Information System (" CTIS "), adding further complexity, cost and potential risk to future clinical and development activity in the** UK **. Significant political** ~~government has passed a new Medicines and Medical Devices Act 2021, which introduces delegated powers in favor of the Secretary of State or an~~ **and economic uncertainty remains about how much the** ~~' appropriate authority' to amend or supplement existing regulations --~~ **relationship** ~~in~~ **between** the **UK and EU** ~~area of medical devices. This allows new rules to be introduced in the future by way of secondary legislation, which aims to allow flexibility in addressing regulatory gaps. There is a possibility that, over time, national laws~~ will **differ as a result** ~~be amended and that consequently the regulatory framework in Great Britain will diverge from that~~ of ~~the EU. As of January 1, 2021, the MHRA is~~ the UK' s **withdrawal** ~~standalone medicines and medical devices regulator~~ . ~~As~~ **These developments, or the perception that any related developments could occur, have had and may continue to have** a ~~result~~ **material adverse effect on global economic conditions and the stability** of **global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. The UK has also experienced significant political instability in 2022, which has seen** ~~the~~ **three** ~~Northern Ireland protocol,~~ different **Prime Ministers hold office** ~~rules will apply in Northern Ireland than in England, Wales, and Scotland, together, Great Britain~~ . **Any of** ~~Broadly, Northern Ireland will continue to follow the~~ **these** ~~EU regulatory regime~~ **factors could depress economic activity and restrict our access to capital** , ~~but its national competent authority will~~

~~remain~~ **which could have a material adverse effect on our business, financial condition and results of operations and reduce** the ~~MHRA~~ **price of our common stock** . The uncertainty regarding new or modified arrangements between the **UK** ~~United Kingdom~~ and other countries following the withdrawal may have a material adverse effect on the movement of personnel, goods, information or data between the **UK** ~~United Kingdom~~ and members of the EU and the United States, including the interruption of or delays in imports into the **UK** ~~United Kingdom~~ of goods originating within the EU and exports from the **UK** ~~United Kingdom~~ of goods originating there. For example, shipments into the **UK** ~~United Kingdom~~ of ~~drug~~ **medicinal product** substance manufactured for us in the EU may be interrupted or delayed and thereby prevent or delay the manufacture in the **UK** ~~United Kingdom~~ of drug product. Similarly, shipments out of the **UK** ~~United Kingdom~~ of drug product to the United States or the EU may be interrupted or delayed and thereby prevent or delay the delivery of drug product to clinical sites. Such a situation could hinder our ability to conduct current and planned clinical trials and have an adverse effect on our business. Our business and operations may suffer in the event of information technology ~~and other~~ system failures or security breaches of or unauthorized access to our systems. We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. Despite the implementation of security measures, our information technology systems and those of our current and future partners, service providers, contractors and consultants are vulnerable to attack and damage from computer viruses, unauthorized access, malware (e. g. ransomware), **malicious code,** natural disasters, terrorism, war, telecommunication and electrical failures, cyberattacks or cyber- intrusions, phishing attacks and other social engineering schemes, employee theft or misuse, human error, fraud, denial or degradation of service attacks, and other security breaches or unauthorized access by persons inside our organization or with access to our internal systems. The risk of a security breach or disruption, particularly through cyberattacks or cyber- intrusions, including by computer hackers, foreign governments and cyber terrorists, generally has increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, our **information technology** systems safeguard important confidential data, including personal data regarding patients enrolled in our clinical trials. As a result of the COVID- 19 pandemic **and continued hybrid working environment** , we may also face increased cybersecurity risks due to our greater reliance on internet technology and the number of our employees who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection ~~,~~ and to remove or obfuscate forensic evidence. We and ~~certain of~~ our service providers are ~~from time to time~~ subject to cyberattacks and security incidents. While we do not believe that we have experienced any significant system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption to our product development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and we have also outsourced elements of our information technology infrastructure. Similar events relating to the ~~computer~~ **information technology** systems of our third- party service providers and vendors could make us vulnerable to disruptions in service and unauthorized access to our confidential or proprietary information, and we could incur liability and reputational damage. Though immaterial to date and despite stringent precautions, we have in the past experienced, and may in the future experience, the inadvertent disclosure of information by our third party service providers. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our business. Furthermore, federal, state **, local** and international laws and regulations can expose us to enforcement actions and investigations by regulatory authorities, and potentially result in regulatory penalties, fines and significant legal liability, if our information technology security efforts fail. We may also be exposed to a risk of loss or litigation and potential liability, which could materially and adversely affect our business, results of operations or financial condition and prospects. We **maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems. We** rely on a set of cloud- based software services and access these services via the Internet for the vast majority of our computing, storage, bandwidth ~~,~~ and other services. Any disruption of or interference with our use of our cloud- based services would negatively affect our operations and could seriously harm our business. We use several distributed computing infrastructure platforms for business operations, or what is commonly referred to as" cloud" computing services **,** and we access these services via the Internet. Any transition of the cloud services currently provided by an existing vendor to another cloud provider would be difficult to implement and will cause us to incur significant time and expense. Given this, any significant disruption of or interference with our use of these cloud computing services would negatively impact our operations and our business would be seriously harmed. If our employees or partners are not able to access our cloud computing services or encounter difficulties in doing so, we may experience business disruption. The level of service provided by our cloud computing vendors, including the ability to secure our confidential information and the confidential information of third parties that is shared with us, may also impact the perception of our company and could seriously harm our business and reputation and create

liability for us. If a cloud computing service that we use experiences interruptions in service regularly or for a prolonged basis, or other similar issues, our business could be seriously harmed. In addition, a cloud computing service may take actions beyond our control that could seriously harm our business, including: • discontinuing or limiting our access to its platform; • increasing pricing terms; • terminating or seeking to terminate our contractual relationship altogether; • establishing more favorable relationships with one or more of our competitors; or • modifying or interpreting its terms of service or other policies in a manner that impacts our ability to run our business and operations. Our cloud computing service providers have broad discretion to change and interpret their terms of service and other policies with respect to us, and those actions may be unfavorable to us. Our cloud computing service providers may also alter how we are able to process data on the platform. If a cloud computing service provider makes changes or interpretations that are unfavorable to us, our business could be seriously harmed. Our efforts to protect the information shared with us may be unsuccessful due to the actions of third parties, software bugs ~~,~~ or other technical malfunctions, employee error or malfeasance ~~,~~ or other factors. In addition, third parties may attempt to fraudulently induce employees or users to disclose information to gain access to our data or third- party data entrusted to us. If any of these events occur, our or third- party information could be accessed or disclosed improperly. Some partners or collaborators may store information that we share with them on their own computing system. If these third parties fail to implement adequate data- security practices or fail to comply with our policies, our data may be improperly accessed or disclosed. And even if these third parties take all these steps, their networks may still suffer a breach, which could compromise our data. Any incidents where our information is accessed without authorization, ~~or~~ is improperly used, or ~~incidents~~ that violate our policies ~~,~~ could damage our reputation and our brand and diminish our competitive position. In addition, affected parties or government authorities could initiate legal or regulatory action against us over those incidents, which could cause us to incur significant expense and liability or result in orders or consent decrees forcing us to modify our business practices. Concerns over our privacy practices, whether actual or unfounded, could damage our reputation and brand and deter users, advertisers ~~,~~ and partners from using our products and services. Any of these occurrences could seriously harm our business. Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could adversely affect our business, results of operations, financial condition and prospects. Legislation in various countries around the world with regard to cybersecurity, privacy and data protection is rapidly expanding and creating a complex compliance environment. We are subject to many federal, state ~~,~~ and foreign laws and regulations, including those related to privacy, rights of publicity, data protection, content regulation, protection of minors ~~,~~ and consumer protection. In the United States, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ~~,~~ and regulations promulgated thereunder (collectively, " HIPAA "), imposes, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information. Most healthcare providers, including research institutions from which we obtain patient health information, are subject to privacy and security regulations promulgated under HIPAA. While we do not believe that we are currently acting as a covered entity or business associate under HIPAA and thus are not directly regulated under HIPAA, any person may be prosecuted under HIPAA' s criminal provisions either directly or under aiding- and- abetting or conspiracy principles. Consequently, depending on the facts and circumstances, we could face substantial criminal penalties if we knowingly receive individually identifiable health information from a HIPAA- covered healthcare provider or research institution that has not satisfied HIPAA' s requirements for disclosure of individually identifiable health information. Certain U. S. states have also adopted comparable privacy and security laws and regulations ~~,~~ which govern the privacy, processing and protection of health- related and other personal information. Such laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. For example, California has enacted the California Consumer Privacy Act (the" CCPA"), which took effect on January 1, 2020. The CCPA creates individual privacy rights for California consumers and increases the privacy and security obligations of entities handling certain personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that **has** ~~is expected to increase~~ **increased the likelihood of and risks associated with** data breach litigation. Additionally, the California Privacy Rights Act (the " CPRA ") ~~was recently enacted in California~~ **generally went into effect on January 1, 2023 and significantly amends the CCPA** . The CPRA ~~significantly amends the CCPA and will impose~~ **imposes** additional data protection obligations on covered companies doing business in California, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data ~~,~~ and opt outs for certain uses of sensitive data. It ~~will~~ also ~~create~~ **creates** a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement. ~~The majority of the provisions will go into effect on January 1, 2023, and additional~~ **Additional** compliance investment and potential business process changes may **also** be required. Similar laws have passed in **other states including** Virginia **, Utah, Connecticut** and Colorado, and have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the United States. We are also or may become subject to rapidly evolving data protection laws, rules and regulations in foreign jurisdictions. For example, the General Data Protection Regulation (the " GDPR "), which became effective in May 2018, imposes stringent data protection requirements for processing the personal data of individuals within the EEA. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to € 20 million or 4 % of the annual global revenues of the noncompliant company, whichever is greater. Among other requirements, the GDPR prohibits the transfer of personal data from the EEA to the United States and other jurisdictions that the European Commission does not recognize as having " adequate " data protection laws unless a data transfer mechanism has been put in place. In July 2020, the Court of Justice of the European Union (the " CJEU ") limited how organizations could lawfully transfer personal data from the EEA to the United States by invalidating the EU- US Privacy Shield for purposes of international transfers and imposing further restrictions on the use of standard contractual clauses (" SCCs "). ~~The~~ **In March 2022, the US and EU**

announced a new regulatory regime intended to replace the invalidated regulations; however, this new EU- US Data Privacy Framework has not been implemented beyond an executive order signed by President Biden on October 7, 2022 on Enhancing Safeguards for United States Signals Intelligence Activities. European ~~Commission published revised SCCs for~~ **court and regulatory decisions subsequent to the CJEU decision of July 2020 have taken a restrictive approach to international** data transfers ~~from the EEA on June 4, 2021. The revised clauses must be used for relevant new data transfers from September 27, 2021 onward; existing SCC arrangements must be migrated to the revised clauses by December 27, 2022. The new SCCs apply only to the transfer of personal data outside of the EEA and not the United Kingdom; the United Kingdom Information Commissioner' s Office launched a public consultation on its draft revised data transfers mechanisms in August 2021 and laid its proposal before Parliament, with the United Kingdom SCCs expected to come into force in March 2022, with a two- year grace period. We will be required to implement the revised SCCs, in relation to relevant existing contracts and certain additional contracts and arrangements, within the relevant time frames. There is some uncertainty around whether the revised clauses can be used for all types of data transfers, particularly whether they can be relied on for data transfers to non- EEA entities subject to the GDPR. These recent developments are likely to require us to review and amend the legal mechanisms by which we make and / or receive personal data transfers to / in the United States~~ . As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the standard contractual clauses cannot be used, and / or start taking enforcement action, we could suffer additional costs, complaints and / or regulatory investigations or fines, and / or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results. Relatedly, following the United Kingdom' s withdrawal from the EEA and the EU ~~,~~ and the expiration of the transition period, from January 1, 2021, companies have to comply with both the GDPR and the **UK** GDPR ~~as incorporated into United Kingdom national law~~ , the latter regime having the ability to separately fine up to the greater of £ 17. 5 million or 4 % of global ~~turnover~~ **revenue** . ~~The relationship between~~ **If and as we continue to expand into** ~~the~~ **other** ~~United Kingdom~~ **foreign countries** and ~~the EU in relation~~ **jurisdictions, we may be subject** to **additional** ~~certain aspects of data protection law~~ **laws** ~~remains unclear,~~ and ~~it is unclear~~ **regulations that may affect** how **we conduct business** ~~United Kingdom data protection laws and regulations will develop in the medium to longer term. On June 28, 2021, the European Commission adopted an adequacy decision in favor of the United Kingdom, enabling data transfers from EU member states to the United Kingdom without additional safeguards. However, the United Kingdom adequacy decision will automatically expire in June 2025 unless the European Commission renews or extends that decision and remains under review by the Commission during this period~~ . Although we work to comply with applicable laws, regulations and standards, our contractual obligations and other legal obligations, these requirements are evolving and may be modified, interpreted and applied in an inconsistent manner from one jurisdiction to another, and may conflict with one another or other legal obligations with which we must comply. Any failure or perceived failure by us or our employees, representatives, contractors, consultants, collaborators ~~,~~ or other third parties to comply with such requirements or adequately address privacy and security concerns, even if unfounded, could result in additional cost and liability to us, damage our reputation, and adversely affect our business and results of operations. Acquisitions or joint ventures could disrupt our business, cause dilution to our stockholders and otherwise harm our business. We may acquire other businesses, products or technologies as well as pursue strategic alliances, joint ventures, technology licenses or investments in complementary businesses. We have limited experience in completing such transactions. Any of these transactions could be material to our financial condition and operating results and expose us to many risks, including: • disruption in our relationships with future customers or with current or future distributors or suppliers as a result of such a transaction; • unanticipated liabilities related to acquired companies; • difficulties integrating acquired personnel, technologies and operations into our existing business; • diversion of management time and focus from operating our business to acquisition integration challenges; • increases in our expenses and reductions in our cash available for operations and other uses; • possible write- offs or impairment charges relating to acquired businesses; and • inability to develop a sales force for any additional product candidates. Foreign acquisitions involve unique risks in addition to those mentioned above, including those related to integration of operations across different cultures and languages, currency risks and the particular economic, political and regulatory risks associated with specific countries. Also, the anticipated benefit of any acquisition may not materialize. Future acquisitions or dispositions could result in potentially dilutive issuances of our equity securities, the incurrence of **additional** debt, contingent liabilities or amortization expenses or write- offs of goodwill, any of which could harm our financial condition. We cannot predict the number, timing or size of future joint ventures or acquisitions, or the effect that any such transactions might have on our operating results **. Healthcare legislative reform discourse and potential or enacted measures may have a material adverse impact on our business and results of operations and legislative or political discussions surrounding the desire for and implementation of pricing reforms may adversely impact our business. In the United States, federal and state legislatures, health agencies and third- party payors continue to focus on containing the cost of health care. Legislative and regulatory proposals, enactments to reform health care insurance programs and increasing pressure from social sources could significantly influence the manner in which our products, if approved, are prescribed and purchased. For example, provisions of the ACA have resulted in changes in the way health care is paid for by both governmental and private insurers, including increased rebates owed by manufacturers under the Medicaid Drug Rebate Program, annual fees and taxes on manufacturers of certain branded prescription drugs, the requirement that manufacturers participate in a discount program for certain outpatient drugs under Medicare Part D and the expansion of the number of hospitals eligible for discounts under Section 340B of the PHSA. Additionally, the Inflation Reduction Act of 2022 includes several provisions such as drug pricing controls and Medicare redesign that are likely to impact our business to varying degrees, but its ultimate effect on our business and the healthcare industry in general is not yet known. We may face uncertainties as a result of efforts to repeal, substantially modify or invalidate some or all of the**

provisions of the ACA. There is no assurance that the ACA, as currently enacted or as amended in the future, will not adversely affect our business and financial results, and we cannot predict how future federal or state legislative or administrative changes relating to healthcare reform will affect our business. There is increasing public attention on the costs of prescription drugs and there have been, and are expected to continue to be, legislative proposals to address prescription drug pricing, which could have significant effects on our business. These actions and the uncertainty about the future of the ACA and healthcare laws may put downward pressure on pharmaceutical pricing and increase our regulatory burdens and operating costs . Risks Related to Our Common Stock The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock, and we could be subject to securities class action litigation as a result. Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies **, and more recently has been a result of disruptions in the global economy, including rising inflation and interest rates, declines in economic growth, international conflict, financial institution failures and continued uncertainty about the ongoing COVID- 19 pandemic** . As a result of this volatility, you may not be able to sell your shares of common stock at or above the price at which you purchase the shares. The market price for our common stock may be influenced by many factors, including: • the success of competitive products or technologies; • actual or anticipated changes in our growth rate relative to our competitors; • results of clinical trials of our product candidates or those of our competitors; • developments related to any future collaborations; • regulatory or legal developments in the United States and other countries; • adverse actions taken by regulatory agencies with respect to our preclinical studies or clinical trials, manufacturing or sales and marketing activities; • any adverse changes to our ~~relationship~~ **relationships** with third party contractors or manufacturers; • development of new product candidates that may address our markets and may make our existing product candidates less attractive; • changes in physician, hospital or healthcare provider practices that may make our product candidates less useful; • announcements by us, our collaborators or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments; • developments or disputes concerning patent applications, issued patents or other proprietary rights; • the recruitment or departure of key personnel; • the level of expenses related to any of our product candidates or product development programs; • failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public; • press reports or other negative publicity, whether or not true, about our business; • the results of our efforts to discover, develop, acquire or in- license additional product candidates or products; • actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts; • variations in our financial results or those of companies that are perceived to be similar to us; • changes in the structure of healthcare payment systems; • market conditions in the pharmaceutical and biotechnology sectors; • speculative trading in and short sales of our stock, as well as trading phenomena such as the " short squeeze "; • general economic, industry and market conditions; and • the other factors described in this" Risk Factors" section. Any of these factors may result in large and sudden changes in the volume and trading price of our common stock. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biopharmaceutical companies have experienced significant stock price volatility in recent years. 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. Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control or significantly influence all matters submitted to stockholders for approval. Based on the number of shares of common stock outstanding as of December 31, ~~2021~~ **2022** , our executive officers, directors and stockholders who own more than 5 % of our outstanding common stock and their respective affiliates hold, in the aggregate, shares representing approximately 70 % of our outstanding voting stock. As a result, if these stockholders were to choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. They may also have interests that differ from yours and may vote in a way with which you disagree, and which may be adverse to your interests. This concentration of ownership control may have the effect of delaying, deferring or preventing a change in control of our company, could deprive our stockholders of an opportunity to receive a premium for their common stock as part of a sale of our company and might ultimately affect the market price of our common stock. A significant portion of our total outstanding shares are eligible to be sold into the market, which could cause the market price of our common stock to drop significantly, even if our business is doing well. Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. Moreover, holders of an aggregate ~~of approximately~~ 18. ~~4~~ **3** million shares of our common stock as of December 31, ~~2021~~ **2022** have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders, including entities affiliated with Flagship Pioneering, until such shares can otherwise be sold without restriction under Rule 144 of the Securities Act or until the rights terminate pursuant to the terms of the investors' rights agreement between us and such holders. We have also registered and intend to continue to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates. We **may not maintain qualification for listing on Nasdaq, which may impair your ability to sell your shares. Our common stock is currently listed on the Nasdaq Global Select Market (" Nasdaq "). Nasdaq requires listed companies to meet certain listing criteria including total number of stockholders, corporate governance requirements, minimum closing bid price, total value of public float, and in some cases total stockholders' equity and market capitalization requirements. If we fail to satisfy the continued listing standards, including with respect to the**

maintenance of a minimum share price, or if Nasdaq, in its discretion, determines that a condition exists that makes further dealings of our Company on the exchange unwarranted, Nasdaq may issue a non- compliance letter or initiate delisting proceedings. Such a delisting would likely have a negative effect on the price of our common stock and would impair our stockholders' ability to sell or purchase our common stock. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the Nasdaq minimum bid price requirement or prevent future non- compliance with Nasdaq' s listing requirements. If for any reason our common stock does not maintain eligibility for listing on Nasdaq, we may list our common stock elsewhere, such as one of the OTC markets, which are generally considered less liquid and more volatile than a national securities exchange, and could mean that certain institutional investors could no longer hold or purchase our stock, and as a result, a purchaser of our common stock may find it more difficult to dispose of, or to obtain accurate quotations as to the price of their shares. This could materially and adversely affect the liquidity of our common stock. We have broad discretion in the use of our cash reserves and may not use them effectively. Our management has broad discretion to use our cash reserves and could use our cash reserves in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline ~~,~~ and delay the development of our product candidates. Pending their use, we may invest our cash reserves in a manner that does not produce income or that loses value. We are an" emerging growth company" and a" smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors. We are an" emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012, (the " JOBS Act ") and may remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of the initial public offering of our common stock, or December 31, 2023, (b) in which we have total annual gross revenue of at least $ 1. ~~07~~ **235** billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our outstanding common stock that are held by non- affiliates exceeds $ 700 million as of the prior June 30, and (2) the date on which we have issued more than $ 1. 0 billion in non- convertible debt during the prior three year period. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include: • being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced" Management' s Discussion and Analysis of Financial Condition and Results of Operations" disclosure; • not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting; • not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor' s report providing additional information about the audit and the financial statements; • reduced disclosure obligations regarding executive compensation; and • exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have elected to take advantage of this extended transition period. We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that our voting and non- voting common shares held by non- affiliates is more than $ 250 million measured on the last business day of our second fiscal quarter, and our annual revenues are more than $ 100 million during the most recently completed fiscal year and our voting and non- voting common shares held by non- affiliates is more than $ 700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies are able to provide simplified executive compensation disclosure, are exempt from the auditor attestation requirements of Section 404 of the Sarbanes- Oxley Act of 2002 (" Section 404") and have certain other reduced disclosure obligations, including, among other things, being required to provide only two years of audited financial statements and not being required to provide selected financial data, supplemental financial information or risk factors. We have elected to take advantage of certain of the reduced reporting obligations, and may in the future take advantage of these or others. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be reduced or more volatile. Provisions in our restated certificate of incorporation and amended and restated bylaws could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management. Provisions in our restated certificate of incorporation and our amended and restated bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, such provisions include those establishing: • a classified board of directors with three- year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors; • no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates; • the exclusive right of our board of directors to elect a director to fill a vacancy created

by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from filling vacancies on our board of directors; • the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquirer; • the ability of our board of directors to alter our bylaws without obtaining stockholder approval; • the required approval of the holders of at least two- thirds of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our restated certificate of incorporation regarding the election and removal of directors; • a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders; • the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and • advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer' s own slate of directors or otherwise attempting to obtain control of us. Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware ~~,~~ which prohibits a person who owns in excess of 15 % of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 % of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Our restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders **,** and our bylaws designate the federal district courts of the United States as the exclusive forum for actions arising under the Securities Act, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees. Our restated certificate of incorporation specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of fiduciary duty owed by any director, officer, employee or stockholder to us or our stockholders, any action asserting a claim arising pursuant to any provision of the General Corporation Law of the State of Delaware or any action asserting a claim governed by the internal affairs doctrine. In addition, our bylaws provide that the federal district courts of the United States are the exclusive forum for any complaint raising a cause of action arising under the Securities Act. We believe these provisions benefit us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes and in the application of the Securities Act by federal judges, as applicable, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi- forum litigation. The provision may limit a stockholder' s ability to bring a claim in a judicial forum that it finds favorable for disputes, and may have the effect of discouraging lawsuits, including those against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation and bylaws has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our restated certificate of incorporation or bylaws to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our restated certificate of incorporation or bylaws 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 results of operations and financial condition. Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain. We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the operation and expansion of our business. Therefore, you should not rely on an investment in our common stock as a source for any future dividend income. Our board of directors has significant discretion as to whether to distribute dividends. Even if our board of directors decides to declare and pay dividends, the timing, amount and form of future dividends, if any, will depend on, among other things, our future results of operations and cash flow, our capital requirements and surplus, our financial condition, contractual restrictions and other factors deemed relevant by our board of directors. Accordingly, the return on your investment in our common stock will likely depend entirely on any future capital appreciation, if any, of our common stock. There is no guarantee that our common stock will appreciate in value or even maintain the price at which you purchased our common stock. Our ability to use net operating losses and research and development tax credits to offset future taxable income or tax liabilities may be subject to certain limitations. As of December 31, ~~2021~~ **2022 , our fiscal year end** , we had approximately $ ~~189~~ **240** . ~~7~~ **3** million and $ ~~187~~ **241** . ~~1~~ **3** million of federal and state net operating losses (" NOLs"), respectively. The federal NOLs include $ 49. 9 million which expire at various dates through 2036, and $ ~~139~~ **190** . ~~7~~ **4** million which carry forward indefinitely. Our ability to use such federal NOLs to offset taxable income is limited to 80 % of taxable income with respect to taxable years beginning after December 31, 2020. Our state NOLs expire at various dates through ~~2041~~ **2042** . As of December 31, ~~2021~~ **2022** , we had federal and state research and development tax credits of $ ~~7~~ **9** . ~~2~~ **6** million and $ ~~3~~ **4** . ~~3~~ **6** million, respectively, which expire at various dates through 2041. A portion of these NOLs and the tax credit carryforwards could expire unused and be unavailable to offset future taxable income or income tax liabilities, respectively. In addition, in general, under Sections 382 and 383 of the **U. S.** Internal Revenue Code of 1986, as amended (the" Code"), a corporation that undergoes an" ownership change" is subject to limitations on its ability to utilize its pre- change NOLs or tax credits to offset future taxable income or tax liabilities. For these purposes, an ownership change generally occurs where the aggregate stock ownership of one or more stockholders or groups of stockholders who owns at least 5 % of a corporation' s stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a specified testing period. Our existing NOLs or tax credits may be subject to limitations arising from previous ownership changes. In addition, future changes in our stock ownership, many of which are outside of our control, could

result in an ownership change under Sections 382 and 383 of the Code. Our state NOLs or tax credits may also be limited or impaired under state law. Our ability to utilize our NOLs or tax credits is also conditioned upon our attaining profitability and generating federal and state taxable income and income tax liabilities. We have incurred significant net losses since our inception and, therefore, we do not know whether or when we will generate the federal or state taxable income or income tax liabilities necessary to utilize our NOLs or tax credits. Accordingly, we may not be able to utilize a material portion of our NOLs or tax credits. In addition, we may be required to pay federal income taxes due to the 80 % limitation on utilization of certain federal NOLs to offset taxable income, even if we have federal NOLs that are otherwise available for use. General Risk Factors We have incurred and expect to continue to incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices. As a public company, we have incurred and expect to continue to incur significant legal, accounting and other expenses that we did not incur as a private company. These expenses will be even greater after we are no longer an emerging growth company and / or a smaller reporting company ~~,~~ **.** The Sarbanes- Oxley Act of 2002, the Dodd- Frank Wall Street Reform and Consumer Protection Act, the listing requirements of ~~The~~ Nasdaq ~~Global Select Market~~ and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and made some activities more time consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to maintain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors. We cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. Pursuant to Section 404 of the Sarbanes- Oxley Act of 2002, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. **The identification of any** ~~If we identify one or more~~ material ~~weaknesses~~ -- **weakness , it** ~~,~~ could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements. Our failure to maintain effective control over financial reporting and disclosure controls and procedures could result in errors in our financial statements, our failure to meet our reporting obligations, reduce investor confidence ~~,~~ and adversely impact our stock price. As a public company, we are required to maintain effective disclosure controls and procedures and internal control over financial reporting, and to report any material weaknesses in such internal controls. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting ~~,~~ such that there is a reasonable possibility that a material misstatement of the annual or interim financial statements will not be prevented or detected on a timely basis **. As previously disclosed, we have identified three material weaknesses to date** . In October 2021, we identified a material weakness relating to an insufficient process for confirming final approvals for the release of reviewed and approved documentation ~~,~~ prior to filing such documentation with the SEC. **In** ~~This material weakness did not result in any financial statement modifications, and there were no changes to our previously disclosed financial results. Additionally, in~~ connection with the preparation of our financial statements in ~~this~~ **our** Annual Report on Form 10- K for the fiscal year ended December 31, 2021, **which we filed with the SEC on March 24, 2022,** we identified a ~~different~~ material weakness relating to the review of certain financial transactions and the preparation and review of account reconciliations ~~,~~ which ~~was~~ **were** not performed using a sufficient level of precision and accuracy. ~~No material financial statement misstatements~~ **In the third quarter of 2022, we identified instances of non-compliance with provisions of the Prior Loan Agreement which resulted in events of default that** were **not** identified ~~in relation to this~~ **or prevented on a timely basis. We, therefore, concluded that there was a** material weakness in our internal ~~control~~ **controls** over financial reporting **, as our controls over debt covenant monitoring and compliance were not operating with sufficient precision and timeliness. These material weaknesses did not result in any financial statement modifications, and there were no changes to our previously disclosed financial results** . The remediation efforts that we take to address a material weakness need to be completed and operating effectively for a sufficient period of time before we are able to deem such material weakness fully remediated. See Part II, Item 9A " Controls and Procedures " for additional information about these material weaknesses and our remediation efforts. If we identify other material weaknesses or identify deficiencies that individually or together constitute significant deficiencies or material weaknesses, or if the additional controls and processes that we implement to remediate any identified material weaknesses prove to be insufficient, our ability to accurately record, process ~~,~~ and report financial information and, consequently, our ability to prepare financial statements within required time periods ~~,~~ could be adversely affected and we may be unable to assure that information required to be disclosed by us in reports that we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. Furthermore,

disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision- making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected. The discovery of additional deficiencies could result in violations of applicable securities laws, stock exchange listing requirements ~~,~~ and agreements to which we are subject, subject us to litigation and investigations, negatively affect investor confidence in our financial statements ~~,~~ and adversely impact our stock price and ability to hinder our ability to access capital markets. If securities or industry analysts do not publish research or reports about our business, or if they issue an adverse or misleading opinion regarding our business, our stock price and trading volume could decline. The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies or clinical trials and / or operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline. **Unfavorable global economic or political conditions could adversely affect our business, financial condition or results of operations. Various macroeconomic factors could adversely affect our business and financial condition, including, for example, changes in inflation, interest rates and foreign currency exchange rates, crises involving banking and financial institutions specifically, and overall economic conditions and uncertainties generally. For instance, if inflation and the resulting increase in interest rates, such as that recently observed in the U. S. and elsewhere, or other factors were to significantly increase costs generally, it may increase our product candidate development and other operating costs, having an adverse effect on our cash flows and results of operations. Additionally, our results of operations could be adversely affected by general conditions in the global financial markets. For example, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the global financial crisis, could result in a variety of risks to our business, including our ability to raise additional capital when needed on acceptable terms, if at all. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption, or cause our customers, if any, to delay making payments for our services. In addition, military conflict such as that ongoing between Russia and Ukraine could disrupt or otherwise adversely impact our operations and those of third parties upon which we rely. Related sanctions, export controls or other actions have and may in the future be initiated by nations including the U. S., the EU or Russia (for example, potential cyberattacks, disruption of energy flows, etc.), which could adversely affect our business and / or our supply chain, our CROs, our CMOs and other third parties with which we conduct business. 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. The increasing focus on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results. There has been increasing public focus by investors, environmental activists, the media and governmental and nongovernmental organizations on a variety of environmental, social and other sustainability matters. We may experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. In addition, we may experience increased costs in order to execute upon our sustainability goals and measure achievement of those goals, which could have an adverse impact on our business and financial condition. In addition, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be adversely impacted.**