Risk Factors Comparison 2024-03-05 to 2023-03-14 Form: 10-K

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Our business is subject to numerous risks. You should carefully consider the following risks and all other information contained in this Annual Report, as well as general economic and business risks, together with any other documents we file with the SEC. If any of the following events actually occur or risks actually materialize, it could have a material adverse effect on our business, operating results and financial condition and cause the trading price of our common stock to decline. Risks Related to Limited Operating History, Financial Position and Capital Requirements We have a limited operating history, have incurred net losses since our inception, and anticipate that we will continue to incur significant losses for the foreseeable future. We may never generate any revenue or become profitable or, if we achieve profitability, may not be able to sustain it. We are a clinical- stage biopharmaceutical company with a limited operating history that may make it difficult to evaluate the success of our business to date and to assess our future viability. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing and optimizing our technology platform, identifying potential product candidates, undertaking research, preclinical studies and clinical trials for our product candidates, establishing and enhancing our intellectual property portfolio, and providing general and administrative support for these operations. IO102- IO103 is in ~~early~~ clinical development and IO112 is in preclinical development, and none of our product candidates have been approved for commercial sale. We have never generated any revenue from product sales and have incurred net losses each year since we commenced operations. For the years ended December 31, **2023 and** 2022 ~~and 2021~~, our net losses were $ **86. 1 million and $** 71. 5 ~~million and $ 67. 9~~ million, respectively. We expect that it will be several years, if ever, before we have a product candidate ready for regulatory approval and commercialization. We expect to incur increasing levels of operating losses over the next several years and for the foreseeable future as we advance our product candidates through clinical development. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. To become and remain profitable, we must develop and eventually commercialize a product or products with significant market potential. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products for which we may obtain marketing approval and satisfying any post- marketing requirements. We may never succeed in these activities and, even if we succeed in commercializing one or more of our product candidates, we may never generate revenue that is significant or large enough to achieve profitability. In addition, as a young business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis and we will continue to incur substantial research and development and other expenditures to develop and market additional product candidates. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment. We will need to obtain substantial additional funding to complete the development and commercialization of our product candidates. If we are unable to raise this capital when needed, we may be forced to delay, reduce or eliminate our product development programs or other operations. Since our inception, we have used substantial amounts of cash to fund our operations and expect our expenses to increase substantially during the next few years. The development of biopharmaceutical product candidates, especially immune-oncology product candidates, is capital intensive. As our product candidates enter and advance through preclinical studies and clinical trials, we will need substantial additional funds to expand our clinical, regulatory, quality and manufacturing capabilities. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to marketing, sales, manufacturing and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company. As of December 31, ~~2022~~ **2023**, we had $ ~~142~~ **143**. ~~6~~ **2** million in cash and cash equivalents. Based upon our current operating plan, we estimate that our existing cash and cash equivalents will be sufficient to fund our operating expenses and capital expenditure requirements ~~through~~ **into** the ~~third~~ **fourth** quarter of ~~2024~~ **2025**. However, our existing cash and cash equivalents may not be sufficient to fund any of our product candidates through regulatory approval, and we ~~may~~ **will** need to raise substantial additional capital to complete the development and commercialization of our product candidates. We have based these estimates on assumptions that may prove to be incorrect or require adjustment as a result of business decisions, and we could utilize our available capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, some of which are outside of our control, including: • the initiation, design, progress, timing, costs and results of drug discovery, preclinical studies and clinical trials of our product candidates, and in particular the clinical trials for IO102- IO103; • the number and characteristics of product candidates that we pursue; • the number of clinical trials needed for regulatory approvals from the FDA, the European Commission (based on recommendation from the EMA), and any other regulatory authority; • the length of our clinical trials, including, among other things, as a result of delays in enrollment, difficulties enrolling sufficient subjects or delays or difficulties in clinical trial site activations; • increased costs associated with conducting our clinical trials, including, among other things, clinical trial site activations and patient enrollment; • successfully ~~complete~~ **completing** ongoing pre- clinical studies and clinical trials; • the outcome, timing and costs of seeking regulatory approvals from the FDA, the European Commission, and any other regulatory authority; • the costs of manufacturing our product candidates, in particular for clinical trials in preparation for marketing approval and in preparation for commercialization; • the costs of any third- party products

used in our combination clinical trials that are not covered by such third party or other sources; • the costs associated with hiring additional personnel and consultants as our preclinical, manufacturing and clinical activities increase; • the receipt of marketing approval and revenue received from any commercial sales of any of our product candidates, if approved; • the cost of commercialization activities for any of our product candidates, if approved, including marketing, sales **, compliance** and distribution costs; • the emergence of competing therapies and other adverse market developments; • the ability to establish and maintain strategic collaboration, licensing or other arrangements and the financial terms of such agreements; • the extent to which we in- license or acquire other products and technologies; • the amount and timing of any payments we may be required to make pursuant to our current or future license agreements; • the costs involved in preparing, filing, prosecuting, maintaining, expanding, defending and enforcing patent claims, including litigation costs and the outcome of such litigation; • our need and ability to retain key management and hire scientific, technical, business, ~~and~~ medical **, and compliance** personnel; • our implementation of additional internal systems and infrastructure, including operational, financial **, compliance** and management information systems; • ~~or~~ **our** costs associated with expanding our facilities or building out our laboratory space; • the effects of the ~~recent~~ disruptions to and volatility in the credit and financial markets in the United States and worldwide from **public health emergencies** ~~the COVID- 19 pandemic~~ , and ~~the~~ **geopolitical** conflict ~~between Russia and~~ **(such as in** Ukraine **and the Middle East)** ; and • the costs of operating as a public company. We will require additional capital to achieve our business objectives. Additional funds may not be available on a timely basis, on favorable terms, or at all, and such funds, if raised, may not be sufficient to enable us to continue to implement our long- term business strategy. Further, our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide ~~resulting from the ongoing COVID- 19 pandemic~~ . If we are unable to raise sufficient additional capital, we could be forced to curtail our planned operations and the pursuit of our growth strategy. Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates. Until such time, if ever, as we can generate substantial product revenue, we expect to finance our operations through equity offerings, debt financings or other capital sources, including potentially grants, collaborations, licenses or other similar arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of holders of our common stock. Additional debt financing, if available, may involve agreements that include covenants further limiting or restricting our ability to take specific actions, such as further limitations on our ability to incur additional debt, make capital expenditures or declare dividends. If we raise funds through collaborations or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Risks Related to the Discovery, Development and Regulatory Approval of Our Product Candidates ~~Our development efforts are in the early stages.~~ All of our product candidates are in clinical development or in preclinical development. ~~if~~ **If** we are unable to advance our product candidates through clinical development, obtain regulatory approval and ultimately commercialize our product candidates, or experience significant delays in doing so, our business will be materially harmed. There is no assurance that clinical trials of IO102- IO103, or any other future clinical trials of our product candidates, will be successful or will generate positive clinical data and we may not receive marketing approval from the FDA, European Commission **(based on recommendation from the EMA)** , or other regulatory authorities for any of our product candidates. We have limited experience submitting INDs to the FDA ~~. IO112 is in initial clinical development, currently being studied in an investigator- initiated study~~ . There can be no assurance that the FDA will permit any of our future INDs, including any IND for IO112, to go into effect in a timely manner or at all. Without an IND for a product candidate, we will not be permitted to conduct clinical trials in the United States of such product candidate. Biopharmaceutical development is a difficult, long, time- consuming, expensive and uncertain process, and delay or failure can occur at any stage of any of our clinical trials. For example, we have experienced longer than expected lead times in clinical trial site activation and patient enrollment in our clinical trials. Failure to obtain regulatory approval for our product candidates will prevent us from commercializing and marketing our product candidates. The success in the development of our product candidates will depend on many factors, including: • timely and successful completion of preclinical studies; • sufficiency of our financial and other resources to complete the necessary preclinical studies and clinical trials; • obtaining and maintaining patent, trademark and trade secret protection and ~~regulator~~ **regulatory** exclusivity for our product candidates and otherwise protecting our rights in our intellectual property portfolio; • submission of INDs and CTAs for and receipt of allowance to proceed with our planned clinical trials or other future clinical trials; • initiating, enrolling, and successfully completing clinical trials, including investigator- initiated clinical trials over which we have limited control; • obtaining positive results from our preclinical studies and clinical trials that support a demonstration of efficacy, safety, and durability of effect for our product candidates; • receiving approvals for commercialization of our product candidates from applicable regulatory authorities; • the outcome, timing and cost of meeting regulatory requirements established by the FDA, European Commission (based on recommendation from the EMA), and other regulatory authorities; • establishing sales, marketing and distribution capabilities and successfully launching commercial sales of our products, if and when approved, whether alone or in collaboration with others; • maintaining a continued acceptable safety, tolerability and efficacy profile of any approved products; • setting acceptable prices for our product and obtaining coverage and adequate reimbursement from third- party payors; • acceptance of our products, if and when approved, by patients, the medical community and third- party payors; • manufacturing our product candidates at an acceptable cost; and • maintaining and growing an organization of scientists, medical and clinical professionals and business ~~people~~ **professionals** who can develop and commercialize our products and technology. Many of these factors are beyond our control,

including the time needed to adequately complete clinical testing, the regulatory submission process and potential threats to our intellectual property rights. It is possible that none of our product candidates will ever obtain regulatory approval, even if we expend substantial time and resources seeking such approval. If we do not achieve one or more of these factors in a timely manner or at all, or any other factors impacting the successful development of biopharmaceutical products, we could experience significant delays or an inability to successfully develop our product candidates, which would materially harm our business. The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate that we advance in clinical trials, including IO102- IO103, may not achieve favorable results in later clinical trials, if any, or receive marketing approval. The research and development of drugs and biological products is extremely risky. Only a small percentage of product candidates that enter the development process ever receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. The outcome of clinical testing is uncertain. We may face unforeseen challenges in our product candidate development strategy, and we can provide no assurances that we will ultimately be successful in our current and future clinical trials or that our product candidates will be able to receive regulatory approval. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later- stage clinical trials. For example, it is not uncommon for product candidates to exhibit unforeseen safety or efficacy issues when tested in humans despite promising results in preclinical animal models. In particular, while IO102- IO103 in combination with an anti- PD- 1 monoclonal antibody has been investigated in a Phase 1 / 2 trial in 30 metastatic melanoma patients at **Herlev** University Hospital of Copenhagen, we do not know how IO102- IO103 will perform in our ongoing Phase 3 clinical trial combining IO102- IO103 with an anti- PD- 1 monoclonal antibody in first line treatment of advanced melanoma patients, **nor do we know how candidates in** our ongoing Phase 2 basket trial, IOB- 022, ~~or~~ **our ongoing** ~~in future clinical trials, including the planned~~ Phase 2 basket trial, IOB- 032 **or in future clinical trials will perform** . Future results of preclinical and clinical testing of our product candidates are also less certain due to the novel and relatively untested nature of the approach of our T- win ~~technology~~ **®** platform. In general, clinical trial failure may result from a multitude of factors including flaws in study design, dose selection, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits. As such, failure in clinical trials can occur at any stage of testing. A number of companies in the biopharmaceutical industry, including immune- oncology companies, have suffered setbacks in the advancement of clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Our product candidates are based on novel technologies that target the highly immunosuppressive tumor microenvironment, which makes it difficult to predict the results, timing, and cost of product candidate development and likelihood of obtaining regulatory approval. We have concentrated our research and development efforts on product candidates using our T- win ~~technology~~ platform, and our future success depends on the successful development of this approach. Our product candidates target the tumor microenvironment which is highly immunosuppressive. We have not yet succeeded and may not succeed in demonstrating efficacy and safety for any product candidates based on our platform technologies in clinical trials or in obtaining marketing approval thereafter, and use of our platform technologies may not ever result in marketable products. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners or establishing our own commercial manufacturing capabilities, which may prevent us from completing our clinical trials or commercializing any products on a timely or profitable basis, if at all. In addition, the clinical trial requirements of the FDA, and other regulatory authorities and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be less predictable, more expensive and longer than for other, better known or extensively studied pharmaceutical or other product candidates. There is no assurance that the approaches offered by our products will gain broad acceptance among doctors or patients or that governmental agencies or third- party medical insurers will be willing to provide reimbursement coverage for proposed product candidates. Since our current product candidates and any future product candidates will represent novel approaches to treating various conditions, it may be difficult, in any event, to accurately estimate the potential revenues from these product candidates. Accordingly, we may spend significant capital trying to obtain approval for product candidates that have an uncertain commercial market. The market for any products that we successfully develop will also depend on the cost of the product. We do not yet have sufficient information to reliably estimate what it will cost to commercially manufacture our current product candidates, and the actual cost to manufacture these products could materially and adversely affect the commercial viability of these products. If we do not successfully develop and commercialize products based upon our approach or find suitable and economical sources for materials used in the production of our products, we will not become profitable, which would materially and adversely affect the value of our common stock. The ~~immuno-~~ oncology industry is also rapidly developing, and our competitors may introduce new technologies improving the immune response to cancer that render our technologies obsolete or less attractive. New technology could emerge at any point in the development cycle of our product candidates. We are investigating IO102- IO103 in clinical trials in melanoma and other solid tumors, and our third product candidate, IO112, targets an immune resistance pathway known as Arginase 1 which is highly expressed in solid cancer indications. If our product candidates do not show any functionality in the solid tumor microenvironment **,** our development plans, financial position, results of operations and prospects may be materially adversely affected. While we plan to develop product candidates for use in solid tumors, including IO102- IO103 and IO112, our product candidates may not show any functionality in the solid tumor microenvironment. The cellular environment in which solid tumor cells thrive is generally hostile to T cells due to factors such as the presence of immunosuppressive cells, humoral factors and limited access to nutrients. Our product candidates may not be able to access the solid tumor, and even if they do, they may not be able to exert anti- tumor effects in a hostile tumor microenvironment. In addition, the safety profile of our product candidates may differ in a solid tumor setting. As a result, our product candidates may not demonstrate efficacy in solid tumors. If we are unable to make our product

candidates function in solid tumors, our development plans, financial position, results of operations and prospects may be materially adversely affected. We have experienced, and may in the future experience delays, or difficulties in clinical trial site activations and the enrollment and / or retention of patients in clinical trials, which could delay or prevent our receipt of necessary regulatory approvals. Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients. Patient enrollment, which is an important factor in the timing of clinical trials, is affected by many factors, including clinical trial site activation, the size and nature of the patient population and competition for patients eligible for our clinical trials with competitors which may have ongoing clinical trials for product candidates that are under development to treat the same indications as one or more of our product candidates, or approved products for the conditions for which we are developing our product candidates. Trials may be subject to delays as a result of patient enrollment taking longer than anticipated or patient withdrawal. As a result of **public health emergencies** ~~the on- going COVID- 19 pandemic~~ and ~~continuing~~ resource constraints on CROs, ~~us,~~ prospective clinical trial sites and others, we **may** ~~are currently experiencing~~ **experience** longer than expected lead times in clinical trial site activation and patient enrollment in our clinical trials. Furthermore, enrollment for our **clinical** ~~Phase 3 potentially registrational trial~~ **trials** may take longer than anticipated due to other monotherapies and combination therapies being investigated in the first- line setting at this time. 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 to adequately power our studies in order to draw meaningful conclusions from them or as may be required by the FDA, **European Commission (based on recommendation from the** EMA **)** , or comparable foreign regulatory authorities. We cannot predict how successful we will be at enrolling subjects in future clinical trials. Subject enrollment is affected by other factors including: • the pace of clinical trial site activation; • the severity and difficulty of diagnosing the disease under investigation; • the eligibility and exclusion criteria for the trial in question; • the size of the patient population and process for identifying patients; • our ability to recruit clinical trial investigators with the appropriate competencies and experience; • the design of the trial protocol; • the perceived risks and benefits of the product candidate in the trial, including relating to cell therapy approaches; • the availability of competing commercially available therapies and other competing therapeutic candidates' clinical trials for the disease or condition under investigation, including for melanoma and other cancers in a first- line setting; • the willingness of patients to be enrolled in our clinical trials; • the efforts to facilitate timely enrollment in clinical trials; • ~~potential disruptions caused by the COVID- 19 pandemic, including difficulties in initiating clinical sites, enrolling and retaining participants, diversion of healthcare resources away from clinical trials, travel or quarantine policies that may be implemented, and other factors; •~~ the patient referral practices of physicians; • the ability to monitor patients adequately during and after treatment; and • the proximity and availability of clinical trial sites for prospective patients **. The FDA may also modify or enhance clinical trial requirements, which may affect enrollment and retention of patients. In August 2023, the FDA published a guidance document, " Informed Consent, Guidance for IRBs, Clinical Investigators, and Sponsors, " which supersedes past guidance and finalizes draft guidance on informed consent. The FDA' s new guidance presents evolving requirements for informed consent which may affect recruitment and retention of patients in clinical trials. Effects on recruitment and retention of patients may hinder or delay a clinical trial, which may increase costs and delay clinical programs** . Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing. Furthermore, we expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and we will have limited influence over their performance. Interim " top- line " and preliminary results 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 publish interim top- line or preliminary results from our clinical trials. Interim results from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top- line results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data 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, and should be viewed with caution until the final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly. The regulatory approval processes of the FDA, European Commission (based on recommendation from the EMA), and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. ~~if~~ **If** we are not able to obtain required regulatory approval for our product candidates, our business will be substantially harmed. The time required to obtain approval or other marketing authorizations by the FDA, European Commission (based on recommendation from the EMA), and comparable foreign regulatory authorities is unpredictable, and it typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, and the type and amount of clinical data necessary to gain approval may change during the course of a product candidate' s clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate, and it is possible that we may never obtain regulatory approval for any product candidates we may seek to develop in the future. Neither we nor any current or future collaborator is permitted to market any drug product candidates in the United States until we receive regulatory approval of a BLA from the FDA, and we cannot market it in the EU until we receive a MAA from the European Commission (based on recommendation from the EMA), or in the UK until we receive regulatory approval from the Medicines and Healthcare Products Regulatory Agency (MHRA) or other required regulatory approval in other countries. To date, we have had only limited discussions with the FDA and EMA regarding clinical development

programs or regulatory approval for any product candidate within the United States and EU, respectively. In addition, we have had no discussions with other comparable foreign authorities regarding clinical development programs or regulatory approval for any product candidate outside of those jurisdictions. Prior to obtaining approval to commercialize any drug product candidate in the United States or abroad, we must demonstrate with evidence from well- controlled clinical trials, and to the satisfaction of the FDA, European Commission (based on recommendation from the EMA), or other foreign regulatory authorities, that such product candidates are safe and effective for their intended uses. Results from preclinical studies and clinical trials can be interpreted in different ways. Even if we believe the preclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA, the European Commission (based on recommendations from the EMA), and other comparable foreign regulatory authorities. The FDA or European Commission (based on recommendations from the EMA) may also require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or after approval, or it may object to elements of our clinical development programs. Our product candidates could fail to receive regulatory approval for many reasons, including the following: • the FDA, EMA, or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials, or with our interpretation of clinical trial results; • we may be unable to demonstrate to the satisfaction of the FDA, EMA, or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication; • the results of clinical trials may not meet the level of statistical significance required by the FDA, European Commission (based on recommendation from the EMA), or comparable foreign regulatory authorities for approval; • we may be unable to demonstrate that a product candidate' s clinical and other benefits outweigh its safety risks; • the FDA, European Commission (based on recommendation from the EMA), or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third- party manufacturers with which we contract for clinical and commercial supplies; and • the approval policies or regulations of the FDA, European Commission, EMA, or comparable foreign authorities may significantly change in a manner rendering our clinical data insufficient for approval. Of the large number of products in development, only a small percentage successfully complete ~~the~~ FDA, European Commission (based on recommendation from the EMA), or foreign regulatory approval processes and are commercialized. The lengthy approval and marketing authorization process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval and marketing authorization to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects. In the EU, the EMA' s Committee for Advanced Therapies (CAT) is responsible for assessing the quality, safety, and efficacy of advanced therapy medicinal products (ATMPs). ATMPs include gene therapy medicines, somatic- cell therapy medicines and tissue- engineered medicines. The role of the CAT is to prepare a draft opinion on an application for marketing authorization for a gene therapy medicinal candidate that is submitted to EMA' s Committee for Medicinal Products for Human Use (CHMP) for final adoption. In the EU, the development and evaluation of ATMPs follow relevant EU guidelines. European Commission or EMA may issue new guidelines concerning the development and marketing authorization for ATMPs and require that we comply with these new guidelines. We have invested a significant portion of our time and financial resources in the development of our clinical and preclinical product candidates. Our business is dependent on our ability to successfully complete preclinical and clinical development of, obtain regulatory approval for, and, if approved, successfully commercialize IO102- IO103, IO112 and any future product candidates in a timely manner. Even if we eventually complete clinical testing and receive approval of a BLA or other comparable foreign marketing application for IO102- IO103, IO112 or any future product candidates, the FDA, European Commission (based on recommendation from the EMA) or other comparable foreign regulatory authorities may grant approval or other marketing authorization contingent on the performance of costly additional clinical trials, including post- marketing clinical trials. The FDA, European Commission (based on recommendations from the EMA) or other comparable foreign regulatory authorities may also approve or authorize for marketing a product candidate for a more limited indication or patient population than we originally request, and the FDA, European Commission (based on recommendations from the EMA) or other comparable foreign regulatory authorities may not approve or authorize the labeling that we believe is necessary or desirable for the successful commercialization of a product candidate. Any delay in obtaining, or inability to obtain, applicable regulatory approval or other marketing authorization would delay or prevent commercialization of that product candidate and would materially adversely impact our business and prospects. In addition, the FDA, European Commission (based on recommendations from the EMA), or other comparable foreign regulatory authorities and regulatory review committees described above may change their policies, issue additional regulations or revise existing regulations, or take other actions, which may prevent or delay approval of our future products under development on a timely basis. Such policy or regulatory changes could impose additional requirements upon us that could delay our ability to obtain approvals, increase the costs of compliance or restrict our ability to maintain any marketing authorizations we may have obtained. Our preclinical studies and clinical trials may fail to demonstrate the safety and efficacy of our product candidates, or serious adverse or unacceptable side effects may be identified during the development of our product candidates, which could prevent, delay or limit the scope of regulatory approval of our product candidates, limit their commercialization, increase our costs or necessitate the abandonment or limitation of the development of some of our product candidates. To obtain the requisite regulatory approvals for the commercial sale of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical testing and clinical trials that our product candidates are safe and effective for use in each target indication. These trials are expensive and time consuming, and their outcomes are inherently uncertain. Failures can occur at any time during the development process. Preclinical studies and clinical trials often fail to demonstrate safety or efficacy of the product candidate studied for the target indication, and most product candidates that begin clinical trials are never approved. We may fail to demonstrate with evidence from adequate and well- controlled trials, and to the satisfaction of the FDA, European Commission (based on recommendation from the EMA), or comparable foreign regulatory authorities, that our product candidates are safe and effective for their intended uses. Possible adverse reactions and adverse side effects that could occur with immuno- oncology treatments can be

severe. For example, we have reported to FDA some serious and unexpected suspected adverse reactions from the ~~IO102-~~ **IOB** - ~~112~~ **012** trial to FDA, which involved pulmonary tuberculosis, enterocolitis, hypovolemic shock, and diabetic ketoacidosis. **As part of routine safety monitoring and pharmacovigilance evaluation on ongoing and planned trials, we continue to review data and perform additional assessments,** ~~Depending~~ **depending** on an evaluation of the available data, we may decide or be required to perform additional preclinical studies or to halt or delay further clinical development of our product candidates or to limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe, or more acceptable from a risk- benefit perspective, which may limit the commercial expectations for the product candidate, if approved. Our clinical trials could also be suspended or terminated and the FDA, **European Commission (based on recommendation from the** EMA **)** , or comparable foreign regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Even if this does not occur, reports of serious reactions could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if we elect, or are required, to not initiate, delay, suspend or terminate any future clinical trial of any of our product candidates, the commercial prospects of such product candidates may be harmed and our ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm our ability to develop other product candidates, and may harm our business, financial condition and prospects significantly. If our product candidates are associated with side effects in clinical trials or have characteristics that are unexpected, we may need to abandon their development or limit development to more narrow uses in which the side effects or other characteristics are less prevalent, less severe or more acceptable from a risk- benefit perspective. The FDA, **European Commission (based on recommendation from the** EMA **)** , an institutional review board (IRB) or ethics committee (EC), which are local institutional boards or committees, as applicable, that review, approve and oversee basic and clinical research conducted as the institution participating in the clinical trial, or comparable foreign regulatory authorities, may also require that we suspend, discontinue, or limit our clinical trials based on safety information, or that we conduct additional animal or human studies regarding the safety and efficacy of our product candidates which we have not planned or anticipated. Such findings could further result in regulatory authorities failing to provide marketing authorization for our product candidates or limiting the scope of the approved indication, if approved. Many product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented further development of the product candidate. As an organization, we have never conducted pivotal clinical trials, and we may be unable to do so for any product candidates we may develop. We will need to successfully complete clinical trials meeting requirements for approval of the FDA or comparable foreign regulatory authorities, known as pivotal trials, to market IO102- IO103, IO112, **IO170** or any future product candidate. ~~Carrying out~~ **Conducting and successfully completing** pivotal clinical trials is a complicated process. ~~As an~~ **Consequently, we may be unable to successfully and efficiently execute and complete necessary** ~~organization, we have not previously conducted any later stage or pivotal~~ clinical trials **in a way that leads to BLA submission and approval of IO102- IO103, IO112, IO170 or future product candidates** . In order to do so, we will need to expand our clinical development and regulatory capabilities, and we may be unable to recruit and train qualified personnel. We also expect to continue to rely on third parties to conduct our pivotal clinical trials. ~~Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to BLA submission and approval of IO102- IO103, IO112, or future product candidates.~~ We **also** may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates. Some data for product candidates comes from clinical trials conducted outside the United States, EU and the UK, and the FDA, **European Commission (based on recommendation from the** EMA **)** , or comparable foreign regulatory authorities may not accept data from such trials. Although we believe that the patient population in the Phase 1 / 2 trial with IO102- IO103 in combination with an anti- PD- 1 monoclonal antibody in 30 metastatic melanoma patients is representative of the population for which we intend to label our IO102- 103 product candidate in the United States, the trial was conducted in Europe, our ongoing IOB- 013 / KN- D18 and IOB- 022 trials include sites outside of the United States, and we may conduct additional trials in the future outside of the United States, Europe and the ~~UK~~ **United Kingdom** . The acceptance of data from clinical trials conducted outside the United States or another jurisdiction by the FDA may be subject to certain conditions or may not be accepted at all. Similarly, the **European Commission (based on recommendation from the** EMA **)** , and other equivalent foreign regulatory authorities may not accept data from trials conducted outside their jurisdiction. In cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (1) the data are applicable to the U. S. population and U. S. medical practice; and (2) the trials were performed by clinical investigators of recognized competence and pursuant to good clinical practice (GCP) regulations; and (3) 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 general, the patient population for any clinical trials conducted outside the United States must be representative of the population for whom we intend to label the product candidate in the United States. Additionally, the FDA' s clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. Many foreign regulatory authorities have similar approval requirements for clinical trials. In addition, such 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, **European Commission (based on recommendation from the** EMA **)** , or any comparable foreign regulatory authority will accept data from trials conducted outside of the applicable jurisdiction. If the FDA, **European Commission (based on recommendation from the** EMA **)** , 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 product candidates that we may develop not receiving approval for commercialization in the applicable

jurisdiction. Breakthrough therapy designation by the FDA for any product candidate may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that the product candidate will receive marketing approval **.** IO102- IO103 combined with an anti- PD- 1 monoclonal antibody in first line metastatic melanoma patients has been granted BTD from the FDA. We may also, in the future, apply for BTD, or the equivalent thereof in foreign jurisdictions (where available), for our product candidates or programs. A breakthrough therapy is defined as a product candidate that is intended, alone or in combination with one or more other drugs, to treat a serious or life- threatening disease or condition, and preliminary clinical evidence indicates that the 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. For product candidates that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Product candidates designated as breakthrough therapies by the FDA are also eligible for priority review if supported by clinical data at the time of the submission of the BLA. BTD is within the discretion of the FDA. Accordingly, even if we believe that one of our product candidates meets the criteria for BTD, 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, including the breakthrough therapy designation of IO102- IO103 combined with an anti- PD- 1 monoclonal antibody in first line metastatic melanoma patients, may not result in a faster development process, review or approval compared to product candidates considered for approval under conventional FDA procedures and it would not assure ultimate approval by the FDA. In addition, even after a product candidate qualifies as a breakthrough therapy, the FDA may later decide that the product candidate no longer meets the conditions for qualification or it may decide that the time period for FDA review or approval will not be shortened. We may submit a BLA for our product candidates under the Accelerated Approval Pathway. If we are unable to obtain licensure of our biological candidates through the Accelerated Approval ~~Program~~ **Pathway** in the United States, we may be required to conduct additional nonclinical and clinical studies and trials beyond those that we currently contemplate, which could increase the expense of obtaining, reduce the likelihood of obtaining and / or delay the timing of obtaining, necessary marketing approval. Even if we receive licensure from the FDA through the Accelerated Approval Program, if any required confirmatory post- marketing trial does not verify clinical benefit, or if we do not comply with rigorous post- marketing requirements, the FDA may seek to withdraw the approval. We may seek approval under the Accelerated Approval ~~pathway~~ **Pathway** for our IO102- IO103, IO112 or any other product candidates. For any approval to market a product, we must provide the FDA and foreign regulatory authorities with clinical data that adequately demonstrate the safety, efficacy, purity and potency of the product for the indication applied for in the BLA, or other respective regulatory filings. The Accelerated Approval ~~Program~~ **Pathway** is one of several approaches used by the FDA to make prescription drugs and biologics more rapidly available for the treatment of serious or life- threatening diseases. Section 506 (c) of the FDCA provides that the FDA may grant accelerated approval to " a product for a serious or life- threatening condition upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. " Approval through the Accelerated Approval ~~Program~~ **Pathway** is typically subject, however, to the requirement that the applicant conduct additional post- marketing clinical trials to verify and describe the product' s clinical benefit. Typically, clinical benefit is verified when post- marketing clinical trials show that the product provides a clinically meaningful positive therapeutic effect, that is, an effect on how a patient feels, functions, or survives. If such confirmatory post- marketing trial fails to confirm the product' s clinical profile or risks and benefits, the FDA may withdraw its approval of the product. The FDA has broad discretion with regard to approval through the Accelerated Approval ~~Program~~ **Pathway** , and even if we believe that the Accelerated Approval ~~Program~~ **Pathway** is appropriate for our product candidates, we cannot assure you that the FDA will ultimately agree. Furthermore, even if we do obtain approval through the Accelerated Approval ~~Program~~ **Pathway** , we may not experience a faster development process, review or approval compared to conventional FDA procedures. Even if we receive approval for one or more of our product candidates through the Accelerated Approval ~~Program~~ **Pathway** , we will be subject to rigorous post- marketing requirements, possibly including the completion of one or more confirmatory post- marketing trials as the FDA may require, to verify the clinical benefit of the product, and submission to the FDA of all promotional materials prior to their dissemination. The FDA could seek to withdraw the approval for multiple reasons, including if we fail to conduct any required confirmatory post- marketing trial with due diligence, our confirmatory post- marketing trial does not confirm the predicted clinical benefit, other evidence shows that the product is not safe, effective, pure or potent under the conditions of use, or we disseminate promotional materials that are found by the FDA to be false and misleading. Moreover, Congress has recently enacted changes to the Accelerated Approval ~~Program~~ **Pathway** that could impact our ability to obtain Accelerated Approval, or increase the burdens associated with post- marketing requirements in the event we do obtain Accelerated Approval. In particular, the FDA must specify certain conditions for required post- approval studies for products that receive Accelerated Approval, which may include enrollment targets and milestones, including the target date for study completion, by the time the biologic is licensed. FDA may also require post- approval studies to be underway at the time of Accelerated Approval or within a specified time period following Accelerated Approval for such biologics. Any delay in obtaining, or inability to obtain, approval or licensure through the Accelerated Approval ~~Program~~ **Pathway** , or any issues in maintaining approval or licensure granted under the Accelerated Approval ~~Program~~ **Pathway** , would delay or prevent commercialization of our products, and could materially adversely affect our business, financial condition, results of operations, cash flows and prospects. Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to post- market study

requirements, marketing and labeling restrictions, and even recall or market withdrawal if unanticipated safety issues are discovered following approval. In addition, we may be subject to penalties or other enforcement action if we fail to comply with regulatory requirements. If the FDA, the European Commission (based on recommendation from the EMA), or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, storage, advertising, promotion, import, export, recordkeeping, monitoring, and reporting for our product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, establishment registration and listing, as well as continued compliance with current Good Manufacturing Practice requirements (cGMPs) and GCP requirements for any clinical trials that we conduct post- approval. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing studies, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. The FDA may require a REMS in order to approve our product candidates, which could entail requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third- party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things: • restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls; • revision to the labeling, including limitations on approved uses or the addition of additional warnings, contraindications or other safety information, including boxed warnings; • imposition of a REMS, which may include distribution or use restrictions; • requirements to conduct additional post- market clinical trials to assess the safety of the product; • fines, warning letters or other regulatory enforcement action; • refusal by the FDA to approve pending applications or supplements to approved applications filed by us; • product seizure or detention, or refusal to permit the import or export of products; and • injunctions or the imposition of civil or criminal penalties; In the EU, the European Commission (based on recommendation from the EMA) ~~may~~ **will** require an equivalent risk management plan (RMP). The FDA' s, European Commission' s, EMA' s, and other comparable foreign regulatory authorities' policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability. We anticipate that our current product candidates and any future product candidates will be used in combination with third- party drugs or biologics, some of which are still in development, and we have limited or no control over the supply, regulatory status, or regulatory approval of such drugs or biologics. Our T- win ~~technology~~ **® platform** targets both immune suppressive host and tumor cells in the TME initiating a dynamic process of activating the host immune system, which response can be further exploited by concurrent or subsequent therapies as checkpoint inhibitors such as the dominant PD- 1 monoclonal antibodies, pembrolizumab and nivolumab. Accordingly, it is expected that our product candidates, if approved, would be used in combination with third- party drugs or biologics. For example, IO102- IO103 in combination with an anti- PD- 1 monoclonal antibody was investigated in a Phase 1 / 2 trial in 30 metastatic melanoma patients at **Herlev** University Hospital of Copenhagen, and we are conducting a Phase 3 clinical trial, the IOB- 013 / KN- D18 trial, combining IO102- IO103 with an pembrolizumab in first line advanced melanoma patients. Our ability to develop and ultimately commercialize our current product candidates and any future product candidates used in combination with pembrolizumab, nivolumab, or any other checkpoint inhibitor immunotherapies will depend on our ability to access such drugs or biologics on commercially reasonable terms for the clinical trials and their availability for use with the commercialized product, if approved. We cannot be certain that current or potential future commercial relationships will provide us with a steady supply of such drugs or biologics on commercially reasonable terms or at all. Any failure to maintain or enter into new successful commercial relationships, or the expense of purchasing checkpoint inhibitor immunotherapies or other comparator therapies in the market, may delay our development timelines, increase our costs and jeopardize our ability to develop our current product candidates and any future product candidates as commercially viable therapies. If any of these occur, our business, financial condition, results of operations, stock price and prospects may be materially harmed. Moreover, the development of product candidates for use in combination with another product or product candidate may present challenges that are not faced for single agent product candidates. We are currently developing IO102- IO103 and IO112 and may develop other future product candidates for use in combination with checkpoint inhibitors and ~~may develop IO102- IO103 and IO112, or any future product candidates for use with~~ other therapies. The FDA, EMA, or comparable foreign regulatory authorities may require us to use more complex clinical trial designs in order to evaluate the contribution of each product and product candidate to any observed effects. It is possible that the results of such trials could show that any positive previous trial results are attributable to the combination therapy and not our current product candidates and any future product candidates. It is also possible that trial results for our product candidates may differ significantly if our product candidates are investigated with different combination therapies in different trials- for example, if we were to investigate our product candidates with one anti- PD- 1 monoclonal antibody in one trial and a different anti- PD- 1 monoclonal antibody in another. Moreover, following product approval, the FDA, EMA, or comparable foreign regulatory authorities may require that products used in conjunction with each other be cross labeled for combined use. To the extent that we do not have rights to the other product, this may require us to work with a third party to satisfy such a requirement. Moreover, developments related to the other product may impact our clinical trials for the combination as well as our commercial prospects should we receive marketing approval. Such developments may include changes to the other product' s safety or efficacy profile, changes to the availability of the approved product, quality, manufacturing and supply issues, and changes to the standard of care. In the event that any of our collaborators or suppliers cannot continue to supply their products

on commercially reasonable terms, we would need to identify alternatives for accessing such checkpoint inhibitor immunotherapies. Additionally, should the supply of products from any collaborator or supplier be interrupted, delayed or otherwise be unavailable to us, our clinical trials may be delayed. In the event we are unable to source an alternative supply, or are unable to do so on commercially reasonable terms, our business, financial condition, results of operations, stock price and prospects may be materially harmed. 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 must prioritize our research programs and will need to focus our discovery and development on select product candidates and indications. Correctly prioritizing our research and development activities is particularly important for us due to the breadth of potential product candidates and indications that we believe could be pursued using our platform technologies. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later 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 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 also 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. Our success largely depends on the success of our limited number of product candidates. If any of these candidates fail in clinical trials or are not approved for commercialization, our ability to generate revenue and achieve profitability could be impacted. We expect initially to focus on the development of our lead dual epitope IO102- IO103. We also expect to continue to develop our ~~third~~ **other** product ~~candidate~~ **candidates** , IO112 **and IO170** . A key part of our strategy, however, is to continue to pursue clinical development of additional product candidates utilizing our T- win ~~technology~~ **®** platform. Developing, obtaining marketing approval for, and commercializing any future product candidates will require substantial additional funding ~~beyond the net proceeds of our IPO~~ and will be subject to the risks of failure inherent in drug product development. We cannot assure you that we will be able to successfully advance any future product candidates through the development process. Even if we obtain approval from the FDA, European Commission (based on recommendation from the EMA) or comparable foreign regulatory authorities to market any future product candidates for the treatment of tumors, we cannot assure that any such product candidates will be successfully commercialized, widely accepted in the marketplace, or more effective than other commercially available alternatives. If we are unable to successfully develop and commercialize additional product candidates our commercial opportunity may be limited and our business, financial condition, results of operations, stock price and prospects may be materially harmed. Difficulty in enrolling patients could delay or prevent clinical trials of our current product candidates and any future product candidates. We may find it difficult to enroll patients in our ongoing clinical trials or any subsequent trials we may conduct and our receipt of necessary regulatory approvals could be delayed or prevented. For example, we have experienced longer than expected lead times in clinical trial site activation and patient enrollment in our clinical trials. Identifying and qualifying patients to participate in clinical studies of our current product candidates and any future product candidates is critical to our success. The timing of completion of our clinical trials depends in part on the speed at which we can recruit patients to participate in testing our current product candidates and any future product candidates, and we may experience delays in our clinical trials if we encounter difficulties in enrollment or patient retention due to other unforeseen factors. We may not be able to initiate or continue clinical trials for our current product candidates and any future product candidates if we are unable to locate and enroll and retain a sufficient number of eligible patients to participate in these trials as required by the FDA, EMA, or comparable foreign regulatory authorities outside the United States. For example, ~~the~~ COVID- 19 ~~pandemic has~~ impacted ~~, and may continue to impact,~~ our ability to initiate clinical sites and recruit, enroll and retain patients **,** or **similar public health emergencies** may divert healthcare resources away from clinical trials. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications as our current product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' product candidates or future product candidates. In addition to the competitive trial environment, the eligibility criteria of our planned clinical trials will further limit the pool of available study participants as we will require that patients have specific characteristics that we can measure to assure their cancer is either severe enough or not too advanced to include them in a study. Additionally, the process of finding patients may prove costly. We also may not be able to identify, recruit and enroll a sufficient number of patients to complete our clinical studies because of the perceived risks and benefits of the product candidates under study, the availability and efficacy of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective patients, and the patient referral practices of physicians. If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. The enrollment of patients further depends on many factors, including: • the eligibility criteria for the clinical trial in question; • the availability of an appropriate screening test, as necessary; • the perceived risks and benefits of the product candidate under study; • the proximity and availability of clinical trial sites for prospective patients; • the design of the clinical trial; • our ability to obtain and maintain patient consents; • reporting of the preliminary results of any of our clinical trials; and • the risk that patients enrolled in clinical trials will drop out of the clinical trials before clinical trial completion. In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our current product candidates and any future product candidates, and this competition ~~will~~ **may** reduce the number and types of patients available to us because some patients who might have opted to enroll in our clinical trials may instead opt to enroll in a clinical trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which ~~will~~ **may** reduce the number of patients who are available for our clinical trials at such clinical trial sites.

Furthermore, even if we are able to enroll a sufficient number of patients for our clinical trials, we may have difficulty maintaining enrollment of such patients in our clinical trials. If we experience delays in the completion of, or termination of, any clinical trial of our current product candidates and any future product candidates, the commercial prospects of our current product candidates and any future product candidates will be harmed, and our ability to generate product revenue from such product candidates could be delayed or prevented. Our future growth depends, in part, on our ability to penetrate multiple markets in which we would be subject to additional regulatory burdens and other risks and uncertainties. Our future profitability will depend, in part, on our ability to commercialize our product candidates, if approved, in markets in the United States, Europe, the ~~UK~~ **United Kingdom**, and other countries where we maintain commercialization rights. As we begin to commercialize our product candidates, if approved, in multiple markets, we are subject to additional risks and uncertainties, including: • foreign currency exchange rate fluctuations and currency controls; • economic weakness, including inflation, or political instability in particular economies and markets ~~; • uncertainties related to Brexit, including potential impacts on costs, exchange rates, flow of goods, manufacturing and operations~~ ; • potentially adverse and / or unexpected tax consequences, including penalties due to the failure of tax planning or due to the challenge by tax authorities on the basis of transfer pricing and liabilities imposed from inconsistent enforcement; • the burden of complying with complex and changing regulatory, tax, accounting and legal requirements, many of which vary between countries; • different medical practices and customs in multiple countries affecting acceptance of drugs in the marketplace; • differing payor reimbursement regimes, governmental payors or patient self- pay systems and price controls; • tariffs, trade barriers, import or export licensing requirements or other restrictive actions; • compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; • workforce uncertainty in countries where labor unrest is common; • reduced or loss of protection of intellectual property rights in some foreign countries, and related prevalence of generic alternatives to therapeutics; and • becoming subject to the different, complex and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties and regulations. These and other risks associated with international operations may adversely affect our ability to attain or maintain profitable operations. Future sales of our products or our product candidates, if they are approved, will be dependent on purchasing decisions of and reimbursement from government health administration authorities, distributors and other organizations. As a result of adverse conditions affecting the global economy and credit and financial markets, including disruptions due to political instability **, geopolitical conflict** or otherwise, these organizations may defer purchases, may be unable to satisfy their purchasing or reimbursement obligations, or may affect milestone payments or royalties for our products or any of our product candidates that are approved for commercialization in the future. Should any of these risks materialize, this could have a material adverse effect on our business, prospects, financial condition and results of operations. Risks Related to Manufacturing and Commercialization The manufacture of our product candidates is complex and we may encounter difficulties in production, particularly with respect to process development or ~~scaling~~ **scale** - ~~out~~ **up** of our manufacturing capabilities. If we encounter such difficulties, our ability to provide supply of our product candidates for clinical trials or our products for patients, if approved, could be delayed or stopped. We have not yet manufactured or processed our product candidates on a commercial scale and may not be able to do so for any of our product candidates. We may encounter difficulties in production, particularly in scaling up or out, validating the production process, and assuring high reliability of the manufacturing process. These problems **may** include delays or break- downs in logistics and shipping, difficulties with production costs and yields, quality control, and product testing, operator error, lack of availability of qualified personnel, as well as failure to comply with strictly enforced federal, state and foreign regulations. Furthermore, if contaminations are discovered in our supply of product candidates or in the manufacturing facilities, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure you that any of these or other issues relating to the manufacture of our product candidates will not occur in the future. Any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to begin new clinical trials at additional expense or terminate clinical trials completely. Manufacturing facilities also require commissioning and validation activities to demonstrate that they operate as designed, and are subject to government inspections by the FDA, EU Member States ~~,~~ **(** coordinated by the EMA ~~,~~ **)** and other comparable foreign regulatory authorities. If we are unable to reliably produce products to specifications acceptable to the regulatory authorities, we may not obtain or maintain the approvals we need to manufacture our products. Further, manufacturing facilities may fail to pass government inspections prior to or after the commercial launch of our product candidates, which would cause significant delays and additional costs required to remediate any deficiencies identified by the regulatory authorities. Any of these challenges could delay completion of clinical trials, require bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidate, impair commercialization efforts, increase our cost of goods, and have an adverse effect on our business, financial condition, results of operations and growth prospects. Changes in product candidate manufacturing or formulation may result in additional costs or delay. As product candidates are developed through preclinical studies to later- stage clinical trials towards approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Any of these changes could cause our current product candidates or any future product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the altered materials. Such changes may also require additional testing, or notification to, or approval by the FDA, European Commission, EMA, or a comparable foreign regulatory authority. This could delay completion of clinical trials, require the conduct of bridging clinical trials or studies, require the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our current product candidates and any future product candidates and / or jeopardize our ability to commence product sales and generate revenue. Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third- party payors and others in the medical community necessary for

commercial success. Even if we obtain marketing approvals from the FDA, European Commission (based on recommendation from the EMA), or other comparable foreign regulatory agencies and are able to initiate commercialization of our clinical- stage product candidates or any other product candidates we develop, the product candidate may not achieve market acceptance among physicians, patients, hospitals, including pharmacy directors **, cancer treatment centers** , and third- party payors and, ultimately, may not be commercially successful. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including: • the clinical indications for which our product candidates are approved; • physicians, hospitals, cancer treatment centers, and patients considering our product candidates as a safe and effective treatment; • the potential and perceived advantages of our product candidates over alternative treatments; • the prevalence and severity of any side effects; • product labeling or product insert requirements of the FDA, European Commission, EMA, or other comparable foreign regulatory authorities; • limitations or warnings contained in the labeling approved by the FDA, European Commission, EMA, or other comparable foreign regulatory authorities; • the timing of market introduction of our product candidates as well as competitive products; • the cost of treatment in relation to alternative treatments; • the amount of upfront costs or training required for physicians to administer our product candidates; • the availability of coverage **from** , adequate reimbursement from, and our ability to negotiate pricing with, third- party payors and government authorities; • the willingness of patients to pay out- of- pocket in the absence of comprehensive coverage and reimbursement by third- party payors and government authorities; • relative convenience and ease of administration, including as compared to alternative treatments and competitive therapies; and • the effectiveness of our sales and marketing efforts and distribution support. Our efforts to educate physicians, patients, third- party payors and others in the medical community on the benefits of our product candidates, if approved, may require significant resources and may never be successful. Such efforts may require more resources than are typically required due to the complexity and uniqueness of our product candidates. Because we expect sales of our product candidates, if approved, to generate substantially all of our product revenue for the foreseeable future, the failure of our product candidates to find market acceptance would harm our business and could require us to seek additional financing. Even if our product candidates, if approved, achieve market acceptance, we may not be able to maintain that market acceptance over time if new products or technologies are introduced that are more favorably received than our products, are more cost effective or render our products obsolete. We may not be able to successfully commercialize our product candidates, if approved, due to unfavorable pricing regulations or third- party coverage and reimbursement policies, which could make it difficult for us to sell our product candidates profitably **.** Obtaining coverage and reimbursement approval for a product from a government or other third- party payor is a time- consuming and costly process, with uncertain results, that could require us to provide supporting scientific, clinical and cost effectiveness data for the use of our products to the payor. There may be significant delays in obtaining such coverage and reimbursement for newly approved products, and coverage may not be available, or may be more limited than the purposes for which the product is approved by the FDA or other comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a product will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new products, 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 product and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost products and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors, by any future laws limiting drug prices and by any future relaxation of laws that presently restrict imports of ~~product~~ **products** from countries where they may be sold at lower prices than in the United States. There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, there is no uniform policy among third- party payors for coverage and reimbursement. Third- party payors often rely upon Medicare coverage policy and payment limitations in setting reimbursement policies, but also have their own methods and approval process apart from Medicare coverage and reimbursement determinations. Therefore, one third- party payor' s determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Coverage and reimbursement by a third- party payor may depend upon a number of factors, including the third- party payor' s determination that use of a product is: • a covered benefit under its health plan; • safe, effective and medically necessary; • appropriate for the specific patient; • cost- effective; and • neither experimental nor investigational. We cannot be sure that reimbursement will be available for any product that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. 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. Reimbursement may impact the demand for, and the price of, any product for which we obtain marketing approval. Even if we obtain coverage for a given product by a third- party payor, the resulting reimbursement payment rates may not be adequate or may require co- payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third- party payors to reimburse all or part of the costs associated with those medications. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our products. Therefore, coverage and adequate reimbursement are critical to a new product' s acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new products when more established or lower cost therapeutic alternatives are already available or subsequently become available. For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself may or may not be available. Instead, the hospital or administering physician may be reimbursed only for providing the treatment or procedure in which our product is used. Further, from time to time, ~~the~~ CMS, the federal agency

responsible for administering the Medicare program, revises the reimbursement amounts paid to health care providers, including the Medicare Physician Fee Schedule and Hospital Outpatient Prospective Payment System, which may result in reduced Medicare payments. We expect to experience pricing pressures in connection with the sale of any of our product candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the successful commercialization of new products. Further, the adoption and implementation of any future governmental cost containment or other health reform initiative may result in additional downward pressure on the price that we may receive for any approved product. Outside of the United States, many countries require approval of the sale price of a product before it can be marketed, and the pricing review period only begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some of these countries, we may be required to conduct a clinical trial that compares the cost- effectiveness of our product candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate 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 negatively impact the revenue, if any, 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 such product candidates obtain marketing approval. Reimbursement and healthcare payment systems vary significantly by country outside the ~~US~~ **United States**, and many countries have instituted price ceilings on specific products and therapies. In the EU and the ~~UK~~ **United Kingdom**, similar political, economic and regulatory developments may affect our ability to profitably commercialize our product candidates, if approved. In addition to continuing pressure on prices and cost containment measures, legislative developments at the EU, ~~UK~~ **United Kingdom** or at ~~a~~ **an** EU Member State level may result in significant additional requirements or obstacles that may increase our operating costs. The delivery of healthcare in the EU ~~and the UK~~, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, law and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most EU Member States and the ~~UK~~ **United Kingdom** have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever- increasing EU and national regulatory burdens on those wishing to develop and market products in these countries, ~~this~~ **these restrictions on pricing and reimbursement** could prevent or delay marketing approval of our product candidates, restrict or regulate post- approval activities and affect our ability to commercialize our product candidates, if approved. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the ~~US~~ **United States**, the EU, ~~UK~~ **United Kingdom** or any other jurisdiction. If we, or any third parties we may engage **,** are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability. If the regulatory authorities in such jurisdictions set prices or make reimbursement criteria that are not commercially attractive for us or our collaborators, our revenues and the potential profitability of our products in those countries would be negatively affected. If the market opportunities for any of our product candidates are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer. We are focused on the development of treatments for cancer. Our projections of addressable patient populations that have the potential to benefit from treatment with our product candidates are based on estimates, including estimated incidence rates of specific forms of cancer. If any of our estimates are inaccurate, the market opportunities for any of our product candidates could be significantly diminished and have an adverse material impact on our business. If any of our product candidates are approved for marketing and commercialization and we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our product candidates, we will be unable to successfully commercialize our product candidates if and when they are approved. We have no sales, marketing or distribution capabilities or experience. To achieve commercial success for any approved product for which we retain sales and marketing responsibilities, we must either develop a sales and marketing organization, which would be expensive and time consuming, or outsource these functions to other third parties. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our product candidates if and when they are approved. There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel. Factors that may inhibit our efforts to commercialize future products on our own include: • our inability to recruit and retain adequate numbers of effective sales and marketing personnel; • the inability of sales personnel to compliantly obtain access to physicians or educate adequate numbers of physicians on the benefits of prescribing any future 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 portfolios; and • unforeseen costs and expenses associated with creating an independent sales and marketing organization. If we enter into arrangements with third parties to perform sales, marketing and distribution services, our product revenue or the profitability of the product revenue to us are likely to be lower than if we were to market and sell any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so

on terms that are favorable to us. In entering into third- party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of ~~the~~ third parties and we cannot assure you that such third parties will establish adequate sales and distribution capabilities or devote the necessary resources and attention to sell and market any future products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates. **If granted,** ~~Regulatory~~ **regulatory** approval by the FDA, European Commission (based on recommendations from the EMA) or comparable foreign regulatory authorities is limited to those specific indications and conditions for which approval has been granted, and we may be subject to substantial fines, criminal penalties, injunctions, or other enforcement actions if we are determined to be promoting the use of our products for unapproved or ~~"~~ off- label ~~"~~ uses, or in a manner inconsistent with the approved labeling, resulting in damage to our reputation and business. We must comply with requirements concerning advertising and promotion for any product candidates for which we obtain marketing approval. Promotional communications with respect to therapeutics are subject to a variety of legal and regulatory restrictions and continuing review by the FDA or comparable foreign regulatory and governmental authorities, Department of Justice, HHS Office of Inspector General, state attorneys general, members of Congress, and the public. When the FDA or comparable foreign regulatory authorities issue regulatory approval for a product candidate, the regulatory approval is limited to those specific uses and indications for which ~~a~~ **the** product ~~is~~ **has been** approved. If we are not able to obtain FDA or comparable foreign regulatory authority approval for desired uses or indications for our current product candidates and any future product candidates, we may not market or promote them for those indications and uses, referred to as off- label uses, and our business, financial condition, results of operations, stock price and prospects will be materially harmed. We also must sufficiently substantiate any claims that we make for our products, including claims comparing our products to other companies' products, and must abide by the FDA or a comparable foreign regulatory or governmental authority' s strict requirements regarding the content of promotion and advertising. While physicians may choose to prescribe products for uses that are not described in the product' s labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, we and any third parties engaged on our behalf are prohibited from marketing and promoting the products for indications and uses that are not specifically approved by the FDA or comparable foreign regulatory authorities. Regulatory authorities in the United States generally do not restrict or regulate the behavior of physicians in their choice of treatment within the practice of medicine. Regulatory authorities do, however, restrict communications by biopharmaceutical companies concerning off- label ~~use~~ **uses** . If we are found to have impermissibly promoted any of our current product candidates and any future product candidates, we may become subject to significant liability and government fines. The FDA and other agencies actively enforce the laws and regulations regarding product promotion, particularly those prohibiting the promotion of off- label uses, and a company that is found to have improperly promoted a product may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off- label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed. In the United States, engaging in the impermissible promotion of our products, following approval, for off- label uses can also subject us to false claims and other litigation under federal and state statutes. These include fraud and abuse and consumer protection laws, which can lead to civil and criminal penalties and fines, **and** agreements with governmental authorities that materially restrict the manner in which we promote or distribute therapeutic products and conduct our business. These restrictions could include corporate integrity agreements, suspension or exclusion from participation in federal and state healthcare programs, and suspension and debarment from government contracts and refusal of orders under existing government contracts. These FCA lawsuits against manufacturers of drugs and biologics have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements pertaining to certain sales practices and promoting off- label uses. In addition, FCA lawsuits may expose manufacturers to follow- on claims by private payors based on fraudulent marketing practices. This growth in litigation has increased the risk that a biopharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, as well as criminal and civil penalties, agree to comply with burdensome reporting and compliance obligations, and be excluded from Medicare, Medicaid, or other federal and state healthcare programs. If we do not lawfully promote our approved products, if any, we may become subject to such litigation and, if we do not successfully defend against such actions, those actions may have a material adverse effect on our business, financial condition, results of operations, stock price and prospects. In the United States, the promotion of biopharmaceutical products are subject to additional FDA requirements and restrictions on promotional statements. If after one or more of our current or future product candidates obtains marketing approval the FDA determines that our promotional activities violate its regulations and policies pertaining to product promotion, it could request that we modify our promotional materials or subject us to regulatory or other enforcement actions, including issuance of warning letters or untitled letters, suspension or withdrawal of an approved product from the market, requests for recalls, payment of civil fines, disgorgement of money, imposition of operating restrictions, injunctions or criminal prosecution, and other enforcement actions. Similarly, industry codes in foreign jurisdictions may prohibit companies from engaging in certain promotional activities and regulatory agencies in various countries may enforce violations of such codes with civil penalties. If we become subject to regulatory and enforcement actions our business, financial condition, results of operations, stock price and prospects will be materially harmed. Furthermore, the use of our products for indications other than those approved by the FDA or comparable foreign regulatory authorities may not effectively treat such conditions. Any such off- label use of our product candidates could harm our reputation in the marketplace among physicians and patients. There may also be increased risk of injury to patients if physicians attempt to use our products for these uses for which they are not approved, which could lead to product liability suits that that might require significant financial and management resources and that could harm our reputation. Even if we obtain FDA or European Commission (based on recommendations from the EMA) approval **of** any of our product candidates in the United States or EU, we may never obtain approval for or commercialize any of them in any other jurisdiction, which would

limit our ability to realize their full market potential **.** In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country- by- country basis regarding safety and efficacy. Approval by the FDA in the United States or the European Commission (based on recommendations from the EMA) in the EU does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not guarantee regulatory approval in any other country. Approval processes vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized. Risks Related to Reliance on Third Parties Some of our product candidates may be studied in clinical trials sponsored by organizations or agencies other than us, or in investigator- initiated clinical trials, which means we will have minimal or no control over the conduct of such trials. We have **supplied** and may continue to supply and otherwise support third party research, including investigator- initiated clinical trials. Investigator-initiated clinical trials pose similar risks as those set forth elsewhere in this " Risk Factor " section relating to our internally-sponsored clinical trials, but because we may not be the sponsors of these trials, we have less control over the protocols, administration or conduct of these trials, including follow- up with patients and ongoing collection of data after treatment. The conduct or findings of these trials may have a negative impact on our development programs notwithstanding that we have little involvement or control over these trials. As a result, we are subject to additional risks associated with the way investigator-initiated trials are conducted. In particular, we may be named in lawsuits that would lead to increased costs associated with legal defense. Additional risks include difficulties or delays in communicating with investigators or administrators, procedural delays and other timing issues and difficulties or differences in interpreting data. Third- party investigators may design clinical trials with clinical endpoints that are more difficult to achieve, or in other ways that increase the risk of negative clinical trial results compared to clinical trials that we may design on our own. Negative results in investigator- initiated clinical trials could have a material adverse effect on our efforts to obtain regulatory approval for our product candidates and the public perception of our product candidates. As a result, our lack of control over the conduct and timing of and communications with the FDA and other regulatory authorities regarding investigator- sponsored trials may expose us to additional risks and uncertainties, many of which are outside our control, and the occurrence of which could adversely affect the commercial prospects for our product candidates. We rely on third parties to conduct, supervise, and monitor our clinical trials and perform some of our research and preclinical studies. If these third parties do not satisfactorily carry out their contractual duties or fail to meet expected deadlines, our development programs may be delayed or subject to increased costs ~~, each of~~ which may have an adverse effect on our business and prospects. We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. As a result, we are and expect to remain dependent on third parties to conduct our current and future preclinical studies and clinical trials. CROs that manage our preclinical studies and clinical trials as well as clinical investigators, including in investigator-initiated clinical trials, and consultants play a significant role in the conduct of our preclinical studies and clinical trials and the subsequent collection and analysis of data. The timing of the initiation and completion of these studies and trials will therefore be partially controlled by such third parties and may result in delays to our development programs. Nevertheless, we are responsible for ensuring that each of our preclinical studies and clinical trials is conducted in accordance with the applicable protocol, legal requirements, and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with Good Laboratory Practice (GLP) and GCP requirements, which are regulations and guidelines enforced by the FDA, the EMA, and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GLP and GCP requirements through periodic inspections of preclinical study sites, trial sponsors, clinical trial investigators and clinical trial sites. If we or any of our CROs or clinical trial sites, including clinical trial sites in investigator- initiated clinical trials, fail to comply with applicable GLP or GCP requirements, the data generated in our preclinical studies and clinical trials may be deemed unreliable, and the FDA, EMA, or comparable foreign regulatory authorities may require us to perform additional preclinical or clinical trials before approving our marketing applications. **Further, requirements regarding clinical trial data may evolve. In June 2023, the FDA published a draft guidance, " E6 (R3) Good Clinical Practice (GCP), " which seeks to unify standards for clinical trial data for ICH member countries and regions. Changes to data requirements may cause the FDA or other foreign regulatory authorities to disagree with data from preclinical studies or clinical trials, and may require further studies.** In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to stop and / or repeat clinical trials, which would delay the marketing approval process. There is no guarantee that any such CROs, clinical trial investigators or other third parties on which we rely will devote adequate time and resources to our development activities or perform as contractually required. ~~These risks are heightened as a result of the efforts of government agencies and the CROs themselves to limit the spread of COVID- 19, including quarantines and shelter- in- place orders.~~ If any of these third parties ~~fail~~ **fails** to meet expected deadlines, **fails to** adhere to our clinical protocols or meet regulatory requirements, otherwise performs in a substandard manner, or terminates its engagement with us, the timelines for our development programs may be extended or delayed or our development activities may be suspended or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow- up

information on subjects enrolled in such clinical trials unless we are able to transfer those subjects to another qualified clinical trial site, which may be difficult or impossible. In addition, clinical trial investigators for our clinical trials or investigator-initiated clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA or any comparable foreign regulatory authority concludes that the financial relationship may have affected the interpretation of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any marketing application we submit by the FDA or any comparable foreign regulatory authority. Any such delay or rejection could prevent us from commercializing our product candidates. 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, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we **may** ~~will not~~ be ~~able~~ **unable** to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and **may** ~~will not~~ be ~~able~~ **unable** to, or may be delayed in our efforts to, successfully commercialize our products. We rely on third parties to manufacture our product candidates, and we expect to continue to rely on third parties for the clinical as well as any future commercial supply of our product candidates and other future product candidates. The development of our current and future product candidates, and the commercialization of any approved products, could be stopped, delayed or made less profitable if any such third party fails to provide us with sufficient clinical or commercial quantities of such product candidates or products, fails to do so at acceptable quality levels or prices or fails to achieve or maintain satisfactory regulatory compliance. We do not currently have, and we do not plan to build, the infrastructure or capability internally to manufacture current product candidates or any future product candidates for use in the conduct of our clinical trials or, if approved, for commercial supply. We rely on, and expect to continue to rely on, CMOs. Reliance on third- party providers may expose us to more risk than if we were to manufacture our product candidates ourselves. We do not control the manufacturing processes of the CMOs we contract with and are dependent on those third parties for the production of our product candidates in accordance with relevant applicable regulations such as cGMP, which includes, among other things, quality control, quality assurance and the maintenance of records and documentation. In complying with the manufacturing regulations of the FDA and other comparable foreign regulatory authorities, we and our third- party suppliers must spend significant time, money and effort in the areas of design and development, testing, production, record- keeping and quality control to assure that the products meet applicable specifications and other regulatory requirements. The failure to comply with these requirements could result in an enforcement action against us, including the seizure of products and shutting down of production. We and any of these third- party suppliers may also be subject to inspections by the FDA, EU Member States ~~,~~ **(** coordinated by the EMA **)** , or comparable foreign regulatory authorities. If any of our third- party suppliers fails to comply with cGMP or other applicable manufacturing regulations, our ability to develop and commercialize our product candidates could suffer significant interruptions. 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 revocation, seizures or recalls of product candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products. Any disruption, such as a fire, natural hazards or vandalism at our CMOs, or any impacts on our CMOs due to ~~the~~ COVID- 19 ~~pandemic~~ , could significantly interrupt our manufacturing capability. We currently do not have alternative production plans in place or disaster- recovery facilities available. In case of a disruption, we will have to establish alternative manufacturing sources. This would require substantial capital on our part, which we may not be able to obtain on commercially acceptable terms or at all. Additionally, we would likely experience months of manufacturing delays as we build facilities or locate alternative suppliers and seek and obtain necessary regulatory approvals. If this occurs, we ~~will~~ **may** be unable to satisfy manufacturing needs on a timely basis, if at all. If changes to CMOs occur, then there also may be changes to manufacturing processes inherent in the setup of new operations for our product candidates and any products that may obtain approval in the future. Any such changes could require the conduct of bridging studies before we can use any materials produced at new facilities or under new processes in clinical trials or, for any products reaching approval, in our commercial supply. Further, business interruption insurance may not adequately compensate us for any losses that may occur and **, in that case,** we would have to bear the additional cost of any disruption. For these reasons, a significant disruptive event of any CMOs could have drastic consequences, including placing our financial stability at risk. Our product candidates and any drugs that we may develop may compete with other product candidates and drugs for access to manufacturing facilities. There are no assurances we would be able to enter into similar commercial arrangements with other manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. If we were to experience an unexpected loss of supply of or if any supplier were unable to meet our clinical or commercial demand for any of our product candidates, we could experience delays in our planned clinical studies or commercialization. For example, **future public health emergencies** ~~the COVID- 19 pandemic~~ may impact our ability to procure sufficient supplies for the development of our current and future product candidates, and the extent of such impacts will depend on the severity and duration of ~~the spread of the virus~~ and the actions undertaken to contain ~~COVID- 19~~ **such public health crisis** or treat its effects. We could be unable to find alternative suppliers of acceptable quality and experience that can produce and supply appropriate volumes at an acceptable cost or on favorable terms. Moreover, our suppliers are often subject to strict manufacturing requirements and rigorous testing requirements, which could limit or delay production. The long transition periods necessary to switch manufacturers and suppliers, if necessary, ~~would~~ **could** significantly delay our clinical trials and, for any product candidates that reach approval, the commercialization of our products, which would materially adversely affect our business, financial condition and results of operation. We depend on third- party suppliers for materials that are necessary for the conduct of preclinical studies and

manufacture of our product candidates for clinical trials, and the loss of these third- party suppliers or their inability to supply us with sufficient quantities of adequate materials, or to do so at acceptable quality levels and on a timely basis, could harm our business. Manufacturing our product candidates requires many reagents, which are substances used in our manufacturing processes to bring about chemical or biological reactions, and other specialty materials and equipment, some of which are manufactured or supplied by small companies with limited resources and experience to support commercial biologics production. We currently depend on a limited number of vendors for certain materials and equipment used in the manufacture of our product candidates. For example, we currently use facilities and equipment at external CMOs, as well as supply sources internal to the collaboration for vector supply. Our use of CMOs increases the risk of delays in production or insufficient supplies as we transfer our manufacturing technology to these CMOs and as they gain experience with our supply requirements. Some of these suppliers may not have the capacity to support clinical trials and commercial products manufactured under cGMP by biopharmaceutical firms or may otherwise be ill- equipped to support our needs. We also do not have supply contracts with many of these suppliers and may not be able to obtain supply contracts with them on acceptable terms or at all. Accordingly, we may experience delays in receiving key materials and equipment to support clinical or commercial manufacturing. For some of these reagents, equipment, and materials, we rely and may in the future rely on sole source vendors or a limited number of vendors. The supply of the reagents and other specialty materials and equipment that are necessary to produce our product candidates could be reduced or interrupted at any time. In such case, identifying and engaging an alternative supplier or manufacturer could result in delay, and we may not be able to find other acceptable suppliers or manufacturers on acceptable terms, or at all. Switching suppliers or manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines. If we change suppliers or manufacturers for commercial production, applicable regulatory agencies may require us to conduct additional studies or trials. If key suppliers or manufacturers are lost, or if the supply of the materials is diminished or discontinued, we may not be able to develop, manufacture and market our product candidates in a timely and competitive manner, or at all. An inability to continue to source product from any of these suppliers, which could be due to a number of issues, including regulatory actions or requirements affecting the supplier, adverse financial or other strategic developments experienced by a supplier, labor disputes or shortages, unexpected demands or quality issues, could adversely affect our ability to satisfy demand for our product candidates, which could adversely and materially affect our product sales and operating results or our ability to conduct clinical trials, either of which could significantly harm our business. As we continue to develop and scale our manufacturing process, we expect that we will need to obtain rights to and supplies of certain materials and equipment to be used as part of that process. We may not be able to obtain rights to such materials on commercially reasonable terms, or at all, and if we are unable to alter our process in a commercially viable manner to avoid the use of such materials or find a suitable substitute, it would have a material adverse effect on our business. Even if we are able to alter our process so as to use other materials or equipment, such a change may lead to a delay in our clinical development and / or commercialization plans. If such a change occurs for **a** product candidate that is already in clinical testing, the change may require us to perform both ex vivo comparability studies and to collect additional data from patients prior to undertaking more advanced clinical trials. These factors could cause the delay of studies or trials, regulatory submissions, required approvals or commercialization of product candidates that we develop, cause us to incur higher costs and prevent us from commercializing our product candidates successfully. Our reliance on third parties requires us to share **certain of** our trade secrets, which increases the possibility that a competitor will discover them or that ~~our~~ **such** trade secrets will be misappropriated or disclosed. Because we rely on third parties to research and develop and to manufacture our product candidates, we must share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third- party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know- how and trade secrets, a competitor' s independent discovery of our trade secrets or other unauthorized use or disclosure ~~would~~ **could** impair our competitive position and may have a material adverse effect on our business. In addition, these agreements typically restrict the ability of our advisors, employees, third- party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with will likely expect to be granted rights to publish data arising out of such collaboration and any joint research and development programs may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third- party collaborators. A competitor' s discovery of our trade secrets ~~would~~ **could** impair our competitive position and have an adverse impact on our business. We may form or seek partnerships, collaborations or strategic alliances or enter into additional licensing arrangements in the future, and we may not realize the benefits of such partnerships, collaborations, alliances or licensing arrangements. We may form or seek partnerships or strategic alliances, create joint ventures or collaborations, or enter into licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any future product candidates that we may develop. For example, we have entered into collaborative agreements with Merck pursuant to which they provide the pembrolizumab used in certain of our trials. Any of these relationships may require us to incur non- recurring and other charges, increase our near and long- term expenditures, ~~require us to~~ share the data with such collaborators ~~or ,~~ restrict our ability to utilize certain data arising out of these collaboration arrangements, issue securities that dilute our existing stockholders or **take**

actions that disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time- consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy and obtain marketing approval. Further, collaborations involving our product candidates are subject to numerous risks, which may include the following: • collaborators have significant discretion in determining the efforts and resources that they will apply to a collaboration; • collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization of our product candidates based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities; • collaborators may delay clinical trials, provide insufficient funding for a clinical trial, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing; • collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates; • collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to their marketing and distribution; • collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability; • disputes, including contract disputes, may arise between us and a collaborator that cause the delay or termination of the research, development or commercialization of our product candidates, or that result in costly litigation or arbitration that diverts management attention and resources; • collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates; and • collaborators may own or co- own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to commercialize such intellectual property. As a result, if we enter into additional collaboration agreements and strategic partnerships or license our product candidates, we may not be able to realize the benefit of such transactions if we are unable to successfully integrate them with our existing operations and company culture, which could delay our timelines or otherwise adversely affect our business. We also cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction. Any delays in entering into new collaborations or strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates in certain geographies for certain indications, which would harm our business prospects, financial condition and results of operations. Risks Related to Our Industry and Business Operations The outbreak of COVID- 19, or similar public health ~~crises~~ **emergencies** , could have a material adverse impact on our business, financial condition and results of operations, including the execution of our planned clinical trials. In December 2019, a novel strain of coronavirus, SARS- CoV- 2, was identified. This virus ~~has since~~ spread globally, including within the United States and **,** while **the COVID- 19 public health emergency expired on May 11, 2023 and** cases and hospitalization are currently on the decline in the United States, there can be no assurances they will not continue at the current rate or increase in the future especially in light of the number of variants that are emerging across the world. Governments in the United States and elsewhere have **historically** taken and ~~are continuing to~~ **may in the future** take severe measures to slow the spread of COVID- 19, including **by** requiring that certain businesses close or conduct only the minimum necessary operations. The pandemic and government measures taken in response ~~have also~~ had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages ~~have~~ occurred, supply chains **were** ~~have been~~ disrupted, facilities ~~and~~ **were closed,** production **was** ~~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, **fell** ~~has fallen~~ . The extent to which COVID- 19 ~~will continue to~~ **and similar public health emergencies may** impact our business and operating results will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID- 19 and **similar public health emergencies and** government measures taken in response. Site activation, participant recruitment and enrollment, participant dosing, distribution of clinical trial materials, study monitoring and data analysis for our planned clinical trials may be delayed due to changes in hospital or university policies, federal, state or local regulations, prioritization of hospital resources toward pandemic efforts, or other reasons related to ~~the pandemic~~ **COVID- 19 or similar public health emergencies** . Additionally, some participants and clinical investigators may not be able to comply with clinical trial protocols **in light of future restrictions imposed by the U. S. and other foreign governments** . For example, quarantines or other travel limitations (whether voluntary or required) may impede participant movement, affect sponsor access to study sites, or interrupt healthcare services, and we may be unable to conduct its planned clinical trials. If the global effort to control ~~the spread of~~ **public health emergencies such as** COVID- 19 ~~and treat COVID- 19 patients~~ continues for an extended period of time, we risk a delay in activating sites and enrolling subjects as previously projected. For example, **during COVID- 19,** we ~~have~~ experienced longer than expected lead times in clinical trial site activation and patient enrollment in our clinical trials. Any delays to our planned clinical trials for IO102- IO103 and any future clinical trials and increased cost associated with the conducting of our clinical trials could impact the use and sufficiency of our existing cash reserves, and we may be required to raise additional capital earlier than it had previously planned. We may be unable to raise additional capital if and when needed, which may result in further delays or suspension of our development plans. Further, infections and deaths related to COVID- 19 ~~are~~ **and similar public health emergencies have disrupted, and may** ~~disrupting~~ --- **disrupt in the future,** certain healthcare and healthcare regulatory systems globally. Such disruptions could divert healthcare resources away from, or materially delay review by, the FDA and comparable foreign regulatory agencies. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de- prioritization of our clinical trials or delay in regulatory review resulting from such disruptions could

materially adversely affect the development and study of its product candidates. We currently utilize third parties to, among other things, manufacture raw materials and our product candidates, components, parts, and consumables, and to perform quality testing. If either we or any third- party in the supply chain for materials used in the production of its product candidates are adversely impacted by restrictions resulting from the COVID- 19 ~~pandemic~~ **or similar public health emergencies**, our supply chain may be disrupted, limiting our ability to manufacture product candidates for its clinical trials. In response to ~~the~~ COVID- 19 ~~pandemic~~, we complied with applicable regulation and limited required on- site staff to essential workers, with the balance of its employees continuing their work primarily outside of our offices. Due to shelter- in- place orders or other mandated local travel restrictions, third parties conducting clinical or manufacturing activities ~~may~~ **were** not be able to access laboratory or manufacturing space, and **, should future public health emergencies necessitate similar action,** our core activities may be significantly limited or curtailed, possibly for an extended period of time. While the potential economic impact brought by and the duration of ~~the pandemic~~ **public health emergencies** may be difficult to assess or predict, ~~it has already~~ **COVID- 19** caused, and **may** ~~is likely to result~~ in ~~further~~ **the future cause**, significant disruption of global financial markets and the trading prices of biopharmaceutical companies **was** ~~have been~~ highly volatile as a result of ~~the~~ COVID- 19 pandemic, which may reduce our ability to access capital either at all or on favorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the global effort to control **future public health emergencies could materially and adversely affect our business. The ultimate impact of the** COVID- 19 ~~infections could materially and adversely affect our business. The ultimate impact of the current pandemic~~, or any other health epidemic, is highly uncertain and subject to change. ~~We do not yet know the full extent of potential~~ **Potential** delays or impacts on our business, our planned clinical trials, healthcare systems or the global economy as a whole ~~. However, these effects~~ could have a material adverse impact on our business, financial condition and results of operations. Disruptions at the FDA, EMA, SEC and other government agencies and regulatory authorities caused by funding shortages or global health concerns could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal governmental functions on which the operation of our business may rely, which could negatively impact our business. The ability of the FDA, EMA, and other comparable foreign regulatory authorities to review and approve new products can be affected by a variety of factors, including government budget and funding levels, the ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at regulatory authorities and government agencies have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities **,** is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies such as the EMA following its post- Brexit relocation and resulting staff changes ~~as well as necessary COVID- 19 prioritizations~~ may also slow the time necessary for new products to be reviewed and / or approved by necessary government agencies, which would adversely affect our business. For example, in ~~recent years, including in~~ 2018 and 2019, the U. S. government shut down several times and certain regulatory agencies, such as the FDA and the SEC, had to furlough critical employees and stop critical activities. If a prolonged government shutdown occurs **in the future**, it could significantly impact the ability of the FDA to review and process our regulatory submissions, which could have a material adverse effect on our business. Further, ~~upon completion of our IPO and~~ in our operations as a public company, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations. ~~Separately~~ **Since March 2020**, ~~in response to the COVID- 19 pandemic,~~ **when foreign and domestic inspections of facilities were largely placed** on **hold** ~~March 10~~, ~~2020~~ the FDA ~~announced its intention~~ **has been working** to **resume** ~~postpone most inspections of foreign manufacturing facilities, and on March 18, 2020, the FDA temporarily postponed~~ routine surveillance **, bioresearch monitoring, and pre- approval** inspections ~~of domestic manufacturing facilities~~ **on a prioritized basis**. **Since April** ~~On July 10, 2020~~ **2021**, the FDA **has conducted limited** ~~announced its intention to resume certain on- site~~ inspections **and employed** ~~of domestic manufacturing facilities subject to a risk- based prioritization system. On April 14, 2021, the FDA issued a guidance document in which the FDA described its plans to conduct voluntary~~ remote interactive evaluations **, using risk management methods,** ~~of certain drug manufacturing facilities and clinical research sites. According~~ to **meet user fee commitments and goal dates. Travel restrictions and** ~~the~~ **other** ~~guidance,~~ **uncertainties may continue to impact oversight operations both domestic and abroad. Should** the FDA ~~intends~~ **determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due** to ~~request such~~ **restrictions on travel, and the FDA does not determine a** remote interactive ~~evaluations~~ **evaluation to** ~~in situations where an in- person inspection would not~~ be ~~prioritized~~ **adequate**, ~~deemed mission- critical, or where direct inspection is otherwise limited by travel restrictions, but where~~ the **agency has** ~~FDA determines that remote evaluation would still be appropriate. In May 2021, the FDA outlined a detailed plan to move toward a more consistent state~~ **stated** ~~of inspectional operations, and in July 2021, the FDA resumed standard inspectional operations of domestic facilities and was continuing to maintain this level of operation as of September 2021. In November 2021, the FDA provided an update to the May 2021 " Resiliency Roadmap for FDA Inspectional Oversight, " noting completion of " mission- critical " work over the previous year. In the update, the FDA noted~~ that it **generally intends** ~~" is continuing~~ to **issue, depending on the circumstances, a** complete **response letter** ~~mission- critical work, prioritize other higher- tiered inspectional needs (e. g., for~~ **or** ~~- cause inspections),~~ **defer action on the application until** ~~and~~ **an** ~~carry out surveillance inspections using risk- based approaches for evaluating public health impact. " Further, ongoing surges in COVID- 19 case numbers, with the emergence of new variants and sub- variants, have contributed to interruptions in FDA' s surveillance capabilities. In light of high positivity rates and hospitalizations associated with COVID- 19, the FDA made temporary changes in late 2021, including temporarily postponing certain~~ inspection **can be completed** ~~activities from December 29, 2021 to January 19, 2022~~. On February 2, 2022, the FDA announced that it would resume domestic surveillance inspections across all product areas on February 7, 2022. **On May 11, 2023,** ~~We cannot predict whether and when the FDA will~~

~~decide to pause or resume inspections due to~~ the COVID- 19 ~~pandemic~~ **public health emergency declared under the Public Health Service (PHS) Act expired** . ~~More recently,~~ **It is unclear how** the FDA **' s policies** ~~has continued to monitor~~ and ~~implement changes to its~~ **guidance will impact any** ~~inspectional~~ **inspections of our** ~~activities~~ - **facilities** ~~to ensure the safety of~~ **, including our clinical trial** ~~its~~ **sites** ~~employees and~~ **. During** ~~those~~ -- **the** ~~of the firms it regulates as it adapts to the evolving~~ COVID- 19 ~~pandemic~~ **public health emergency, a number of companies announced receipt of complete response letters due to the FDA' s inability to complete required inspections for their applications** . Regulatory authorities outside **of** the United States may adopt similar restrictions or other policy measures in response to ~~the~~ COVID- 19 ~~pandemic~~ **and may experience delays in their regulatory activities** . If a prolonged government shutdown occurs, or if global health concerns ~~continue to prevent~~ **impact regular inspections, reviews, or other regulatory activities of** 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 ~~. The United Kingdom' s withdrawal from the EU may cause additional administrative burdens and strain on regulatory authorities in the EU, this may delay our ability to obtain regulatory approvals of our product candidates in the EU and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the EU. The UK formally exited the EU, commonly referred to as Brexit, on January 31, 2020. Under the terms of its departure, the UK entered a transition period (the Transition Period), during which it continued to follow all EU rules. The Transition Period ended on December 31, 2020. On December 30, 2020, the UK and EU signed the Trade and Cooperation Agreement (TCA), which includes an agreement on free trade between the two parties. The TCA does not contain wholesale mutual recognition of regulatory regimes for pharmaceuticals as was hoped. There is mutual recognition of eGMP inspections of manufacturing facilities but it does not include reciprocal arrangements for the recognition of batch testing certification, in order to avoid unnecessary re- testing on importation of products. There is considerable uncertainty resulting from a lack of precedent and the complexity of the UK and the EU' s intertwined legal regimes as to how Brexit will impact the life sciences industry in Europe, including our company, including with respect to ongoing or future clinical trials. The impact will largely depend on the model and means by which the UK' s relationship with the EU is governed post- Brexit and the extent to which the UK chooses to diverge from the EU regulatory framework. The regulatory framework for medicines that existed before the end of the transition period has effectively been preserved in UK domestic legislation as ' retained EU law' which has prevented substantial divergence to the regulation of medicines. However, some changes to the UK legislation have been immediately necessary, including the implementation of the Northern Ireland Protocol (NIP), pursuant to which, the EU pharmaceutical legal framework acquis continues to apply in Northern Ireland (subject to periodic consent of the Northern Ireland Legislative Assembly), and only products compliant with EU law can be placed in the Northern Ireland market- adding an extra layer of regulatory complexity. As companies now need to comply with a separate UK regulatory legal framework in order to commercialize medicinal products in Great Britain (namely, England, Wales and Scotland, as EU law continues to apply in Northern Ireland). The UK government is currently trying to renegotiate fundamental aspects of the Northern Ireland Protocol so this is an unpredictable area for companies in the near future. The Trade and Cooperation Agreement signed between the UK and the EU allows for future deviation from the current regulatory framework and it is not known if and / or when any deviations may occur, which may have an impact on development, manufacture, marketing authorization, commercial sales and distribution of pharmaceutical products. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from or delay us commercializing our product candidates in the UK and / or the European Economic Area (EEA) and restrict our ability to generate revenue and achieve and sustain profitability. In the short term, there is a risk of disrupted import and export processes due to a lack of administrative processing capacity by the respective United Kingdom and EU customs agencies that may delay time- sensitive shipments and may negatively impact our product supply chain~~ . We may be exposed to significant foreign exchange risk. We have operations in Denmark and we incur portions of our expenses, and may in the future derive revenues, in a variety of currencies. As a result, we are exposed to foreign currency exchange risk as our results of operations and cash flows are subject to fluctuations in foreign currency exchange rates. Fluctuations in currency exchange rates have had, and will continue to have, an impact on our results as expressed in U. S. dollars. We currently do not engage in hedging transactions to protect against uncertainty in future exchange rates between particular foreign currencies and the U. S. dollar. We cannot predict the impact of foreign currency fluctuations, and foreign currency fluctuations in the future may adversely affect our financial condition, results of operations and cash flows. Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non- compliance with regulatory standards and requirements and insider trading. We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA and other comparable foreign regulatory authorities, provide accurate information to the FDA and other comparable foreign regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the United States, EU, ~~UK,~~ **United Kingdom** and in other jurisdictions, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us those actions

could have a significant impact on our business, including the imposition of significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, diminished profits and future earnings, additional reporting obligations and oversight if subject to a corporate integrity agreement or other agreement to resolve allegations of non- compliance with these laws, and the curtailment or restructuring of our operations. We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. ~~if~~ **If** the use of our product candidates harms patients or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims. The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in: • impairment of our business reputation; • withdrawal of clinical trial participants; • costs due to related litigation; • distraction of management' s attention from our primary business; • substantial monetary awards to patients or other claimants; • the inability to commercialize our product candidates; and • decreased demand for our product candidates, if approved for commercial sale. We believe our product liability insurance coverage is sufficient in light of our current clinical programs; however, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claims ~~,~~ or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business. Patients with cancer and other diseases targeted by our product candidates are often already in severe and advanced stages of disease and have both known and unknown significant pre- existing and potentially life- threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to **, or perceived to be related to,** our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time- consuming or inconclusive. These investigations may divide the attention of our management team, interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or results of operations. Our future success depends on our ability to retain key members of senior management and to attract, retain and motivate qualified personnel. Our ability to compete in the highly competitive biopharmaceutical industry depends upon our ability to attract and retain highly qualified management, research and development, clinical, financial and business development personnel. We are highly dependent on our management, scientific and medical personnel, including Mai Britt Zocca, Ph. D., our Chief Executive Officer, Amy Sullivan, **M. B. A.,** our Chief Financial Officer ~~, Eva Ehrnrooth~~ **and Qasim Ahmad** , M ~~. D., Ph~~ . D., our Chief Medical ~~Officer, and Muhammad Al- Hajj, Ph. D., our Chief Scientific~~ Officer. Our senior management may terminate their employment with us at any time. We do not maintain " key person " insurance for any of our employees. Recruiting and retaining qualified scientific and clinical personnel and, if we progress the development of any of our product candidates, commercialization, manufacturing and sales and marketing personnel, will be critical to our success. The loss of the services of members of our senior management 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 members of our senior management and key employees may be difficult and may take an extended period of time because of 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 our product candidates. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid- level and senior managers, as well as junior, mid- level and senior scientific and medical personnel. Competition to hire from this limited candidate pool 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 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 strategy will be limited. We expect to expand our clinical 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. As of December 31, ~~2022~~ **2023** we had ~~42~~ **68** full- time employees ~~engaged in research and development activities~~ . As our development progresses, we expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of clinical product development, regulatory affairs, manufacturing and, if any of our product candidates receives marketing approval **, compliance** , 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. We face substantial competition, which may result in others discovering, developing or commercializing products more quickly or marketing them more successfully than us. The development and commercialization of new products is highly competitive. We expect to compete in the segments of the pharmaceutical, biotechnology and other related markets that pursue ~~immuno-~~ oncology treatments. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, 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 regulatory approval from the FDA or other comparable foreign regulatory authorities for their products more rapidly than we may obtain approval for ours, if ever, which could result in our competitors establishing a strong market position before we are able to enter the market or make our development more complicated. Moreover, with the proliferation of new drugs and therapies into oncology, we expect to face increasingly intense competition as new technologies become available. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. The highly competitive nature of and rapid technological changes in the biotechnology and pharmaceutical industries could render our product candidates or our technology obsolete, less competitive or uneconomical. Other products in a similar class as some of our product candidates have already been approved and other products in the same class are further along in development. As more product candidates within a particular class of biopharmaceutical products proceed through clinical development to regulatory review and approval, the amount and type of clinical data that may be required by regulatory authorities may increase or change. Consequently, the results of our clinical trials for product candidates in those classes will likely need to show a risk benefit profile that is competitive with or more favorable than those products and product candidates in order to obtain marketing approval or, if approved, a product label that is favorable for commercialization. If the risk benefit profile is not competitive with those products or product candidates, we may have developed a product that is not commercially viable, that we are not able to sell profitably or that is unable to achieve favorable pricing or reimbursement. In such circumstances, our future product revenue and financial condition would be materially and adversely affected. Specifically, there are many companies that have commercialized or are developing immuno- oncology treatments for cancer including large pharmaceutical and biotechnology companies such as Amgen Inc. (Amgen), AstraZeneca plc (AstraZeneca) ~~and its subsidiary, MedImmune, LLC (MedImmune)~~ , Bristol- Myers Squibb Company (BMS), Merck, Novartis AG (Novartis), Pfizer Inc. (Pfizer) **, Moderna, Regeneron,** and F. Hoffman- La Roche AG (Roche), and Roche' s subsidiary Genentech, Inc. (Genentech). In melanoma specifically, the dominant market players are nivolumab, marketed by BMS and Ono ~~Pharmaceutical Co.~~ , **combination of** ~~Ltd. (Ono),~~ nivolumab & ipilimumab, marketed by BMS and Ono, **combination of nivolumab and relatlimab (LAG- 3 blocking antibody) marketed by BMS** and pembrolizumab, marketed by Merck. We are also aware of several companies testing their compounds in combination with nivolumab or pembrolizumab. **In mid** ~~Select programs in late~~ stage development ~~include lymphocyte activation gene~~ **there is Moderna and Merck with an investigational personalized mRNA cancer vaccine, in combination with pembrolizumab and Regeneron testing their fianlimab anti** - ~~3 (LAG~~ **LAG3 in combination cmiplimab Anti** - **PD** ~~3) assets from BMS (relatlimab) and modified interleukin-~~ **1 in first line melanoma** ~~2 (IL- 2) assets from Nektar Therapeutics bempegaldesleukin)~~ . In earlier stage development there are also BioNTech ~~SE (BioNTech)~~ with NEO- PV- 01 and Karyopharm ~~Therapeutics, Inc. (Karyopharm)~~ with selinexor. Many of our competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, preclinical testing, clinical trials, manufacturing and marketing than we do. Future collaborations and mergers and acquisitions may result in further resource concentration among a smaller number of competitors. Smaller or early- stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors will also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or that maybe necessary for, our programs. The key competitive factors affecting the success of all of our programs are likely to be efficacy, safety, and convenience. If we are not successful in developing, commercializing and achieving higher levels of reimbursement than our competitors, we will not be able to compete against them and our business would be materially harmed. The tax authorities in the jurisdictions in which we operate may challenge our transfer pricing procedures. We are a multinational business that operates in Denmark and other tax jurisdictions, and the tax laws of those jurisdictions generally require that royalty and other payments between affiliated companies in different jurisdictions be the same as those between unrelated companies dealing at arm' s length, and that such prices are supported by contemporaneous documentation. While we believe that we operate in compliance with applicable transfer pricing laws and intend to continue to do so, our transfer pricing procedures are not binding on applicable tax authorities. If tax authorities in any of these jurisdictions were to successfully challenge our transfer prices as not reflecting arm' s length transactions, they could require us to adjust our transfer prices and thereby reallocate our income or deductions to reflect these revised transfer prices, which could result in a higher overall tax liability to us and possibly interest and penalties. Additionally, tax authorities in the jurisdictions in which we operate may challenge our treatment of ~~the~~ **our** ~~Corporate~~ **corporate** ~~Reorganization~~ **reorganization** . No assets (either physical or intangible) were transferred from Denmark to the U. S. pursuant to ~~the~~ **our** ~~Corporate~~ **corporate** ~~Reorganization~~ **reorganization** , nor ~~are~~ **were** any existing business functions or units operating from Denmark ~~being~~ transferred from IO Biotech ApS to IO Biotech, Inc. as part of the ~~Corporate~~ **corporate** ~~Reorganization~~ **reorganization** to form part of our U. S. operations. Accordingly, we did not intend to treat the ~~Corporate~~ **corporate** ~~Reorganization~~ **reorganization** as a deemed sale of

all or part of our business by IO Biotech ApS to IO Biotech, Inc. If Danish tax authorities were to disagree with our position and treat the ~~Corporate~~ **corporate** ~~Reorganization~~ **reorganization** or any of our activities thereafter as a deemed sale, in whole or in part, of intellectual property rights and / or other assets owned by IO Biotech ApS to IO Biotech, Inc., we could be subject to a Danish tax, the current rate of which is 22 %, on the gain realized calculated as the difference between the fair market value and the tax value of the assets, at the time of the deemed sale of the assets from Denmark as determined by the Danish tax authorities. Finally, the nature of our operations can produce conflicting claims from tax authorities in different countries as to the profits to be taxed in the individual countries. The jurisdictions in which we operate have double tax treaties with other jurisdictions, which provide a framework for mitigating the impact of double taxation on our revenues and capital gains. However, mechanisms developed to resolve such conflicting claims are largely untested, can be expected to be very lengthy, and do not always contain a mandatory dispute resolution clause. In recent years, tax authorities around the world have increased their scrutiny of company tax filings, and have become more rigid in exercising any discretion they may have. In general, tax reform efforts, including with respect to transfer pricing, will require us to continually assess our organizational structure and could lead to an increased risk of international tax disputes, an increase in our effective tax rate and an adverse effect on our financial condition. We have net operating losses to be carried forward, which may become devalued if we do not generate sufficient future taxable income, applicable corporate tax rates are reduced or if we experience an ownership change. Our total gross deferred tax assets as of December 31, ~~2022~~ **2023** were $ ~~35~~ **58** . ~~6~~ **4** million. Total gross deferred tax assets is comprised of $ ~~32~~ **53** . ~~8~~ **3** million, $ ~~2~~ **4** . ~~2~~ **5** million and $ 0. 6 million relating to IO Biotech ApS, IO Bio US, Inc. and IO Biotech, Inc., respectively. Our anticipated activities are also expected to result in future significant net operating losses in Denmark resulting in additional deferred tax assets. Utilization of most deferred tax assets is dependent on generating sufficient future taxable income in the appropriate jurisdiction and / or entity. The company has provided a valuation allowance of **(** $ ~~32~~ **53** . ~~7~~ **1)** million, $ ~~1~~ **(4** . ~~7~~ **3)** million and $ **(** 0. ~~6~~ **5)** million on our net deferred tax assets in IO Biotech ApS, IO Bio US, Inc. and IO Biotech, Inc., respectively, as of December 31, ~~2022~~ **2023** . Based on all available evidence, it is considered more likely than not that all the recorded deferred tax assets will not be realized in a future period. Additionally, most of our deferred tax assets are determined by reference to applicable corporate income tax rates in Denmark and the **United States** ~~U. S.~~ . Accordingly, in the event of a reduction of any such corporate income tax rates, the carrying value of certain of our deferred tax assets would decrease. Moreover, our ability to use our net operating losses and other deferred tax assets to offset future taxable income in Denmark and the U. S. may be limited if we experience an ownership change. We may experience ownership changes in the future as a result of our IPO or subsequent shifts in our stock ownership, some of which are outside the Company' s control. For Danish income tax purposes, an ownership change will generally occur when one, or several shareholders together, at once or successively, acquire shares representing more than 50 percent of the share capital or voting power. Although such an ownership change entails no reduction of the amount of net operating losses to be carried forward, the utilization is restricted to exclude offsetting against positive net capital income (e. g. income from interest, dividend and royalty) on net operating losses incurred in a previous income year, where the ownership differs by 50 percent (under section 12D of the Danish Corporate Tax Act). The restriction may limit future offsetting against net operating profits, when the ownership change is due to the listing on an exchange. For U. S. federal income tax purposes, an ownership change will generally occur when the percentage of our stock (by value) owned by one or more " 5 % shareholders " (as defined in the U. S. Internal Revenue Code of 1986, as amended) has increased by more than 50 % over the lowest percentage owned by such shareholders at any time during the prior three years (calculated on a rolling basis). We anticipate that we will incur losses in the United States in the foreseeable future related to our research and development activities. Due to potential ownership changes under Section 382 of the Code, we may be limited in our ability to realize a tax benefit from the use of such losses, whether or not we attain profitability in future years. In addition, our ability to utilize any future net operating losses may be limited by Pub. L. 115- 97, enacted in 2017 and commonly known as the Tax Cuts and Jobs Act of 2017 (TCJA). Under the TCJA, the amount of our net operating losses that we are permitted to deduct in any taxable year is limited to 80 % of our taxable income in such year, where taxable income is determined without regard to the net operating loss deduction itself, while allowing unused net operating losses to be carried forward indefinitely. For these reasons, a material devaluation in our deferred tax assets due to insufficient taxable income, lower corporate income tax rates or ownership change would have an adverse effect on our results of operations and financial condition. We may be subject to current taxation on some of the income of our foreign subsidiaries even absent any cash distributions. Because we hold directly or indirectly all of the shares of our foreign subsidiaries, including IO Biotech ApS, such subsidiaries are treated as controlled foreign corporations (CFC) for U. S. federal income tax purposes. For U. S. federal income tax purposes, IO Biotech, Inc. will therefore need to include in its taxable income each year its " global intangible low- taxed income " and IO Biotech ApS' s " subpart F income, " if any, even if no distributions are made. Our foreign subsidiaries may directly become subject to U. S. federal income tax and be subject to a branch profits tax in the United States, which could reduce our after- tax returns and the value of our shares. We currently intend to conduct substantially all of our businesses and operations in a manner such that our foreign subsidiaries will not be treated as engaged in a trade or business in the United States and will not be subject to additional U. S. income tax or branch profits tax. However, it is not entirely clear when a foreign subsidiary is treated as being engaged in a trade or business in the United States for U. S. federal income tax purposes. Accordingly, we cannot assure you that the Internal Revenue Service (IRS) will not contend, perhaps successfully, that our foreign subsidiaries were engaged in a trade or business in the United States or are subject to more U. S. income tax than they currently incur. A foreign corporation deemed to be so engaged would be subject to U. S. federal income tax on its income that is treated as effectively connected with the conduct of that trade or business, as well as to branch profits tax on its " dividend equivalent amount, " unless the corporation is entitled to relief under an applicable tax treaty, which is determined on an annual basis. Our business operations and current and future relationships with investigators, health care professionals, consultants, third- party payors and customers are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, transparency laws and other healthcare

laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties. Healthcare providers and others play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Although we do not currently have any products on the market, our operations and current and future arrangements with investigators, healthcare professionals, customers and third- party payors, may be subject to various U. S. federal and state healthcare laws and regulations, including, without limitation, the U. S. federal Anti- Kickback Statute, the U. S. federal civil and criminal false claims laws and the Physician Payments Sunshine Act and regulations. These laws may impact, among other things, our current business operations, including our clinical research activities, and proposed sales, marketing and education programs and constrain the business of financial arrangements and relationships with healthcare providers and other parties through which we may market, sell and distribute our products for which we obtain marketing approval. In addition, we may be subject to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. See Part I, Item 1, " Government Regulations – Other Regulatory Matters – Other Healthcare Laws " for additional detail. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including certain arrangements with physicians who receive stock, warrants or stock options as compensation for services provided to us, do not comply with current or future statutes, regulations, agency guidance 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 the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U. S. government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non- compliance with these laws and the delay, reduction, termination or restructuring of our operations. Further, defending against any such actions can be costly and time- consuming, and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations. Healthcare legislative reform measures may have a material adverse effect on our business and results of operations **.** The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our current product candidates and any future product candidates, restrict or regulate post- approval activities and affect our ability to profitably sell a product for which we obtain marketing approval. Changes in regulations, statutes or the interpretation of existing regulations could impact our business in the future by requiring, for example: (1) changes to our manufacturing arrangements; (2) additions or modifications to product labeling; (3) the recall or discontinuation of our products; or (4) additional record- keeping requirements. If any such changes were to be imposed, they could adversely affect the operation of our business. In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ACA was passed, which substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacted the U. S. pharmaceutical industry. The ACA, among other things, subjected biological products to potential competition by lower- cost biosimilars, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs and biologics that are inhaled, infused, instilled, implanted or injected, ~~and~~ increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program ~~and~~ **,** extended the rebate program to individuals enrolled in Medicaid managed care organizations, **and** established annual fees and taxes on manufacturers of certain branded prescription drugs and biologics. Since its enactment, there have been judicial, executive and Congressional challenges to certain aspects of the ACA. See Part I, Item 1, " Government Regulation – Healthcare Reform " for additional detail on recent challenges to the ACA. We expect that the ACA, new laws, and other healthcare reform measures that may be adopted in the future may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product. 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. We cannot predict the initiatives that may be adopted in the future. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or such third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability. **Upcoming changes in the pharmaceutical product legislation in certain jurisdictions may have an adverse effect on the data and market exclusivity available for our products. The EU Pharma Law Review initiated by the European Commission on April 6, 2023 could have a significant impact on the RDP available for innovative medicinal products in the EU. If adopted in current form, the EU Pharma Law Proposal would reduce the current baseline for data exclusivity from eight to six years, extendable under certain conditions. Such RDP reduction could lead to faster access to the EU market for generics and biosimilars. The EU Pharma Law Proposal also proposes changes the current orphan market exclusivity approach. If adopted in the current form, the EU Pharma Law Proposal would in most cases reduce the duration of orphan market exclusivity.** We are subject to a variety of privacy and data security laws, and our failure to comply with them could harm our business. We maintain a large quantity of sensitive information, including confidential business and personal information in connection with the conduct of our clinical trials and related to our employees, and we are subject to laws and regulations governing the privacy and security of such information. In the United States, there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure and protection of personal information, including federal and state health

information privacy laws, federal and state security breach notification laws, and federal and state consumer protection laws. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues, including with respect to regulatory enforcement and private litigation, which may affect our business and is expected to increase our compliance costs and exposure to liability. In the United States, numerous federal and state laws and regulations could apply to our operations or the operations of our partners, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations (e. g., Section 5 of the Federal Trade Commission (FTC) Act), that govern the collection, use, disclosure, and protection of health-related and other personal information. In addition, we may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that ~~are~~ **may be** subject to privacy and security requirements under HIPAA, as amended by HITECH and regulations promulgated thereunder. Depending on the facts and circumstances, we could be subject to significant penalties if we obtain, use, or disclose, or are subject to an actual or alleged data breach regarding, individually identifiable health information in a manner that is not authorized or permitted by HIPAA **. In 2023, the SEC finalized rules requiring enhanced disclosures regarding cybersecurity risk management, strategy, and governance, as well as the timely reporting of material cybersecurity incidents. These rules mandate disclosures about our processes for identifying, assessing, and managing cybersecurity risks, the role of management and the board of directors in overseeing these risks, and specific incidents that materially affect us** . In the EEA, we are subject to the EU GDPR, which took effect in May 2018. The EU GDPR governs the collection, use, disclosure, transfer or other processing of personal data (i. e., data which identifies an individual or from which an individual is identifiable), including clinical trial data, and grants individuals various data protection rights (e. g., the right to erasure of personal data). The EU GDPR imposes a number of obligations on companies, including inter alia: (1) accountability and transparency requirements, and enhanced requirements for obtaining valid consent; (2) obligations to consider data protection as any new products or services are developed and to limit the amount of personal data processed; (3) obligations to implement appropriate technical and organizational measures to safeguard personal data and to report certain personal data breaches to the supervisory authority without undue delay (and no later than 72 hours where feasible); and (4) additional, more onerous requirements around the processing of special categories of personal data (including health data and genetic data). In addition, the EU 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 EU (CJEU) in the Schrems II decision 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 use of the standard contractual clauses (SCCs), including a requirement for companies to carry out a transfer impact assessment, which among other things, assesses laws governing access to personal data in the recipient country and considers whether supplementary measures that provide privacy protections additional to those provided under SCCs will need to be implemented to ensure an essentially equivalent level of data protection to that afforded in the EEA. The European Commission subsequently issued new SCCs in June 2021 to account for the decision of the CJEU and recommendations made by the European Data Protection Board and which are in turn relatively more onerous. At present, there are few, if any, viable alternatives to the SCCs. However, on October 7, 2022, the Biden administration introduced an Executive Order to facilitate a new Trans- Atlantic Data Privacy Framework which will act as a successor to the invalidated EU- US Privacy Shield. On December 13, 2022, the European Commission also published its draft adequacy decision to reflect its view that the new Executive Order and Trans-Atlantic Data Privacy Framework, is able to meet the concerns raised in Schrems II. If the draft adequacy decision is approved and implemented, the agreement will facilitate the transatlantic flow of personal data and provide additional safeguards to data transfer mechanisms (including SCCs and Binding Corporate Rules) for companies transferring personal data from the EU to the US. However, before parties rely on the new framework, there are still legislative and regulatory steps that must be undertaken both in the US and in the EU. The EU GDPR imposes substantial fines for breaches and violations (up to the greater of € 20 million or 4 % of consolidated annual worldwide gross revenue), and confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the EU GDPR. The EU GDPR increases our responsibility and liability in relation to personal data that we process, and additional mechanisms put in place to address compliance with the EU GDPR must be kept under review as the legislative and regulatory landscape for data protection in the EU continues to evolve. Relatedly, following Brexit, the EU GDPR has been implemented in the United Kingdom (as the UK GDPR). The UK GDPR sits alongside the UK Data Protection Act 2018 which implements certain derogations in the EU GDPR into UK law. Under the UK GDPR, companies not established in the UK but that process personal data in relation to the offering of goods or services to individuals in the UK, or to monitor their behavior will be subject to the UK GDPR – the requirements of which are (at this time) largely aligned with those under the EU GDPR and as such, may lead to similar compliance and operational costs with potential fines of up to £ 17. 5 million or 4 % of global turnover. The UK Government has published its own form of SCCs, known as the International Data Transfer Agreement (~~the "~~ IDTA ~~"~~) and International Data Transfer Addendum (UK Addendum) to the EU SCCs. The UK Information Commissioner' s Office (~~the "~~ ICO ~~"~~) has also published its own version of the transfer impact assessment and recently revised guidance on international transfers, although entities may choose to adopt either the EU or UK style transfer impact assessment. In terms of international data transfers between the UK and US, it is understood that the UK and the US are also negotiating an adequacy agreement. Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time- intensive process, and we may be required to **devote additional resources to and** put in place additional mechanisms ensuring compliance with the new data protection **and disclosure** rules **. Despite our efforts to comply with these laws and regulations, the inherent complexity of data security and cyber threats, and the newness of some of these requirements, such as the SEC' s cybersecurity disclosure requirements, present a risk of non-**

compliance or insufficient disclosure, which could invite regulatory scrutiny and affect our operational and financial performance . Furthermore, the laws are not consistent, and compliance in the event of a widespread data breach is costly. In addition, states are constantly adopting new laws or amending existing laws, requiring attention to frequently changing regulatory requirements. For example, California enacted the California Consumer Privacy Act (the CCPA), which took effect on January 1, 2020, became enforceable by the California Attorney General on July 1, 2020, and was the first comprehensive state privacy law in the United States. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used by requiring covered companies to provide new disclosures to California consumers (as that term is broadly defined) and provide such consumers new ways to opt- out of certain sales of personal information. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Further, the California Privacy Rights Act (the CPRA), which further amended the CCPA, went into effect on January 1, 2023. The CCPA, as amended by the CPRA, imposes additional data protection obligations on 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 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 **went** ~~will go~~ into effect on January 1, 2023, and additional compliance investment and potential business process changes may be required. Although the CCPA currently exempts certain health- related information, including clinical trial data, the CCPA (as amended by the CPRA) may increase our compliance costs and potential liability. Similar laws have been adopted in other states ~~(for example Nevada, Virginia and Colorado)~~ or proposed in other states and at the federal level, and if passed, such laws may have potentially conflicting requirements that would make compliance challenging. For example ~~, on March 2, 2021~~ , the Nevada Privacy of Information Collected on the Internet from Consumers Act went into effect on October 1, 2021, the Virginia Consumer Data Protection Act went into effect on January 1, 2023, the Colorado Privacy Act ~~goes~~ **went** into effect on July 1, 2023, the Connecticut Data Privacy Act ~~goes~~ **went** into effect July 1, 2023, and the Utah Consumer Privacy Act ~~goes~~ **went** into effect December 31, 2023 **. Additionally, newly introduced state laws related to health privacy may result in additional compliance costs. For example, the state of Washington recently passed the " My Health My Data " Act, which will regulate " consumer health data, " defined as " personal information that is linked or reasonably linkable to a consumer and that identifies a consumer' s past, present, or future physical or mental health. " The " My Health My Data " Act provides exemptions for personal data used or shared in research, including data subject to 45 C. F. R. Parts 46, 50, and 56. Additionally, Nevada recently enacted a consumer health data privacy bill, and other states could adopt health- specific privacy laws that could impact our business** . The Federal Trade Commission (FTC) and many state attorneys general are interpreting existing federal and state consumer protection laws to impose evolving standards for the collection, use, dissemination and security of health- related and other personal information. For instance, the FTC has promulgated standards for fair information practices, which concern consumer notice, choice, security and access, and also require notice of certain health information breaches outside the HIPAA context. Privacy laws require us to publish statements that describe how we handle personal information and choices individuals may have about the way we handle their personal information. Violating individuals' privacy rights, publishing false or misleading information about security practices, or failing to take appropriate steps to keep individuals' personal information secure may constitute unfair or deceptive acts or practices in violation of Section 5 of the FTC Act. Additionally, the FTC ~~recently~~ published an advance notice of proposed rulemaking on commercial surveillance and data security ~~,~~ **in 2022** and **may** ~~is seeking comment on whether it should~~ implement new trade regulation rules or other regulatory alternatives concerning the ways in which companies (1) collect, aggregate, protect, use, analyze, and retain consumer data, as well as (2) transfer, share, sell, or otherwise monetize that data in ways that are unfair or deceptive **in the coming years** . Federal regulators, state attorneys general and plaintiffs' attorneys have been and will likely continue to be active in this space, and if we do not comply with existing or new laws and regulations related to patient health information, we could be subject to criminal or civil sanctions. Any actual or perceived failure by us to comply with applicable privacy and data security laws and regulations could result in regulatory investigations, reputational damage, orders to cease / change our processing of our data, enforcement notices, and / or assessment notices (for a compulsory audit). We may also face civil claims including representative actions and other class action type litigation (where individuals have suffered harm), potentially amounting to significant compensation or damages liabilities, as well as associated costs, diversion of internal resources, and reputational harm. Risks Related to Intellectual Property If we are unable to obtain and maintain sufficient intellectual property protection for our platform technologies and product candidates, or if the scope of the intellectual property protection is not sufficiently broad, our competitors could develop and commercialize products similar or identical to ours, and our ability to successfully commercialize our products may be adversely affected. We rely upon a combination of patents, know- how and confidentiality agreements to protect the intellectual property related to our products and technologies and to prevent third parties from copying and surpassing our achievements, thus eroding our competitive position in our market. Our success depends in large part on our ability to obtain and maintain patent protection for our T- win ~~technology~~ ® platform, product candidates and their uses, as well as our ability to operate without infringing the proprietary rights of others. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel discoveries and technologies that are important to our business. We cannot guarantee that our pending and future patent applications will result in patents being issued or that issued patents will afford sufficient protection of our product candidates or their intended uses against competitors, nor can there be any assurance that the patents issued will not be infringed, designed around, invalidated by third parties, or **that they** will effectively prevent others from commercializing competitive technologies, products or product candidates. Obtaining and enforcing patents is expensive and time- consuming, and we may not be able to file and prosecute all necessary or desirable patent applications or maintain and / or enforce patents that may issue based on our patent applications, at

a reasonable cost or in a timely manner ~~, including delays as a result of the COVID- 19 pandemic impacting our or our licensors' operations~~ . It is also possible that we will fail to identify patentable aspects of our research and development results before it is too late to obtain patent protection. Although we enter into non- disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, **CROs** ~~contract research organizations~~ , **CMOs** ~~contract manufacturers~~ , consultants, advisors and other third parties, any of these parties may breach these agreements and disclose such results before a patent application is filed, thereby jeopardizing our ability to seek patent protection. Composition of matter patents for biological and pharmaceutical product candidates often provide a strong form of intellectual property protection for those types of products, as such patents provide protection without regard to any method of use. However, we cannot be certain that the claims in our pending patent applications directed to composition of matter of our product candidates will be considered patentable by the United States Patent and Trademark Office (USPTO) or by patent offices in foreign countries, or that the claims in any of our issued patents will be considered valid and enforceable by courts in the United States or foreign countries. Method of use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products " off- label. " Although off- label prescriptions may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute. The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal, scientific, and factual questions and has in recent years been the subject of much litigation, resulting in court decisions, including **United States** Supreme Court decisions, which have increased uncertainties as to the ability to enforce patent rights in the future. The standards that the USPTO and its foreign counterparts use to grant patents are not always applied predictably or uniformly. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States, or vice versa. The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. For example, we may not be aware of all third- party intellectual property rights potentially relating to our product candidates or their intended uses, and as a result the impact of such third- party intellectual property rights upon the patentability of our own patents and patent applications, as well as the impact of such third- party intellectual property upon our freedom to operate, is highly uncertain. Patent applications in the United States and other jurisdictions are typically not published until 18 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 our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. As a result, the issuance, inventorship, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending patent applications may be challenged in patent offices in the United States and abroad. The issuance of a patent is not conclusive as to its inventorship, ownership, scope, validity or enforceability. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. For example, our pending patent applications may be subject to third- party pre- issuance submissions of prior art to the USPTO or our issued patents may be subject to post- grant review (PGR) proceedings, oppositions, derivations, reexaminations, interference or inter partes review proceedings, in the United States or elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such challenges may result in loss of exclusivity or in patent claims being narrowed, invalidated, or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. Any failure to obtain or maintain patent protection with respect to our product candidates or their uses could have a material adverse effect on our business, financial condition, results of operations and prospects. In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know- how that is not patentable, processes for which patents are difficult to enforce and any other elements of our discovery and development processes that involve proprietary know- how, information or technology that is not covered by patents. We may also rely on trade secret protection as temporary protection for concepts that may be included in a future patent filing. However, trade secret protection will not protect us from innovations that a competitor develops independently of our proprietary know how. If a competitor independently develops a technology that we protect as a trade secret and files a patent application on that technology, then we may not be able to patent that technology in the future, may require a license from the competitor to use our own know- how, and if the license is not available on commercially- viable terms, then we may not be able to launch our product. Although we require all of our employees to assign their inventions to us, and require all of our employees, consultants, advisors and any third parties who have access to our proprietary know- how, information or technology to enter into confidentiality agreements, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Furthermore, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent unauthorized material disclosure of our intellectual property to third parties, we will not be able to establish or maintain a competitive advantage in our market, and this scenario could materially adversely affect our business, financial condition and results of operations. Intellectual property rights do not necessarily address all potential threats to our

competitive advantage. The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example: • others may be able to make product candidates that are the same as or similar to ours but that are not covered by the claims of the patents that we own or have exclusively licensed; • we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed; • we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions; • others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights; • it is possible that noncompliance with the USPTO and foreign governmental patent agencies requirement for a number of procedural, documentary, fee payment and other provisions during the patent process can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction; • it is possible that our pending patent applications will not lead to issued patents; • issued patents that we own or have exclusively licensed may be revoked, modified, or held invalid or unenforceable, as a result of legal challenges by our competitors; • our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets; • we may not develop additional proprietary technologies that are patentable; • we cannot predict the scope of protection of any patent issuing based on our patent applications, including whether the patent applications that we own or in- license will result in issued patents with claims that directed to our product candidates or uses thereof in the United States or in other foreign countries; • there may be significant pressure on the U. S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; • countries other than the United States may have patent laws less favorable to patentees than those upheld by U. S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates; • the claims of any patent issuing based on our patent applications may not provide protection against competitors or any competitive advantages, or may be challenged by third parties; • if enforced, a court may not hold that our patents are valid, enforceable and infringed; • we may need to initiate litigation or administrative proceedings to enforce and / or defend our patent rights which will be costly whether we win or lose; • we may choose not to file a patent application in order to maintain certain trade secrets or know- how, and a third party may subsequently file a patent application covering such intellectual property; • we may fail to adequately protect and police our trademarks and trade secrets; and • the patents of others may have an adverse effect on our business, including if others obtain patents claiming subject matter similar to or improving that covered by our patents and patent applications. Should any of these or similar events occur, they could significantly harm our business, results of operations and prospects. If we fail to comply with our obligations imposed by any intellectual property licenses with third parties that we may need in the future, we could lose rights that are important to our business. We may in the future require licenses to third- party technology and materials. Such licenses may not be available in the future or may not be available on commercially reasonable terms, or at all, which could have a material adverse effect on our business and financial condition. We may rely on third parties from whom we license proprietary technology to file and prosecute patent applications and maintain patents and otherwise protect the intellectual property we license from them. We may have limited control over these activities or any other intellectual property that may be related to our in- licensed intellectual property. For example, we cannot be certain that such activities by these licensors will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. We may have limited control over the manner in which our licensors initiate an infringement proceeding against a third- party infringer of the intellectual property rights, or defend certain of the intellectual property that may be licensed to us. It is possible that the licensors' infringement proceeding or defense activities may be less vigorous than if we conduct them ourselves. Even if we acquire the right to control the prosecution, maintenance and enforcement of the licensed and sublicensed intellectual property relating to our product candidates, we may require the cooperation of our licensors and any upstream licensor, which may not be forthcoming. Therefore, we cannot be certain that the prosecution, maintenance and enforcement of these patent rights will be in a manner consistent with the best interests of our business. If we or our licensor fail to maintain such patents, or if we or our licensor lose rights to those patents or patent applications, the rights we have licensed may be reduced or eliminated and our right to develop and commercialize any of our product candidates that are the subject of such licensed rights could be adversely affected. In addition to the foregoing, the risks associated with patent rights that we license from third parties will also apply to patent rights we may own in the future. Further, if we fail to comply with our diligence, development and commercialization timelines, milestone payments, royalties, insurance and other obligations under our license agreements, we may lose our patent rights with respect to such agreement, which would affect our patent rights worldwide. Termination of our current or any future license agreements would reduce or eliminate our rights under these agreements and may result in our having to negotiate new or reinstated agreements with less favorable terms or cause us to lose our rights under these agreements, including our rights to important intellectual property or technology. Any of the foregoing could prevent us from commercializing our other product candidates, which could have a material adverse effect on our operating results and overall financial condition. In addition, intellectual property rights that we may in- license in the future may be sublicenses under intellectual property owned by third parties, in some cases through multiple tiers. The actions of our licensors may therefore affect our rights to use our sublicensed intellectual property, even if we are in compliance with all of the obligations under our license agreements. Should our licensors or any of the upstream licensors fail to comply with their obligations under the agreements pursuant to which they obtain the rights that are sublicensed to us, or should such agreements be terminated or amended, our ability to develop and commercialize our product candidates may be materially harmed. In the future, we may need to obtain additional licenses of third- party technology that may not be available to us or are available only on commercially unreasonable terms, and which may cause us to operate our business in a more costly or otherwise adverse

manner that was not anticipated. We currently own intellectual property directed to our product candidates and other proprietary technologies, including our T- win ~~technology~~ ® platform. Other pharmaceutical companies and academic institutions may also have filed or are planning to file patent applications potentially relevant to our business. From time to time, in order to avoid infringing these third- party patents, we may be required to license technology from additional third parties to further develop or commercialize our product candidates. Should we be required to obtain licenses to any third- party technology, including any such patents required to manufacture, use or sell our product candidates, such licenses may not be available to us on commercially reasonable terms, or at all. The inability to obtain any third- party license required to develop or commercialize any of our product candidates could cause us to abandon any related efforts, which could seriously harm our business and operations. The licensing or acquisition of third- party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third- party intellectual property rights we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Even if we are able to obtain a license under such intellectual property rights, any such license may be non- exclusive, which may allow our competitors to access the same technologies licensed to us. Moreover, some of our owned and in- licensed patents or patent applications or future patents may be co- owned with third parties. If we are unable to obtain an exclusive license to any such third- party co- owners' interest in such patents or patent applications, such co- owners may be able to license their rights to other third parties, including our competitors, and our competitors could market competing products and technology. In addition, we may need the cooperation of any such co- owners of our patents in order to enforce such patents against third parties, and such cooperation may not be provided to us. Furthermore, our owned and in- licensed patents maybe subject to a reservation of rights by one or more third parties. Any of the foregoing could have a material adverse effect on our competitive position, business, financial conditions, results of operations and prospects. If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates. Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates without infringing the intellectual property and other proprietary rights of third parties. Third parties may allege that we have infringed, misappropriated or otherwise violated their intellectual property. Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and, even if resolved in our favor, is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. In addition, patent holding companies that focus solely on extracting royalties and settlements by enforcing patent rights may target us. There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our product candidates. We cannot be certain that our product candidates and other proprietary technologies we may develop will not infringe existing or future patents owned by third parties. Third parties may assert infringement claims against us based on existing or future intellectual property rights. If we are found to infringe a third party' s intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing candidate product or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing candidate product or product. However, we may not be able to obtain any required 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. 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 investigational products 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. We cannot guarantee that any of our or our licensors' patent searches or analyses, including but not limited to the identification of relevant patents, analysis of the scope of relevant patent claims or determination of the expiration of relevant patents, are complete or thorough. We may not be aware of patents that have already been issued and that a third party, for example, a competitor in the fields in which we are developing our product candidates, might assert are infringed by our current or future product candidates, including claims to compositions, formulations, methods of manufacture or methods of use or treatment that cover our product candidates. It is also possible that patents owned by third parties of which we are aware, but which we do not believe are relevant to our product candidates and other proprietary technologies we may develop, could be found to be infringed by our product candidate. In addition, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates may infringe. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our product candidates or the use of our product candidates.. Our determination of the expiration date of any patent in the United States, Europe or elsewhere that we

consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our competitors in both the United States and abroad, many of which have substantially greater resources and have made substantial investments in patent portfolios and competing technologies, may have applied for or obtained or may in the future apply for and obtain, patents that will prevent, limit or otherwise interfere with our ability to make, use and sell our product candidates. The pharmaceutical and biotechnology industries have produced a considerable number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity may be difficult. For example, in the United States, proving invalidity in court requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents, and there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U. S. patent. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could have a material adverse effect on our business and operations. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. In addition, we may not have sufficient resources to bring these actions to a successful conclusion. We may choose to challenge the enforceability or validity of claims in a third party' s U. S. patent by requesting that the USPTO review the patent claims in an ex- parte re- exam, inter partes review or post- grant review proceedings. These proceedings are expensive and may consume our time or other resources. We may choose to challenge a third party' s patent in patent opposition proceedings in the European Patent Office (EPO), or other foreign patent office. The costs of these opposition proceedings could be substantial, and may consume our time or other resources. If we fail to obtain a favorable result at the USPTO, EPO or other patent office then we may be exposed to litigation by a third party alleging that the patent may be infringed by our product candidates or proprietary technologies. We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful. Competitors or other third parties may infringe our patents, trademarks or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Our pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non- enablement or insufficient written description. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. The outcome following legal assertions of invalidity and unenforceability is unpredictable. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent' s claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention, or decide that the other party' s use of our patented technology falls under the safe harbor to patent infringement under 35 U. S. C. § 271 (e) (1). An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Any of these occurrences could adversely affect our competitive business position, business prospects and financial condition. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks. Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock. Moreover, we cannot assure you that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings. Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties. Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our issued patent, any patents that may be issued as a result of our pending or future patent applications or other intellectual property rights, the risk- adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our stockholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non- litigious action or solution. We may be subject to claims that our employees, consultants, or independent contractors have wrongfully used or disclosed confidential information of third parties. We employ and may

employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and advisors do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that we or our employees, consultants, or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our future patents. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. There is no guarantee of success in defending these claims, and even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees. 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 product candidates. As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States could increase the uncertainties and costs, and may diminish our ability to protect our inventions, obtain, maintain, and enforce our intellectual property rights and, more generally, could affect the value of our intellectual property or narrow the scope of our owned and licensed patents. Patent reform legislation in the United States and other countries, including the Leahy- Smith America Invents Act (the Leahy- Smith Act), signed into law on September 16, 2011, could increase those uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy- Smith Act includes a number of significant changes to U. S. patent law. These include 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. These include allowing third- party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO administered post-grant proceedings, including post- grant review, inter partes review, and derivation proceedings. Further, because of a lower evidentiary standard in these USPTO post- grant proceedings compared to the evidentiary standard in United States federal courts necessary to invalidate a patent claim, a third party could potentially provide evidence in a USPTO proceeding sufficient for the USPTO to hold a claim invalid even though the same evidence would be insufficient to invalidate the claim if first presented in a district court action. Accordingly, a third party may attempt to use the USPTO procedures to invalidate our patent claims that would not have been invalidated if first challenged by the third party as a defendant in a district court action. Thus, the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. After March 2013, under the Leahy- Smith Act, the United States transitioned to a first inventor to file system in which, assuming that the other statutory requirements are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third- party was the first to invent the claimed invention. A third party that files a patent application in the USPTO after March 2013, but before we file an application covering the same invention, could therefore be awarded a patent covering an invention of ours even if we had made the invention before it was made by such third party. This will require us to be cognizant going forward of the time from invention to filing of a patent application, but circumstances could prevent us from promptly filing patent applications on our inventions. Since patent applications in the United States and most other countries are confidential for a period of time after filing or until issuance, we cannot be certain that we or our licensors were the first to either (i) file any patent application related to our product candidates and other proprietary technologies we may develop or (ii) invent any of the inventions claimed in our or our licensor' s patents or patent applications. Even where we have a valid and enforceable patent, we may not be able to exclude others from practicing the claimed invention where the other party can show that they used the invention in commerce before our filing date. Thus the Leahy- Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. 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. 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. For example, in the 2013 case Assoc. for Molecular Pathology v. Myriad Genetics, Inc., the U. S. Supreme Court held that certain claims to DNA molecules are not patentable. While we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U. S. Congress or the USPTO may impact the value of our patents. Obtaining and maintaining patent protection depends on compliance with various procedural, document submissions, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements. Periodic maintenance fees, renewal fees, annuities fees and various other governmental fees on patents and / or patent applications are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent and / or patent application. The USPTO and various foreign governmental patent agencies also require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse ~~, including due to the effect of the COVID- 19 pandemic on us or our patent maintenance vendors,~~ 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. Non- compliance 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. If we fail to maintain the patents and patent applications covering our product candidates, our competitive position would be adversely affected. Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time. The term of any individual patent depends on applicable law in the country where the patent is granted. In the United States, provided all maintenance fees are timely paid, a patent generally has a term of 20 years from its application filing date or earliest claimed non- provisional filing date. Extensions may be available under certain circumstances, but the life of a patent and, correspondingly, the protection it affords is limited. Even if we or our licensors obtain patents covering our product candidates, when the terms of all patents covering a product expire, our business may become subject to competition from competitive medications **or vaccines** , including generic medications **or vaccines** . Given the amount of time required for the development, testing and regulatory review and approval of new product candidates, patents protecting such candidates may expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. If we do not obtain patent term extension in the United States under the Hatch- Waxman Act and in foreign countries under similar legislation, thereby potentially extending the term of marketing exclusivity for our product candidates, our business may be harmed. In the United States, a patent that covers an FDA- approved drug or biologic may be eligible for a term extension designed to restore the period of the patent term that is lost during the premarket regulatory review process conducted by the FDA. Depending upon the timing, duration and conditions of FDA marketing approval of our product candidates, one or more of our U. S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, as amended (the Hatch- Waxman Act), which permits a patent term extension of up to five years for a patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. In Europe, our product candidates may be eligible for term extensions based on similar legislation. In either jurisdiction, however, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Even if we are granted such extension, the duration of such extension may be less than our request. If we are unable to obtain a patent term extension, or if the term of any such extension is less than our request, the period during which we can enforce our patent rights for that product will be in effect shortened and our competitors may obtain approval to market competing products sooner. The resulting reduction of years of revenue from applicable products could be substantial. We enjoy only limited geographical protection with respect to certain patents and we may not be able to protect our intellectual property rights throughout the world. Filing, prosecuting and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive, and even in countries where we have sought protection for our intellectual property, such protection can be less extensive than ~~those~~ in the United States. The requirements for patentability may differ in certain countries, particularly developing countries, and the breadth of patent claims allowed can be inconsistent. 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. In- licensing patents covering our product candidates in all countries throughout the world may similarly be prohibitively expensive, if such opportunities are available at all. And in- licensing or filing, prosecuting and defending patents even in only those jurisdictions in which we develop or commercialize our product candidates may be prohibitively expensive or impractical. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection or licensed patents to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but where enforcement is not as strong as that in the United States or Europe. These products may compete with our product candidates, and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States and Europe, and many companies have encountered significant difficulties in protecting and defending proprietary rights in such jurisdictions. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets or other forms of intellectual property, particularly those relating to biotechnology products, which could make it difficult for us to prevent competitors in some jurisdictions from marketing competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, are likely to result in substantial costs and divert our efforts and attention from other aspects of our business, and additionally could put ~~at risk~~ our or our licensors' patents **at risk** of being invalidated or interpreted narrowly, could increase the risk of our or our licensors' patent applications not issuing, or could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, while damages or other remedies may be awarded to the adverse party, which may be commercially significant. If we prevail, damages or other remedies awarded to us, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition in those

jurisdictions. In some jurisdictions **,** including **certain** European countries, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties under patents relevant to our business, or if we or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions. We may rely on trade secret and proprietary know- how which can be difficult to trace and enforce and, if we are unable to protect the confidentiality of our trade secrets, our business and competitive position ~~would~~ **could** be harmed. In addition to seeking patents for some of our technology and current product candidates or any future product candidates, we may also rely on trade secrets, including unpatented know- how, technology and other proprietary information, to maintain our competitive position. Elements of our current product candidates or any future product candidates, including processes for their preparation and manufacture, as well as our T- win ~~technology~~ **®** platform, may involve proprietary know- how, information, or technology that is not covered by patents, and thus for these aspects we may consider trade secrets and know- how to be our primary intellectual property. Any disclosure, either intentional or unintentional, by our employees, the employees of third parties with whom we share our facilities or third party consultants and vendors that we engage to perform research, clinical trials or manufacturing activities, or misappropriation by third parties (such as through a cybersecurity breach) of our trade secrets or proprietary information could enable competitors to duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Trade secrets and know- how can be difficult to protect. We require our employees to enter into written employment agreements containing provisions of confidentiality and obligations to assign to us any inventions generated in the course of their employment. We enter into written agreements that include confidentiality and intellectual property obligations to protect each party' s property, potential trade secrets, proprietary know- how, and information. We further seek to protect our potential trade secrets, proprietary know- how, and information in part, by entering into non- disclosure and confidentiality agreements with parties who are given access to them, such as our corporate collaborators, outside scientific collaborators, CROs, CMOs, consultants, advisors and other third parties. With our consultants, contractors, and outside scientific collaborators, these agreements typically include invention assignment obligations. 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. 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. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we would have no right to prevent them 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 or other third party, our competitive position would be harmed. We may become subject to claims challenging the inventorship or ownership of our patents and other intellectual property. We may be subject to claims that former employees, collaborators or other third parties have an interest in our patents or other intellectual property as an inventor or co- inventor. The failure to name the proper inventors on a patent application can result in the patents issuing thereon being unenforceable. Inventorship disputes may arise from conflicting views regarding the contributions of different individuals named as inventors, the effects of foreign laws where foreign nationals are involved in the development of the subject matter of the patent, conflicting obligations of third parties involved in developing our product candidates or as a result of questions regarding co- ownership of potential joint inventions. Litigation may be necessary to resolve these and other claims challenging inventorship and / or ownership. Alternatively, or additionally, we may enter into agreements to clarify the scope of our rights in such intellectual property. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. 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. Our licensors may have relied on third- party consultants or collaborators or on funds from third parties, such as the U. S. government, such that our licensors are not the sole and exclusive owners of the patents we may in- license in the future. If other third parties have ownership rights or other rights to our in- licensed patents, they may be able to license such patents to our competitors, and our competitors could market competing products and technology. This could have a material adverse effect on our competitive position, business, financial conditions, results of operations, and prospects. In addition, while it is our policy to require our employees and contractors who may be involved in the conception or 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, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self- executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations, and prospects. 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 current or future trademarks or trade names may be challenged, infringed, circumvented or declared generic or descriptive or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections of our applications by the USPTO or in other foreign jurisdictions. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our

trademarks, and our trademarks may not survive such proceedings. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected. We may license our trademarks and tradenames to third parties, such as distributors. Although these license agreements may provide guidelines for how our trademarks and tradenames may be used, a breach of these agreements or misuse of our trademarks and tradenames by our licensees may jeopardize our rights in or diminish the goodwill associated with our trademarks and trade names. Moreover, any name we have proposed to use with our product candidate in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. Similar requirements exist in Europe. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA (or an equivalent administrative body in a foreign jurisdiction) objects to any of our proposed proprietary product names, it may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Furthermore, in many countries, owning and maintaining a trademark registration may not provide an adequate defense against a subsequent infringement claim asserted by the owner of a senior trademark. At times, competitors or other third parties may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. If we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks. Risks Related to Our Common Stock The stock price of our common stock may be volatile or may decline regardless of our operating performance and you may lose all or part of your investment. The trading price of our common stock is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control, including limited trading volume. In addition to the factors discussed in this " Risk Factors " section and elsewhere in this Annual Report on Form 10- K, these factors include: • overall performance of the equity markets; • our operating performance and the performance of other similar companies; • ~~the~~ published opinions and third- party valuations by banking and market analysts; • results from our ongoing clinical trials and future clinical trials with our current and future product candidates or of our competitors; • adverse results or delays in clinical trials; • failure to commercialize our product candidates; • unanticipated serious safety concerns related to immuno- oncology or related to the use of our product candidates; • changes in our projected operating results that we provide to the public, our failure to meet these projections or changes in recommendations by securities analysts that elect to follow our common stock; • any delay in our regulatory filings for our product candidates and any adverse development or perceived adverse development with respect to the applicable regulatory authority' s review of such filings, including without limitation the FDA' s issuance of a " refusal to file " letter or a request for additional information; • regulatory or legal developments in the United States and other countries; • the level of expenses related to future product candidates or clinical development programs; • our failure to achieve product development goals in the timeframe we announce; • announcements of acquisitions, strategic alliances or significant agreements by us or by our competitors; • recruitment or departure of key personnel; • the economy as a whole and market conditions in our industry; • trading activity by a limited number of stockholders who together beneficially own a majority of our outstanding common stock; • the expiration of market standoff or contractual lock- up agreements; • the size of our public float; • political uncertainty and / or instability in the United States ~~; • the ongoing~~ and **throughout** ~~future impact of~~ the **world** ~~COVID- 19 pandemic and actions taken to slow its spread~~ ; and • any other factors discussed in this Annual Report on Form 10- K. In addition, the stock markets have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many immuno- oncology companies. Stock prices of many immuno- oncology companies have fluctuated in a manner unrelated or disproportionate to the operating performance of those companies. The trading prices for common stock of other biopharmaceutical companies have also been highly volatile as a result of the ~~COVID- 19 pandemic~~ **high inflation environment and geopolitical conflict in Ukraine and the Middle East** . In the past, stockholders have filed securities class action litigation following periods of market volatility. If we were to become involved in securities litigation, it could subject us to substantial costs, divert resources and the attention of management from our business and adversely affect our business. Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval. As of December 31, ~~2022~~ **2023** , our executive officers, directors, 5 % stockholders and their affiliates beneficially owned approximately ~~81~~ **93** . 7 % of our voting stock. Therefore, these stockholders will have the ability to influence us through their ownership positions. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders. If there are substantial sales of shares of our common stock, the price of our common stock could decline. The price of our common stock could decline if there are substantial sales of our common stock, particularly sales by our directors, executive officers and significant stockholders, or if there is a large number of shares of our common stock available for sale and the market perceives that sales will occur. As of December 31, ~~2022~~ **2023** , we had ~~28~~ **65** , ~~815~~ **880** , ~~267~~ **914** shares of common stock outstanding. Substantially all of our outstanding shares of common stock are currently able to be sold freely in the public market, subject to certain restrictions that may apply to shares of our common stock held by our affiliates **and by certain participants in our August 2023 private placement** . The market price of our common stock could decline as a result of the sale 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 their shares. Delaware law and provisions in our amended and restated certificate of incorporation and bylaws could make a

merger, tender offer or proxy contest difficult, thereby depressing the trading price of our common stock. Our amended and restated certificate of incorporation and bylaws contain provisions that could depress the trading price of our common stock by acting to discourage, delay or prevent a change of control of our company or changes in our management that the stockholders of our company may deem advantageous. These provisions ~~include~~ : • establish a classified board of directors so that not all members of our board of directors are elected at one time; • permit the board of directors to establish the number of directors and fill any vacancies and newly- created directorships; • provide that directors may only be removed for cause and only by the affirmative vote of the holders of at least a majority of the voting power of all then outstanding shares of our capital stock; • require super- majority voting to amend some provisions in our amended and restated certificate of incorporation and bylaws; • authorize the issuance of " blank check " preferred stock that our board of directors could use to implement a stockholder rights plan; • prohibit stockholders from calling special meetings of stockholders; • prohibit stockholder action by written consent, which requires all stockholder actions to be taken at a meeting of our stockholders; • provide that the board of directors is expressly authorized to make, alter or repeal our bylaws; • restrict the forum for certain litigation against us to Delaware; and • establish advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted upon by stockholders at annual stockholder meetings. Any provision of our amended and restated certificate of incorporation or bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock. Our amended and restated certificate of incorporation designates a state or federal court located within the state of Delaware as the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to choose the judicial forum for disputes with us or our directors, officers or employees. Our amended and restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, to the fullest extent permitted by law, the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf under Delaware law; (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders; (3) any action arising pursuant to any provision of the Delaware General Corporation Law (DGCL), our amended and restated certificate of incorporation or bylaws; (4) any other action asserting a claim that is governed by the internal affairs doctrine; or (5) any other action asserting an " internal corporate claim, " as defined in Section 115 of the DGCL, shall be the Court of Chancery of the State of Delaware (or, if the Court of Chancery does not have jurisdiction, the federal district court for the District of Delaware) in all cases subject to the court having jurisdiction over indispensable parties named as defendants. These exclusive- forum provisions do not apply to claims under the Securities Act or the Securities Exchange Act of 1934, as amended (the Exchange Act). To the extent that any such claims may be based upon federal law claims, Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder. Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. However, our amended and restated certificate of incorporation contains a federal forum provision which provides that unless the ~~company~~ **Company** consents in writing to the selection of an alternative forum, the federal district courts of the United States of America will be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Any person or entity purchasing or otherwise acquiring any interest in any of our securities shall be deemed to have notice of and consented to this provision. This exclusive forum provision may limit a stockholder' s ability to bring a claim in a judicial forum of its choosing for disputes with us or our directors, officers or other employees, which may discourage lawsuits against us and our directors, officers and other employees. If a court were to find the exclusive forum provision in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving the dispute in other jurisdictions, which could harm our results of operations. Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall. Additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner, we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders. Pursuant to ~~our~~ **the IO Biotech, Inc.** 2021 Equity Incentive Plan (the 2021 **Equity** Plan), **we are** ~~our management is~~ authorized to grant stock options and other equity- based awards to our employees, directors and consultants **. In addition** , ~~which~~ **pursuant to the IO Biotech, Inc. 2023 Inducement Award Plan (2023 Inducement Plan), we are eligible to grant stock options and other** equity- based awards **to employees as an inducement for them to join us. Equity- based awards granted under the 2021 Equity Plan and the 2023 Inducement Plan** would ~~also~~ cause dilution to our stockholders. The number of shares of our common stock reserved for issuance under ~~our~~ **the** 2021 **Equity** Plan will automatically increase on January 1 of each calendar year, starting on January 1, 2022 through January 1, 2031, by an amount equal to the lesser of (1) 4 % of the total number of shares of our common stock outstanding on the last day of the calendar month before the date of each automatic increase; or (2) a lesser number of shares determined by our board of directors prior to the applicable January 1st. If our board of directors elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, which could cause our stock price to fall **. The maximum number of shares reserved for issuance under the 2023 Inducement Plan is 1, 976, 427 shares** . We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any

return to stockholders will therefore be limited to the appreciation of their stock. 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 shares less attractive to investors. We are an " emerging growth company " as defined in the Jumpstart Our Business Startups Act (the JOBS Act), and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including: • 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 • not being required to hold a non- binding advisory vote on executive compensation or obtain stockholder approval of any golden parachute payments not previously approved. In addition, as an " emerging growth company " the JOBS Act allows us to delay adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements are made applicable to private companies, unless we later irrevocably elect not to avail ourselves of this exemption. We have elected to use this extended transition period under the JOBS Act. As a result, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or revised accounting standards that are applicable to public companies, which may make comparison of our financials to those of other public companies more difficult. We will remain an emerging growth company until the earliest of (1) the end of the fiscal year following the fifth anniversary of our initial public offering; (2) the last day of the fiscal year during which our annual gross revenues are $ 1. 235 billion or more; (3) the date on which we have, during the previous three- year period, issued more than $ 1. 0 billion in non- convertible debt securities; and (4) the end of any fiscal year in which the market value of our common stock held by non- affiliates exceeded $ 700. 0 million as of the end of the second quarter of that fiscal year. We are also a " smaller reporting company meaning that the market value of our stock held by non- affiliates is less than $ 700 million and our annual revenue was less than $ 100 million during the most recently completed fiscal year. Smaller reporting companies may take advantage of certain reduced disclosure obligations, including, among other things, providing only two years of audited financial statements in our Annual Report on Form 10- K, and, similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations regarding executive compensation. To the extent we take advantage of such reduced disclosure obligations, it may also make comparison of our financial statements with other public companies difficult or impossible. We will remain a smaller reporting company until the last day of the fiscal year in which (i) the market value of our common stock held by non- affiliates exceeds $ 250 million as of the end of that year' s second fiscal quarter and our annual revenues exceeds $ 100 million during such completed fiscal year, or (ii) the market value of our common stock held by non- affiliates exceeds $ 700 million, regardless of our annual revenue, as of the end of that year' s second fiscal quarter. Investors may find our common stock less attractive to the extent we ~~will~~ 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 more volatile. General Risk Factors We ~~will~~ incur significantly increased costs as a result of operating as a public company, and our management **is** ~~will be~~ required to devote substantial time to new compliance initiatives. As a public company, we ~~will~~ incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes- Oxley Act of 2002 **, as amended** (the Sarbanes- Oxley Act), as well as rules subsequently implemented by the SEC ~~,~~ and Nasdaq **,** have imposed various requirements on public companies. In July 2010, the Dodd- Frank Wall Street Reform and Consumer Protection Act (the Dodd- Frank Act) was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd- Frank Act that require the SEC to adopt additional rules and regulations in these areas such as " ~~say~~ **Say** on ~~pay~~ **Pay** " and proxy access. Recent legislation permits smaller " emerging growth companies " to implement many of these requirements over a longer period and up to five years from the pricing of our IPO. We **have** ~~intend to take~~ **taken** advantage of this new legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel ~~will~~ need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations ~~will~~ increase our legal and financial compliance costs and ~~will~~ make some activities more time- consuming and costlier **than when we were a private company** . For example, ~~we expect~~ these rules and regulations ~~to~~ make it more difficult and more expensive for us to obtain director and officer liability insurance ~~and we may be required to incur substantial costs to maintain our current levels of such coverage~~ . Failure to build our finance infrastructure and improve our accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies. As a public company, we operate in an increasingly demanding regulatory environment, which requires us to comply with the Sarbanes- Oxley Act, the regulations of Nasdaq, the rules and regulations of the SEC, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes- Oxley Act include establishing corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud. Commencing with our fiscal year ending December 31, 2022, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting in our Form 10- K filing for that **and each subsequent** year, as required by Section 404 of the Sarbanes- Oxley Act. Prior to our IPO, we were not required to test our

internal controls within a specified period and, as a result, we may experience difficulty in meeting these reporting requirements. For example, in connection with the audit of our financial statements for the years ended December 31, 2021 and 2020, we and our independent registered public accounting firm identified a material weakness in our internal control over financial reporting. This material weakness was not previously remediated, and in connection with the preparation of our consolidated financial statements for the year ended December 31, 2021, the Company identified an error, which resulted in a restatement as disclosed in our Current Report on Form 8- K filed on December 17, 2021. For the year ended December 31, 2022, this material weakness **was** ~~has been~~ remediated **and no additional material weaknesses were identified for the year ended December 31, 2023** , but we could experience further difficulty with internal control over financing reporting in the future. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system' s objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected. If we are not able to comply with the requirements of Section 404 of the Sarbanes- Oxley Act in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed, investors could lose confidence in our reported financial information and we could be subject to sanctions or investigations by Nasdaq, the SEC or other ~~regulatory~~ authorities. Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud. We are subject to the periodic reporting requirements of the Exchange Act. We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports 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. We believe that any 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 ~~. These limitations led to an error that the Company identified in connection with the preparation of our consolidated financial statements, which resulted in a restatement as disclosed in our Current Report on Form 8- K filed on December 17, 2021~~ . For example, our directors or executive officers could inadvertently fail to disclose a new relationship or arrangement causing us to fail to make any related party transaction disclosures. 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. Future changes in financial accounting standards or practices may cause adverse and unexpected revenue fluctuations and adversely affect our reported results of operations. Future changes in financial accounting standards may cause adverse, unexpected revenue fluctuations and affect our reported financial position or results of operations. Financial accounting standards in the United States are constantly under review and new pronouncements and varying interpretations of pronouncements have occurred with frequency in the past and are expected to occur again in the future. As a result, we may be required to make changes in our accounting policies. Those changes could affect our financial condition and results of operations or the way in which such financial condition and results of operations are reported. We intend to invest resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from business activities to compliance activities. See the section titled " Management' s Discussion and Analysis of Financial Condition and Results of Operations — Recent Accounting Pronouncements. " Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations. New income, sales, use, or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations, or ordinances could be interpreted, changed, modified, or applied adversely to us. For example, the TCJA enacted many significant changes to the U. S. tax laws. Future guidance from the IRS and other tax authorities with respect to the TCJA may affect us, and certain aspects of the TCJA could be repealed or modified in future legislation. For example, the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) modified certain provisions of the TCJA. In addition, it is uncertain if and to what extent various states will conform to the TCJA or any newly enacted federal tax legislation. For example, the U. S. government recently enacted the IRA which, among other things, significantly changes the taxation of certain business entities, including by imposing a 1 % excise tax on certain share buybacks, effective for tax years beginning in 2023. If and when applicable, it is possible that the 1 % excise tax on share buybacks could result in an additional tax liability over the regular federal corporate tax liability in a given year. Any resulting tax liability could adverse impact our business, financial condition, results of operation, and liquidity. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the TCJA or future reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one ~~-~~time charges, and could increase our future U. S. tax expense. In addition, ~~the~~ recent **and upcoming** presidential and congressional elections in the United States could also result in significant changes in, and uncertainty with respect to, tax legislation, regulation and government policy directly affecting us and our business. For example, the United States government may enact significant changes to the taxation of business entities including, among others, a permanent increase in the corporate income tax rate, an increase in the tax rate applicable to the global intangible low- taxed income and elimination of certain exemptions, and the imposition of minimum taxes or surtaxes on certain types of income. The likelihood of these changes being enacted or implemented is unclear. Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price. The global credit and financial markets have recently experienced extreme volatility and disruptions, including as a result of recent

developments in the U. S. banking sector ~~as well as~~ **and geopolitical conflict in Ukraine and** the **Middle East** ~~consequences of the COVID- 19 pandemic~~ , leading to increased inflation, diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, and uncertainty about economic and bank- system stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic downturn, which could directly affect our ability to attain our drug- candidate- development goals on schedule and on budget. We will have broad discretion in the use of our existing cash and cash equivalents and may not use them effectively or in ways that increase the value of our share price. We cannot specify with any certainty the particular uses of our existing cash and cash equivalents. We will have broad discretion in the application of our existing cash and cash equivalents, including working capital and other general corporate purposes, and you and other stockholders may disagree with how we spend or invest our cash and cash equivalents. The failure by our management to apply these funds effectively could adversely affect our business and financial condition. Pending their use, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value. These investments may not yield a favorable return to our investors. Our internal information technology systems, or those of our third- party CROs or other contractors or consultants, may fail or suffer security breaches, loss or leakage of data, and other disruptions, which could result in a material disruption of our product candidates' development programs, compromise sensitive information related to our business or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business. We are increasingly dependent upon information technology systems, infrastructure and data to operate our business. In the ordinary course of business, we collect, store and transmit confidential information (including but not limited to 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. We have also outsourced elements of our operations to third parties, and as a result we manage a number of third- party contractors who have access to our confidential information. Despite the implementation of security measures, given their size and complexity and the increasing amounts of confidential information that they maintain, our internal information technology systems and those of our third- party CROs and other contractors and consultants are potentially vulnerable to breakdown or other damage or interruption from service interruptions, system malfunction, natural disasters, terrorism, war and telecommunication and electrical failures, as well as security breaches from inadvertent or intentional actions by our employees, contractors, consultants, business partners, and / or other third parties, or from cyber- attacks by malicious third parties (including the deployment of harmful malware, ransomware, extortion, account takeover attacks, degradation of service attacks, denial- of- service attacks, " phishing, " or social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information), which may compromise our system infrastructure or lead to data leakage. We have technology security initiatives and disaster recovery plans in place to mitigate our risk to these vulnerabilities, but these measures may not be adequately designed or implemented to ensure that our operations are not disrupted or that data security breaches do not occur. 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 reputational damage. Hackers and data thieves are increasingly sophisticated and operate large- scale and complex automated attacks which may remain undetected until after they occur. We cannot assure you that our data protection efforts and our investment in information technology will prevent significant breakdowns, data leakages, breaches in our systems or other cyber incidents that could have a material adverse effect upon our reputation, business, operations or financial condition. For example, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs and the development of our product candidates could be delayed. In addition, the loss of clinical trial data for our product candidates could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. Furthermore, significant disruptions of our internal information technology systems or security breaches could result in the loss, misappropriation, and / or unauthorized access, use, or disclosure of, or the prevention of access to, confidential information (including trade secrets or other intellectual property, proprietary business information, and personal information), which could result in financial, legal, business, and reputational harm to us. Like all businesses we may be increasingly subject to ransomware or other malware that could significantly disrupt our business operations, or disable or interfere with necessary access to essential data or processes. Numerous recent attacks of this nature have also involved exfiltration and disclosure of sensitive or confidential personal or proprietary information, or intellectual property, when victim companies have not paid the cyber criminals substantial ransom payments. For example, any such event that leads to unauthorized access, use, disclosure, unavailability, or compromised integrity of personal or other sensitive or essential information, including personal information regarding our clinical trial subjects or employees, could harm our reputation directly, compel us to comply with federal and / or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, increase the costs we incur to protect against such information security breaches, such as increased investment in technology, render key personnel unable to perform duties or communicate throughout the organization and otherwise subject us to fines and other liability under laws and regulations that protect the privacy and security of personal information, which could result in significant legal and financial exposure and reputational damages that could potentially have an adverse effect on our business. The costs of mitigating cybersecurity risks are significant and are likely to increase in the future. These costs include, but are not limited to, retaining the services of cybersecurity providers; compliance costs arising out of existing and future cybersecurity, data protection and privacy laws and

regulations; and costs related to maintaining redundant networks, data backups and other damage- mitigation measures. We also cannot be certain that our existing insurance coverage will continue to be available on acceptable terms or in amounts sufficient to cover the potentially significant losses that may result from a security incident or breach or that the insurer will not deny coverage of any future claim. Our operations as a global company subject us to various risks, and our failure to manage these risks could adversely affect our business, results of operations, cash flows, financial condition and / or prospects. We face significant operational risks as a result of doing business globally, such as: • fluctuations in currency exchange rates (in particular, **between** U. S. dollars, Euros and Danish Kroner); • potentially adverse tax consequences, including the complexities of foreign value- added tax systems, tax inefficiencies related to our corporate structure, and potential restrictions on the repatriation of earnings; • export restrictions, trade regulations and foreign tax laws; • customs clearance and shipping delays; • the burdens of complying with a wide variety of foreign laws and different legal standards; and • increased financial accounting and reporting burdens and complexities. If one or more of these risks are realized, it could have a material adverse effect on our business, results of operations, cash flows, financial condition and / or prospect. Global economic and political instability and conflicts, such as the conflict ~~between~~ **in** Russia and Ukraine **and conflicts in the Middle East** , could adversely affect our business, financial condition or results of operations. Our business could be adversely affected by unstable economic and political conditions within the United States and foreign jurisdictions and geopolitical conflicts, such as the conflict **in** ~~between Russia and~~ Ukraine **and conflicts in the Middle East** . While we do not have any operations in ~~either country~~ **Russia or Ukraine** at this time, the current military conflict, and related sanctions, as well as export controls or actions that may be initiated by nations **and regions** including the United States, the **EU** ~~European Union~~ or Russia (e. g., potential cyberattacks, disruption of energy flows, disruptions to supply chains, etc.) and other potential uncertainties could adversely affect our business. **Certain of our clinical trial sites are located in Israel and conflicts in the Middle East may delay, limit or hinder ongoing, planned or future trials and affect enrollment and retention of patients. Inability to enroll or retain patients and limitations or delays in clinical trials could increase costs and cause setbacks in product development.** In the event geopolitical tensions fail to abate or deteriorate further, additional governmental sanctions may be enacted adversely impacting the global economy, which could adversely affect our business, financial condition or results of operations. We or the third parties upon whom we depend may be adversely affected by earthquakes, fires or other natural disasters **and / or terrorism** and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster. If earthquakes, fires, other natural disasters, terrorism and similar unforeseen events beyond our control prevent us from using all or a significant portion of our headquarters or other facilities, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. We do not have a disaster recovery or business continuity plan in place and may incur substantial expenses as a result of the absence or limited nature of our internal or third- party service provider disaster recovery and business continuity plans, which could have a material adverse effect on our business. In addition, the long- term effects of climate change on general economic conditions and the pharmaceutical manufacturing and distribution industry in particular are unclear, and changes in the supply, demand or available sources of energy and the regulatory and other costs associated with energy production and delivery may affect the availability or cost of goods and services, including raw materials and other natural resources, necessary to run our business. Furthermore, certain parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our ability to conduct our clinical trials, our development plans and business. We are subject to certain U. S. and foreign anti- corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations. We can face serious consequences for **any** violations **of such laws** . U. S. and foreign anti- corruption, anti- money laundering, export control, sanctions, and other trade laws and regulations (collectively, Trade Laws) prohibit, among other things, companies and their employees, agents, CROs, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government- affiliated hospitals, universities, and other organizations. We also expect to continue our non- U. S. activities, which may increase over time. We expect to rely on third parties for research, preclinical studies, and clinical trials and / or to obtain necessary permits, licenses, patent registrations, and other marketing approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities. If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business. We, and the third parties with whom we share our facilities, 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. Each of our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Each of 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. We could be held liable for any resulting damages in the event of contamination or injury resulting from the use of hazardous materials by us or the third parties with whom we share our facilities, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties. Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. ~~We~~ **Although we maintain general liability insurance, 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 **, and our general liability insurance may not probe sufficient coverage against any potential liabilities** . In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research and development. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions. We could be subject to securities class action litigation. 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 pharmaceutical 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. If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline. The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no or only very few securities analysts commence coverage of us, or if industry analysts cease coverage of us, the trading price for our common stock could be negatively affected. If one or more of the analysts who cover us downgrade our common stock or publish inaccurate or unfavorable research about our business, our common stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, demand for our common stock could decrease, which might cause our common stock price and trading volume to decline. Failure to meet investor and stakeholder expectations regarding environmental, social and corporate governance, or " ESG " matters may damage our reputation. There is an increasing focus from certain investors, employees and other stakeholders concerning ESG matters. Additionally, public interest and legislative pressure related to public companies' ESG practices continue to grow. If our ESG practices fail to meet investor, employee or other stakeholders' evolving expectations and standards for responsible corporate citizenship in areas including environmental stewardship, Board of Directors and employee diversity, human capital management, corporate governance and transparency, our reputation, brand, appeal to investors and employee retention may be negatively impacted, which could have a material adverse effect on our business or financial condition. ~~123~~ **121**