Risk Factors Comparison 2024-02-26 to 2023-02-28 Form: 10-K

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You should consider carefully these risk factors together with all of the information included or incorporated by reference in this Annual Report in addition to our financial statements and the notes to our financial statements. This section includes forward-looking statements. The following is a discussion of the risk factors that we believe are material to us at this time. These risks and uncertainties are not the only ones facing us, and there may be additional matters that we are unaware of or that we currently consider immaterial. All of these could adversely affect our business, results of operations, financial condition and cash flows. Summary of Risk Factors Risks Related to Our Financial Condition and Capital Requirements ● Risks related to our need for additional capital to fund our operations. ● Risks related to the Merger Agreement and related Settlement Agreement with Kolltan. ~~● Risks related to U. S. federal income tax reform.~~ Risks Related to Development and Regulatory Approval of Drug Candidates ● Risks related to our ability to fund and complete the research and development activities and obtain regulatory approval for our program assets. ● Risks related to the extensive **and lengthy** regulatory scrutiny to which we are subject. ● Risks related to our ability to commence, enroll, manage and complete our clinical trials. ● Risk of serious adverse or unacceptable side effects identified related to our drug candidates. ● We may enter collaboration agreements for our lead drug candidates that may not meet our expectations. Risks Related to Commercialization of Our Drug Candidates ● Risks related to delays, difficulties or unanticipated costs in establishing sales, marketing and distribution capabilities. ● Risks related to the acceptance of our drug candidates by physicians, patients and third- party payors. ● Risks related to reimbursement decisions by third- party payors. ● Risks, including the terms of FDA approval, that could affect the demand for and sales and profitability of any of our drug candidates. ● Risks related to the failure to obtain regulatory approvals in foreign jurisdictions and risks related to international operations if we do obtain regulatory approval in foreign jurisdictions. Risks Related to Reliance on Third Parties ● Risks related to our reliance on third parties. Risks Related to Business Operations ● Risks related to strategic transactions. ● Risks related to managing our growth. ● Risks related to our ability to integrate and modify our technologies to create new drugs. ● Risks related to computer systems that we and third parties use and potential security breaches. ● Risks related to hazardous materials. ● Risks related to product liability claims. ~~● Risks related to the global economy and supply chain disruptions.~~ Risks Related to Intellectual Property ● Risks related to intellectual property. Regulatory Risks ● Risks related to the regulatory approval process for our drugs. ● Risks related to changes in product candidate manufacturing or formulation. ● Risks related to our compliance with laws and regulations. Risks Related to Our Capital Stock ● Risks related to our history of losses and uncertainty of future profitability. ● Risks relates to the volatility of our common stock. ● Risks related to our use of our net operating loss carryforwards. General Risk Factors ● Risks related to internal controls over financial reporting. ● Risks that our competitors may develop technologies that make ours obsolete. ● Risks related to health epidemics and outbreaks. ● Risks related to the **global economy and supply chain disruptions. ● Risks related to the** loss of our key executives and scientists. ● Risks that our employees may engage in misconduct or other improper activities. ● Risks related to our compliance with the Nasdaq Listing Rules. ~~22Risks~~ -- **Risks** Related to Our Financial Condition and Capital RequirementsWe currently have no product revenue and will need to raise capital to operate our business. To date, we have generated no product revenue and cannot predict when and if we will generate product revenue. We had an accumulated deficit of $ 1. ~~3~~ **4** billion as of December 31, ~~2022~~ **2023** . Until, and unless, we complete clinical trials and other development activity, and receive approval from the FDA and other regulatory authorities, for our drug candidates, we cannot sell our drugs and ~~will~~ **23will** not have product revenue. We expect to spend substantial funds to continue the research, development and testing of our products that are in the preclinical and clinical testing stages of development and to prepare to commercialize products in anticipation of FDA approval. Therefore, for the foreseeable future, we will have to fund all of our operations and development expenditures from cash on hand, equity or debt financings, licensing fees and grants. Additional financing will be required to meet our liquidity needs. If we do not succeed in raising additional funds on acceptable terms, we might not be able to complete planned preclinical and clinical trials or obtain approval of any drug candidates from the FDA and other regulatory authorities. In addition, we could be forced to discontinue product development, reduce or forego sales and marketing efforts, forego attractive business opportunities or curtail operations. Any additional sources of financing could involve the issuance of our equity securities, which would have a dilutive effect on our stockholders. No assurance can be given that additional financing will be available to us when needed on acceptable terms, or at all. We cannot be certain that we will achieve or sustain profitability in the future. Failure to achieve profitability could diminish our ability to sustain operations, pay dividends on our common stock, obtain additional required funds and make required payments on our present or future indebtedness. We expect to incur future losses and we may never become profitable. We have incurred operating losses of $ **154. 5 million, $** 115. 2 million ~~,~~ **and** $ 71. 2 million ~~and $ 63. 4 million~~ during **2023,** 2022 ~~,~~ **and** 2021 ~~and 2020~~ , respectively, and expect to incur an operating loss in ~~2023~~ **2024** and beyond. We believe that operating losses will continue in ~~2023~~ **2024** and beyond because we are planning to incur significant costs associated with the development of our drug candidates. During the years ended December 31, **2023,** 2022 ~~,~~ **and** 2021 ~~and 2020~~ , we incurred $ **32. 4 million, $** 23. 8 million ~~,~~ **and** $ 8. 0 ~~million and $ 4. 9~~ million in clinical trial expense and $ **24. 1 million, $** 4. 5 million ~~,~~ **and** $ 1. 7 ~~million and $ 1. 2~~ million in contract manufacturing expense. Our net losses have had and will continue to have an adverse effect on, among other things, our stockholders' equity, total assets and working capital. We expect that losses will fluctuate from quarter to quarter and year to year, and that such fluctuations may be substantial. We cannot predict when we will become profitable, if at all. We will need additional capital to fund our operations, including the development, manufacture and potential commercialization of our drug

candidates. If we do not have or cannot raise additional capital when needed, we may be unable to develop and ultimately commercialize our drug candidates successfully. We expect to incur significant costs as we develop our drug candidates. The continuing development and commercialization of our drug candidates requires additional capital beyond our current resources. As of December 31, ~~2022~~ **2023** , we had cash, cash equivalents and marketable securities of $ ~~305~~ **423** . ~~0~~ **6** million. During the next twelve months and beyond, we will take further steps to raise additional capital to fund our long- term liquidity needs. Our capital raising activities may include, but may not be limited to, one or more of the following: ● licensing of drug candidates with existing or new collaborative partners; ● possible business combinations; ● issuance of debt; or ● issuance of common stock or other securities via private placements or public offerings. While we may seek capital through a number of means, there can be no assurance that additional financing will be available on acceptable terms, if at all, and our negotiating position in capital- raising efforts may worsen as existing resources are used. There is also no assurance that we will be able to enter into further collaborative relationships. Additional equity financing may be dilutive to our stockholders; debt financing, if available, may involve significant cash payment obligations and covenants that restrict our ability to operate as a business; and licensing or strategic collaborations may result in royalties or other terms which reduce our economic potential from drug candidates under development. If we are unable to raise the funds necessary to meet our liquidity needs, we may ~~23have~~ -- **have** to delay or discontinue the development of one or more programs, discontinue or delay ongoing or anticipated clinical trials, discontinue or delay our commercial manufacturing efforts, discontinue or delay our efforts to expand into additional indications for our drug product candidates, license out programs earlier than expected, raise funds at significant discount or on other unfavorable terms, if at all, or sell all or part of our business. ~~Our~~ **24Our** stockholders may be subject to substantial dilution if we elect to pay future milestone consideration to the former Kolltan stockholders in shares of common stock. If we elect to pay future milestone consideration in cash, we would likely need to raise additional capital. In connection with the agreement pursuant to which we acquired Kolltan in 2016 (the " Merger Agreement ") as modified by the definitive settlement agreement (the " Settlement Agreement ") we entered on July 15, 2022 related to litigation arising from the Kolltan merger, in the event that ~~certain specified milestones related to the successful completion of a Phase 2 clinical trial of CDX- 0159 or~~ regulatory approval by the United States Food and Drug Administration or European Medicines Agency of certain drug candidates are achieved, we will be required to pay to the former stockholders of Kolltan **a** milestone ~~payments~~ - **payment of $ 52, 500, 000** , which milestone ~~payments~~ - **payment** may be made, at our sole election, in cash, in shares of our common stock or a combination of both, subject to provisions of the Merger Agreement. ~~Pursuant to the Settlement Agreement, as of December 31, 2022 we may be obligated to make milestone payments of up to $ 65, 000, 000.~~ If we elect to issue shares of our common stock to make ~~these~~ **this** milestone ~~payments~~ - **payment** , you will experience further dilution. We may require additional capital to fund ~~any~~ **the** milestone ~~payments~~ - **payment** in cash, depending on the facts and circumstances at the time such ~~payments~~ - **payment** ~~become~~ **becomes** due. The number of shares of our common stock issuable in connection with a milestone payment, if any, will be determined based on the average closing price per share of our common stock for the five trading day period ending three calendar days prior to the achievement of such milestone. If we elect to pay the ~~Kolltan Milestones~~ - **milestone payment** in shares of our common stock, our stockholders would experience substantial dilution ~~. U. S. federal income tax reform could adversely affect us. On March 27, 2020, in response to COVID- 19, U. S. Congress enacted the Coronavirus Aid, Relief, and Economic Security Act (the " CARES Act "). The CARES Act modified the Tax Cuts and Jobs Act (" TCJA ") by, among other things, eliminating the limitation on the deduction of net operating losses to 80 % of current year taxable income for tax years beginning before January 1, 2021, and increasing the amount of interest expense that may be deducted from 30 % to 50 % of adjusted taxable income for tax years beginning in 2019 or 2020. We continue to examine the impact of this tax reform legislation, as well as any additional regulatory guidance that may be issued, may have on our business. For example, change of administration could result in additional tax legislative activity that could have a material adverse effect on the Company~~ . Risks Related to Development and Regulatory Approval of Drug CandidatesOur long- term success depends heavily on our ability to fund and complete the research and development activities and obtain regulatory approval for our program assets. Only a small minority of all research and development programs ultimately result in commercially successful drugs. Clinical failure can occur at any stage of clinical development. Clinical and preclinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical or preclinical trials. In addition, data obtained from trials are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a drug candidate. As part of development, we also must show that we can formulate and manufacture our product candidates in compliance with regulatory requirements. We will need substantial additional financing to complete the development of our drug candidates and comply with the regulatory requirements governing this process. Further, even if we complete the development of our drug candidates and gain marketing approvals from the FDA and comparable foreign regulatory authorities in a timely manner, we cannot be sure that such drug candidates will be commercially successful in the pharmaceutical market. If the results of clinical trials, the anticipated or actual timing of marketing approvals, or the market acceptance of any of our drug candidates, if approved, do not meet the expectations of investors or public market analysts, the market price of our common stock would likely decline. ~~24Our~~ -- **Our** drug candidates are subject to extensive regulatory scrutiny. All of our drug candidates are at various stages of development, and our activities and drug candidates are significantly regulated by a number of governmental entities, including the FDA in the United States and by comparable authorities in other countries. These entities regulate, among other things, the manufacture, testing, safety, effectiveness, labeling, documentation, advertising and sale of drugs and drug candidates. We or our partners must obtain regulatory approval for a drug candidate in all of these areas before we can commercialize any of our drug candidates. Product development within this regulatory framework takes a number of years and involves the expenditure of substantial resources. This process typically requires extensive preclinical and clinical testing, which

may take longer or cost more than we anticipate, and may prove unsuccessful due to numerous factors. Many drug candidates that initially appear promising ultimately do not reach the market because they are found to be unsafe or ineffective when tested. Companies in the pharmaceutical, biotechnology and immunotherapeutic drug industries have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier trials. Our inability to commercialize a drug candidate would impair our ability to earn future revenues. ~~If~~ **25Premarket review of our product candidates by the FDA and / or other regulatory authorities is a lengthy and uncertain process and approval may be delayed, limited or denied, any of which would adversely affect our ability to generate operating revenues. We are not permitted to market our drug product candidates in the United States until we receive approval of an application by the FDA. The time required to obtain approval by the FDA is unpredictable, but typically takes multiple years following the commencement of clinical trials, and depends upon numerous factors, including the substantial discretion of the FDA and the type, complexity and novelty of the product candidates involved. Similar processes are used in countries outside of the U. S. We have not submitted a marketing application such as BLA or NDA to the FDA or any similar application to any other regulatory authority in any jurisdiction. The FDA has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. For example, the FDA: ● could determine that the information provided by us as part of an IND or BLA / NDA is inadequate, contains clinical deficiencies or otherwise fails to demonstrate safety and effectiveness of any of our product candidates for any indication; ● may not find the data from pre- clinical and clinical trials sufficient to support the submission of a marketing application or to obtain marketing approval, including any findings that the safety risks outweigh clinical and other benefits of our product candidates; ● may require us to perform additional studies to demonstrate the safety, efficacy, pharmacokinetics, or other properties of our product candidates prior to approval, or require such studies as a condition of approval; ● may disagree with our clinical trial designs or our interpretation of data from product development manufacturing data, bioequivalence studies and / or clinical trials, or may change the requirements for approval even after it has reviewed and commented on the design for our trials; ● may identify deficiencies in the manufacturing processes or facilities of third- party manufacturers with which we enter into agreements for the supply of the API used in our product candidates; ● may identify deficiencies in our own manufacturing processes or our proposed scale- up of the manufacturing processes or facilities for the production of our product candidates; ● may approve our product candidates for fewer or more limited indications than we request, or may grant approval contingent on the performance of costly post- approval clinical trials; ● may change its approval policies or adopt new regulations; or ● may not approve the labeling claims that we believe are necessary or desirable for the successful commercialization of our product candidates. The time and expense of the approval process, as well as the unpredictability of future clinical trial results and other contributing factors, may result in our failure to obtain regulatory approval to market, in the United States or other jurisdictions, barzolvolimab and other drug candidates that we are developing or may seek to develop in the future, which would significantly harm our business, results of operations and prospects. In such case, we may also not have the resources to conduct new clinical trials and / or we may determine that further clinical development of any such drug candidate is not justified and may discontinue any such programs. 26If** our drug candidates do not pass required tests for safety and effectiveness, we will not be able to obtain regulatory approval and derive commercial revenue from them. In order to succeed, we will need to obtain regulatory approval for our drug candidates. The FDA has not approved any of our drug candidates for sale to date. Our drug candidates are in various stages of preclinical and clinical testing. Preclinical tests are performed at an early stage of a product' s development and provide information about a drug candidate' s safety and effectiveness before initiating human clinical trials. Preclinical tests can last years. If a product passes its preclinical tests satisfactorily and we determine that further development is warranted, we would file an IND application for the product with the FDA, and, if the FDA gives its approval, we would begin Phase 1 clinical tests. Phase 1 testing generally lasts between 6 and 24 months. If Phase 1 test results are satisfactory and the FDA gives its approval, we can begin Phase 2 clinical tests. Phase 2 testing generally lasts between 6 and 36 months. If Phase 2 test results are satisfactory and the FDA gives its approval, we can begin Phase 3 pivotal studies. Phase 3 studies generally last between 12 and 48 months. Once clinical testing is completed and a BLA or NDA is filed with the FDA, it may take more than a year to receive FDA approval. In all cases we must show that a drug candidate is both safe and effective before the FDA, or drug approval agencies of other countries where we intend to sell the product, will approve it for sale. Our research and testing programs must comply with drug approval requirements both in the United States and in other countries, since we are developing our drug candidates with the intention to, or could later decide to, commercialize them both in the U. S. and abroad. A product may fail for safety or effectiveness at any stage of the testing process. A major risk we face is the possibility that none of our products under development will come through the testing process to final approval for sale, with the result that we cannot derive any commercial revenue from them after investing significant amounts of capital in multiple stages of preclinical and clinical testing. Success in early clinical trials does not ensure that later clinical trials will be successful, and we cannot assure you that any of the clinical trials that we may conduct will demonstrate consistent or adequate efficacy and safety to obtain regulatory approval. The results of preclinical studies and early clinical trials may not be predictive of the results of later- stage clinical trials, and interim results of a clinical trial do not necessarily predict final results. Preclinical and clinical data are susceptible to various interpretations and analyses, and many companies that have believed their drug candidates performed satisfactorily in preclinical studies and early- stage clinical trials have nonetheless failed to replicate such results in later- stage clinical trials and subsequently failed to obtain marketing approval. Drug candidates in later- stage clinical trials may fail to show the desired safety and efficacy despite having progressed through preclinical and initial clinical trials, even if certain analyses of primary or secondary endpoints in those early trials showed trends towards efficacy. Later- stage clinical trials with larger numbers of patients or longer durations of therapy may also reveal safety concerns that were not identified in earlier smaller or shorter trials. Our failure to demonstrate efficacy

and safety data sufficient to support marketing approval for any of our other drug candidates would substantially harm our business, prospectus, financial condition and results of operations. Product testing is critical to the success of our drug candidates but subject to delay or cancellation if we have difficulty enrolling patients. As our portfolio of drug candidates moves from preclinical testing to clinical testing, and then through progressively larger and more complex clinical trials, we will need to enroll an increasing number of patients with the appropriate characteristics. At times we ~~25have --~~ **have** experienced difficulty enrolling patients, and we may experience more difficulty as the scale of our clinical testing program increases. The factors that affect our ability to enroll patients are largely uncontrollable and include principally the following: ● the nature of the clinical test; ● the size of the patient population; ● patients' willingness to receive a placebo or less effective treatment on the control arm of a clinical study; ● the distance between patients and clinical test sites; and ● the eligibility criteria for the trial. If we cannot enroll patients as needed, our costs may increase, or we may be forced to delay or terminate testing for a product. ~~We~~ **27We** may have delays in commencing, enrolling and completing our clinical trials, and we may not complete them at all. We have not completed the clinical trials necessary to obtain FDA approval to market any of our drug candidates in development. Clinical trials for our products in development may be delayed or terminated as a result of many factors, including the following: ● inability to reach agreements on acceptable terms with prospective contract research organizations (CROs) and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites; ● difficulty in enrolling patients in our clinical trials; ● inability to maintain necessary supplies of study drug and comparator to maintain predicted enrollment rates at clinical trial sites; ● patients failing to complete clinical trials due to dissatisfaction with the treatment, side effects or other reasons; ● failure by regulators to authorize us to commence a clinical trial; ● suspension or termination by regulators of clinical research for many reasons, including concerns about patient safety, bias or failure of our contract manufacturers to comply with cGMP requirements; ● delays or failure to obtain clinical supply for our products necessary to conduct clinical trials from contract manufacturers, including commercial grade- clinical supply for our Phase 3 clinical trials; ● inability to identify and maintain a sufficient number of trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indication as our product candidates; ● drug candidates demonstrating a lack of efficacy during clinical trials; ● inability to continue to fund clinical trials or to find a partner to fund the clinical trials; ● competition with ongoing clinical trials and scheduling conflicts with participating clinicians; and ● delays in completing data collection and analysis for clinical trials. Any delay or failure to commence, enroll or complete clinical trials, fulfill regulatory requirements and obtain FDA approval for our drug candidates could have a material adverse effect on our cost to develop and commercialize, and our ability to generate revenue from, a particular drug candidate. ~~26If~~ **If** serious adverse or unacceptable side effects are identified during the development of our drug candidates, such events could prevent us from obtaining regulatory approval or achieving market acceptance of our drug candidates, and we may need to abandon or limit our development of some of our drug candidates. If our drug candidates are associated with serious adverse events or undesirable side effects in clinical trials or have characteristics that are unexpected, such events could prevent us from obtaining regulatory approval or achieving market acceptance of our drug candidates, and we may need to abandon their development or limit development to more narrow uses or subpopulations in which the serious adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk- benefit perspective. In pharmaceutical development, many drugs that initially show promise in early- stage testing are later found to cause side effects that prevent further development of the drug. Currently marketed therapies for the treatment of cancer and inflammatory diseases are generally limited to some extent by their toxicity. In addition, some of our drug candidates would be chronic therapies or be used in pediatric populations, for which safety concerns may be particularly important. Use of our drug candidates as monotherapies may also result in adverse events consistent in nature with those associated with other marketed therapies. In addition, when used in combination with other marketed therapies, our drug candidates may exacerbate adverse events associated with the marketed therapy. ~~Our~~ **28Our** drug candidates, including barzolvolimab, are monoclonal antibodies, which are biologics. Side effects from biologics may include hypersensitivity; severe reactions such as anaphylaxis or cytokine release syndrome; immune- mediated adverse reactions that may occur in any organ system or tissue, such as pneumonitis, colitis, hepatitis, endocrinopathies, nephritis, and dermatologic reactions; as well as infusion- related reactions, cellulitis, sepsis, pneumonia, urinary tract infection, fatigue, rash, and diarrhea. Most biologics, including ~~some of~~ our drug candidates, are injected, either subcutaneously or intravenously. There are risks inherent in subcutaneous injections, such as injection- site reactions (including redness, itching, swelling, pain, and tenderness) and other side effects. In addition, there are risks inherent in intravenous administration such as infusion- related reactions (including nausea, pyrexia, rash, and dyspnea). These and other complications or side effects could harm further development and / or commercialization of our antibody- based products and product candidates utilizing this method of administration. In addition to the safety, efficacy, manufacturing, and regulatory hurdles faced by our product candidates, the administration of biologics frequently causes an immune response, sometimes resulting in the creation of antibodies against the drug candidate which can impact the safety and / or efficacy associated with the treatment. We may expend our resources to pursue a particular drug candidate or indication and forgo the opportunity to capitalize on drug candidates or indications that may ultimately be more profitable or for which there is a greater likelihood of success. Because we have limited financial and managerial resources, we intend to focus on developing drug candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for regulatory approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that may prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially viable drug candidates. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug 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 the drug candidate. We may be unable to manage multiple late- stage clinical trials for a variety of drug candidates simultaneously. As our current clinical trials progress, we may need to manage multiple late- stage clinical trials simultaneously in order to continue developing all of our current products. The management of late- stage clinical trials is more complex and time consuming than early- stage trials. Typically, early- stage trials involve several hundred patients in no more than 10 to 30 clinical sites. Late- stage (Phase 3) trials may involve up to several thousand patients in up to several hundred clinical sites and may require facilities in several countries. Therefore, the project management required to supervise and control such an extensive program in a compliant manner is substantially larger than early- stage programs. As the need for these resources is not known until some months before the trials begin, it is necessary to recruit large numbers of experienced and talented individuals very quickly. If the labor market does not allow this ~~27team --~~ **team** to be recruited quickly, ~~the sponsor is~~ **we could be** faced with a decision to delay the program or to initiate it with inadequate management resources. This may result in recruitment of inappropriate patients, inadequate monitoring of clinical investigators and inappropriate handling of data or data analysis. Consequently, it is possible that conclusions of efficacy or safety may not be acceptable to permit filing of a BLA or NDA for any one of the above reasons or a combination of several. Failure to successfully validate, develop and obtain regulatory approval for companion diagnostics for our drug candidates, if needed, could harm our drug development strategy and operational results. As an element of our clinical development approach, we may seek to screen and identify subsets of patients that express a certain biomarker or that have a certain genetic alteration who may derive meaningful benefit from our development drug candidates. To achieve this, one or more of our drug development programs may be dependent on the development and commercialization of a companion diagnostic by us or by third- party collaborators. Companion diagnostics are developed in conjunction with clinical programs for the associated drug candidate. Companion diagnostics are subject to regulation as medical devices and must themselves be approved for marketing by the FDA or certain other foreign regulatory agencies before the related drug candidate may be commercialized. The approval of a companion diagnostic as part of the product label will limit the use of the drug candidate to only those patients who express the specific biomarker it was developed to detect. We or our third- party collaborators may also experience ~~delays~~ **29delays** in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners or negotiating insurance reimbursement for such companion diagnostic, all of which may prevent us from completing our clinical trials or commercializing our drugs on a timely or profitable basis, if at all. We and our third- party collaborators may encounter difficulties in developing and obtaining approval for these companion diagnostics. Any delay or failure by us or third- party collaborators to develop or obtain regulatory approval of a companion diagnostic could delay or prevent approval of our related drug candidates or, if regulatory approval is obtained, delay or limit our ability to commercialize our related drug candidates. Any delay in obtaining regulatory approval would have an adverse impact on our ability to earn future revenues. It is possible that none of the drug candidates that we develop will obtain the regulatory approvals necessary for us to begin commercializing them. The time required to obtain FDA and other approvals is unpredictable but in general takes years following the commencement of clinical trials, depending upon the nature of the drug candidate. Any analysis we perform of data from clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular drug candidate including, but not limited to, loss of patent term during the approval period. Furthermore, if we, or our partners, do not reach the market with our products before our competitors offer products for the same or similar uses, or if we, or our partners, are not effective in marketing our products, our revenues from product sales, if any, will be reduced. We face intense competition in our development activities. We face competition from many companies in the United States and abroad, including a number of large pharmaceutical companies, firms specialized in the development and production of vaccines, adjuvants and vaccine and immunotherapeutic delivery systems and major universities and research institutions. Most of our competitors have substantially greater resources, more extensive experience in conducting preclinical studies and clinical testing and obtaining regulatory approvals for their products, greater operating experience, greater research and development and marketing capabilities and greater production capabilities than those of ours. These companies might succeed in obtaining regulatory approval for competitive products more rapidly than we can for our products, especially if we experience any delay in obtaining required regulatory approvals. We may enter into collaboration agreements for the licensing, development and ultimate commercialization of some of our drug candidates including, where appropriate, for our lead drug candidates. In such cases, we will depend greatly on our third- party collaborators to license, develop and commercialize such drug candidates, and they may not meet our expectations. We may enter into co- development and commercialization partnerships for our drug candidates where appropriate. The process of identifying collaborators and negotiating collaboration agreements for the licensing, development and ultimate commercialization of some of our drug candidates may cause delays and increased costs. We may not be able to enter into collaboration agreements on terms favorable to us or at all. Furthermore, some of those agreements may give substantial responsibility over our drug candidates to the collaborator. Some collaborators may be unable or unwilling to devote sufficient resources to develop our drug candidates as their agreements require. They often face business risks similar to ours, and this could interfere with their efforts. Also, collaborators may ~~28choose --~~ **choose** to devote their resources to products that compete with ours. If a collaborator does not successfully develop any one of our products, we will need to find another collaborator to do so. The success of our search for a new collaborator will depend on our legal right to do so at the time and whether the product remains commercially viable. If we enter into collaboration agreements for one or more of our lead drug candidates, the success of such drug candidates will depend in great part upon our and our collaborators' success in promoting them as superior to other treatment alternatives. We believe that our drug candidates can be proven to offer disease treatment with notable advantages over drugs in terms of patient compliance and effectiveness. However, there can be no assurance that we will be able to prove these advantages or that the advantages will be sufficient to support the successful commercialization of our drug

candidates. ~~Risks~~ **30Risks** Related to Commercialization of Our Drug CandidatesWe may face delays, difficulties or unanticipated costs in establishing sales, marketing and distribution capabilities or seeking a partnership for the commercialization of our drug candidates, even if regulatory approval is obtained. We may retain full economic rights to our drug candidates or seek favorable economic terms through advantageous commercial partnerships. As a result, we may have full responsibility for commercialization of one or more of our drug candidates if and when they are approved for sale. We currently lack sufficient marketing, sales and distribution capabilities to carry out this strategy. If any of our drug candidates are approved by the FDA, we will need a drug sales force with technical expertise prior to the commercialization of any of our drug candidates. We may not succeed in developing such sales and distribution capabilities, the cost of establishing such sales and distribution capabilities may exceed any product revenue, or our direct marketing and sales efforts may be unsuccessful. We may find it necessary to enter into strategic partnerships, co- promotion or other licensing arrangements. To the extent we enter into such strategic partnerships, co- promotion or other licensing arrangements, our product revenues are likely to be lower than if we directly marketed and sold such drugs, and some or all of the revenues we receive will depend upon the efforts of third parties, which may not be successful and may not be within our control. If we are unable to enter into such strategic partnerships, co- promotion or other licensing arrangements on acceptable terms or at all, we may not be able to successfully commercialize our existing and future drug candidates. If we are not successful in commercializing any drug candidates for which we obtain regulatory approval, either on our own or through collaborations with one or more third parties, our future product revenue will suffer, and we may never achieve profitability or become unable to continue the operation of our business. If our drug candidates for which we obtain regulatory approval do not achieve broad acceptance from physicians, patients and third- party payors, we may be unable to generate significant revenues, if any. Even if we obtain regulatory approval for our drug candidates, our approved drugs may not gain market acceptance among physicians and patients. We believe that effectively marketing our drug candidates, if any of them are approved, will require substantial efforts, both prior to commercial launch and after approval. Physicians may elect not to prescribe our drugs, and patients may elect not to request or take them, for a variety of reasons, including: ● limitations or warnings contained in a drug' s FDA- approved labeling; ● changes in the standard of care or the availability of alternative drugs for the targeted indications for any of our drug candidates; ● limitations in the approved indications for our drug candidates; ● the approval, availability, market acceptance and reimbursement for the companion diagnostic, where applicable; ● demonstrated clinical safety and efficacy compared to other drugs; ● significant adverse side effects; ● effectiveness of education, sales, marketing and distribution support; ● timing of market introduction and perceived effectiveness of competitive drugs; ~~29~~ ● cost- effectiveness; ● adverse publicity about our drug candidates or favorable publicity about competitive drugs; ● convenience and ease of administration of our drug candidates; and ● willingness of third- party payors to reimburse for the cost of our drug candidates. If our future drugs fail to achieve market acceptance, we will not be able to generate significant revenues and may never achieve profitability. ~~Even~~ **31Even** if any of our drug candidates receive FDA approval, the terms of the approval may limit such drug' s commercial potential. Additionally, even after receipt of FDA approval, such drug would be subject to substantial, ongoing regulatory requirements. The FDA has complete discretion over the approval of our drug candidates. If the FDA grants approval, the scope of the approval may limit our ability to commercialize such drug, and in turn, limit our ability to generate substantial product revenue. For example, the FDA may grant approval contingent on the performance of costly post- approval clinical trials or subject to warnings or contraindications or under a Risk Evaluation and Mitigation Strategy (REMS) drug safety program. Additionally, even after granting approval, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for such drug will be subject to extensive and ongoing regulatory requirements. In addition, manufacturers of our drug candidates are required to comply with cGMP regulations, which include requirements related to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Further, regulatory authorities must inspect and approve these manufacturing facilities before they can be used to manufacture our drug candidates, and these facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. If we or a third party discover previously unknown problems with a drug, such as adverse events of unanticipated severity or frequency, or problems with the facility where the drug is manufactured, a regulatory authority may impose restrictions on that product, the manufacturer or us, including requiring withdrawal of the drug from the market or suspension of manufacturing. If we, our drug candidates or the manufacturing facilities for our drug candidates fail to comply with regulatory requirements of the FDA and / or other non- U. S. regulatory authorities, we could be subject to administrative or judicially imposed sanctions, including the following: ● warning letters; ● civil or criminal penalties and fines; ● injunctions; ● consent decrees; ● suspension or withdrawal of regulatory approval; ● suspension of any ongoing clinical studies; ● voluntary or mandatory product recalls and publicity requirements; ● refusal to accept or approve applications for marketing approval of new drugs; ● restrictions on operations, including costly new manufacturing requirements; or ● seizure or detention of drugs or import bans. The regulatory requirements and policies may change, and additional government regulations may be enacted with which we may also be required to comply. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. If we are not able to maintain regulatory compliance, we may not be permitted to market our future products and our business may suffer. ~~30Reimbursement~~ **32Reimbursement** decisions by third- party payors may have an adverse effect on pricing and market acceptance of any of our drug candidates. If there is not sufficient reimbursement for our future drugs, it is less likely that such drugs will be widely used. Market acceptance and sales of any of our drug candidates for which we obtain regulatory approval will depend on reimbursement policies and may be affected by future health care reform measures in both the United States and foreign jurisdictions. Government authorities and third- party payors, such as private health insurers and health maintenance organizations, decide which drugs they will cover and establish payment levels. In addition, government authorities and these third- party payors are increasingly attempting to contain health care costs by demanding price discounts or rebates and limiting

both the types and variety of drugs that they will cover and the amounts that they will pay for these drugs. In addition, we might need to conduct post- marketing studies in order to demonstrate the cost- effectiveness of any future drugs to such payors' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on payments allowed for lower- cost products that are already reimbursed, may be incorporated into existing payments for other products or services and may reflect budgetary constraints and / or imperfections in Medicare or Medicaid data used to calculate these rates. Net prices for drugs may be reduced by mandatory discounts or rebates required by government health care programs. Such programs, or regulatory changes or relaxation of laws that restrict imports of drugs from other countries, could reduce the net price we receive for any future marketed drugs. In addition, our future drugs might not ultimately be considered cost- effective. We cannot be certain that reimbursement will be available for any drug candidates that we develop. Also, we cannot be certain that reimbursement policies will not reduce the demand for, or the price paid for, any future drugs. If reimbursement is not available or is available on a limited basis, we may not be able to successfully commercialize any drug candidates that we develop. Other factors could affect the demand for and sales and profitability of any drug candidates that we may commercialize in the future. In general, other factors that could affect the demand for and sales and profitability of our future drugs include, but are not limited to: ● the timing of regulatory approval, if any, of competitive drugs; ● our or any other of our partners' pricing decisions, as applicable, including a decision to increase or decrease the price of a drug, and the pricing decisions of our competitors; ● government and third- party payor reimbursement and coverage decisions that affect the utilization of our future drugs and competing drugs; ● negative safety or efficacy data from new clinical studies conducted either in the U. S. or internationally by any party, which could cause the sales of our future drugs to decrease or a future drug to be recalled; ● the degree of patent protection afforded our future drugs by patents granted to or licensed by us and by the outcome of litigation involving our or any of our licensor' s patents; ● marketing exclusivity, if any, awarded by the FDA to our drugs; ● the outcome of litigation involving patents of other companies concerning our future drugs or processes related to production and formulation of those drugs or uses of those drugs; ● the increasing use and development of alternate therapies; ● the rate of market penetration by competing drugs; and ● the termination of, or change in, existing arrangements with our partners. ~~31Any~~ -- **Any** of these factors could have a material adverse effect on the sales of any drug candidates that we may commercialize in the future. ~~Failure~~ **33Failure** to obtain regulatory approvals in foreign jurisdictions will prevent us from marketing our products internationally. We may seek approval for our drug candidates outside the United States and may market future products in international markets. In order to market our future products in the European Economic Area, or EEA, and many other foreign jurisdictions, we must obtain separate regulatory approvals. Specifically, in the EEA, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. Before granting the MA, the European Medicines Agency or the competent authorities of the member states of the EEA make an assessment of the risk- benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy. The approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Clinical studies conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals, and even if we file, we may not receive necessary approvals to commercialize our products in any market. If we obtain approval to commercialize any approved products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business. If our drug candidates are approved for commercialization outside of the United States, we expect that we will be subject to additional risks related to international operations and entering into international business relationships, including: ● different regulatory requirements for drug approvals; ● reduced protection for intellectual property rights, including trade secret and patent rights; ● unexpected changes in tariffs, trade barriers and regulatory requirements; ● economic weakness, including inflation, ~~rising~~ **uncertain** interest ~~rates~~ **rate environments** or political instability in particular foreign economies and markets; ● compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; ● foreign taxes, including withholding of payroll taxes; ● foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country; ● workforce uncertainty in countries where employment regulations are different than, and labor unrest is more common than, in the United States; ● production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; ● business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters, including earthquakes, hurricanes, floods and fires; and ● difficulty in importing and exporting clinical trial materials and study samples. ~~32Risks~~ **34Risks** Related to Reliance on Third PartiesWe rely on third parties to plan, conduct and monitor our clinical tests, and their failure to perform as required would interfere with our product development. We rely on third parties to conduct a significant portion of our clinical development activities. These activities include clinical patient recruitment and observation, clinical trial monitoring, clinical data management and analysis, safety monitoring and project management. We conduct project management and medical and safety monitoring in- house for some of our programs and rely on third parties for the remainder of our clinical development activities. If any of these third parties is unable to perform in a quality and timely manner, and at a feasible cost, our clinical studies will face delays. Further, if any of these third parties fails to perform as we expect or if their work fails to meet regulatory standards, our testing could be delayed, cancelled or rendered ineffective. We rely on contract manufacturers over whom we have limited control. Should the cost, delivery and quality of clinical materials manufactured by us in our Fall River facility or supplied by contract manufacturers vary to our disadvantage,

our business operations could suffer significant harm. We have limited experience in commercial manufacturing. We rely on CMOs to manufacture drug substance and drug product for any late- stage clinical studies of our drug candidates as well as for future commercial supplies. Our ability to conduct late- stage clinical trials, manufacture and commercialize our drug candidates, if regulatory approval is obtained, depends on the ability of such **CMOs** ~~third parties~~ to manufacture our drug candidates on a large scale at a competitive cost and in accordance with cGMP and foreign regulatory requirements, if applicable. We also rely on CMOs for labeling and storage for studies inside and outside the US. In order for us to establish our own commercial manufacturing facility, we would require substantial additional funds and would need to make facility modifications, hire and retain significant additional personnel and comply with extensive cGMP regulations applicable to such a facility. The commercial manufacturing facility would also need to be licensed for the production of our drug candidates by the FDA and meet other regulatory standards **. We therefore work with CMOs under established manufacturing arrangements that comply with the FDA' s requirements and other regulatory standards, although there is no assurance that the manufacturing will be successful. We also currently manufacture barzolvolimab and CDX- 585 drug substance in our Fall River facility for our current and planned Phase 1 and Phase 2 clinical trials. All products are then filled at CMOs** . Prior to approval of any drug candidate, the FDA must review and approve validation studies for both drug substance and drug product. The manufacturing processes for our drug candidates and immunotherapeutic delivery systems utilize known technologies. We believe that the products we currently have under development can be scaled up to permit manufacture in commercial quantities. However, there can be no assurance that we will not encounter difficulties in scaling up the manufacturing processes. Significant scale- up of manufacturing may result in unanticipated technical challenges and may require additional validation studies that the FDA must review and approve. CMOs may encounter difficulties in scaling up production, including problems involving supply chain, raw material suppliers, production yields, technical difficulties, scaled- up product characteristics, quality control and assurance, shortage of qualified personnel, capacity constraints, changing priorities within the CMOs, compliance with FDA and foreign regulations, environmental compliance, production costs and development of advanced manufacturing techniques and process controls. Any of these difficulties, if they occur and are not overcome to the satisfaction of the FDA or other regulatory agency, could lead to significant delays and possibly the termination of the development program for such drug candidate. These risks become more acute as we scale up for commercial quantities, where reliable sources of drug substance and drug product become critical to commercial success. The commercial viability of any of our drug candidates, if approved, will depend on the ability of our contract manufacturers to produce drug substance and drug product on a large scale. Failure to achieve this level of supply can jeopardize and prevent the successful commercialization of the drug ~~. We operate our own cGMP manufacturing facility in Fall River, Massachusetts, to produce drug substance for our current and planned early- stage clinical trials. Our Fall River manufacturing facility has 250L and 1000L bioreactor capacity and is able to manufacture in compliance with FDA and EU regulations, allowing us to distribute potential products to clinical sites in the U. S., EU and ROW for early- stage clinical trials. We have manufactured barzolvolimab and CDX- 585 drug substance in our Fall River facility for our current and planned Phase 1 and Phase 2 clinical trials. All products are then filled at CMOs. Any manufacturing failures, supply chain delays or compliance issues at our Fall River facility or at our CMOs could cause delays in our Phase 1 and Phase 2 clinical studies for these drug candidates. Our barzolvolimab drug product is currently administered both intravenously and subcutaneously. In 2022, we manufactured barzolvolimab drug substance at our Fall River facility in subcutaneous form then filled at a CMO to support ongoing and planned clinical trials. The subcutaneous formulation will allow for a potential self- administration at home setting versus the need for intravenous dosing in a hospital or clinic setting. The subcutaneous form could improve the patient experience if the product becomes available commercially. In 2022, we initiated a transfer of our current barzolvolimab manufacturing process to a CMO to allow us to 33produce larger batches in support of late- stage trials and to prepare for potential commercialization. We believe that barzolvolimab can be scaled up to permit manufacturing in commercial quantities. However, there can be no assurance that we will not encounter difficulties in scaling up the manufacturing processes~~ . Our leading drug candidates require specialized manufacturing capabilities and processes. We may face difficulty in securing commitments from U. S. and foreign contract manufacturers as these manufacturers could be unwilling or unable to accommodate our needs. Relying on foreign manufacturers involves peculiar and increased risks, including the risk relating to the difficulty foreign manufacturers may face in complying with cGMP requirements as a result of language barriers, lack of familiarity with cGMP or the FDA regulatory process, supply chain issues or other causes, economic or political instability in or affecting the home countries of our foreign manufacturers, shipping delays, potential changes in foreign regulatory laws governing the sales of our product supplies, fluctuations in foreign currency exchange rates and the imposition or application of trade restrictions. ~~There~~ **35There** can be no assurances that contract manufacturers will be able to meet our timetable and requirements. **While we believe that there is currently sufficient capacity worldwide for the production of our potential products through CMOs, establishing long- term relationships with CMOs and securing multiple sources for the necessary quantities of clinical and commercial materials required can be a challenge due to increasing industry demand for CMO services. Qualifying the initial source of clinical and ultimately commercial material is a time consuming and expensive process due to the highly regulated nature of the pharmaceutical / biotech industry. The key difficulty in qualifying more than one source for each product is the duplicated time and expense in doing so without the potential to mitigate these costs if the secondary source is never utilized.** Further, contract manufacturers must operate in compliance with cGMP and failure to do so could result in, among other things, the disruption of product supplies. As noted above, non- U. S. contract manufacturers may face special challenges in complying with cGMP requirements, and although we are not currently dependent on non- U. S. collaborators or contract manufacturers, we may choose or be required to rely on non- U. S. sources in the future as we seek to develop stable supplies of increasing quantities of materials for ongoing clinical trials of larger scale. **Use of third- party manufacturers also limits our control over and ability to monitor the manufacturing process. As a result, we may not be able to detect a variety of**

problems that may arise and may face additional costs in the process of interfacing with and monitoring the progress of our contract manufacturers. If third- party manufacturers fail to meet our manufacturing needs in an acceptable manner or fail to comply with regulatory requirements, we would face delays and additional costs while we develop internal manufacturing capabilities or find alternate third- party manufacturers. It may not be possible to have multiple third- party manufacturers ready to supply us with needed material at all or without incurring significant costs. Our dependence upon third parties for the manufacture of our products may adversely affect our profit margins and our ability to develop, manufacture, sell and deliver products on a timely and competitive basis **. Any manufacturing failures, supply chain delays or compliance issues at our Fall River facility or at our CMOs could cause delays in our clinical studies for our drug candidates** . We may need to rely on third- party collaborators to develop and commercialize companion diagnostic tests for our drug candidates. We do not have experience or capabilities in developing, administering, obtaining regulatory approval for, or commercializing companion diagnostic tests and will need to rely in large part on third- party collaborators to perform these functions. Companion diagnostic tests are subject to regulation by the FDA and similar regulatory authorities outside of the United States as medical devices and require separate regulatory approval prior to commercialization. We may need to rely on such third- party collaborators to obtain regulatory approval and commercialize such companion diagnostic tests. Such third- party collaborators: ● may not perform its obligations as expected or as required under our collaboration agreement; ● may encounter production difficulties that could constrain the supply of the companion diagnostic test; ● may have difficulties gaining acceptance of the use of the companion diagnostic test in the clinical community; ● may not pursue commercialization of the companion diagnostic test even if they receive any required regulatory approvals; ● may elect not to continue the development or commercialization of the companion diagnostic test based on changes in the third parties' strategic focus or available funding, or external factors such as an acquisition, that divert resources or create competing priorities; ● may be susceptible to third party cyber- attacks on our and their information security systems; ● may not commit sufficient resources to the marketing and distribution of the companion diagnostic test; and ● may terminate their relationship with us. If such third- party collaborators fail to develop, obtain regulatory approval or commercialize the companion diagnostic test, we may not be able to enter into arrangements with another diagnostic company to obtain supplies of an alternative diagnostic test for use ~~in~~ **36in** connection with the development and commercialization of our drug candidates or do so on commercially reasonable terms, which could adversely affect and / or delay the development or commercialization of our drug candidates. ~~34Our~~ -- **Our** reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them. Because we rely on third parties to develop our drug 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, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees and consultants prior to beginning research or disclosing proprietary information. These agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs which may require us to share trade secrets under the terms of research and development partnership or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor' s discovery of our trade secrets would impair our competitive position. We or the third parties upon whom..... material adverse effect on our business. Risks Related to Business OperationsWe may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management. From time to time we may consider strategic transactions, including acquisitions of companies, asset purchases and out- licensing or in- licensing of products, drug candidates or technologies. Additional potential transactions that we may consider include a variety of different business arrangements, including spin- offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations, acquisitions of assets and investments. Any such transaction may require us to incur non- recurring or other charges, may increase our near and long- term expenditures and may pose significant integration challenges or disrupt our management or business, which could adversely affect our operations and financial results. For example, these transactions may entail numerous operational and financial risks, including: ● exposure to unknown liabilities; ● disruption of our business and diversion of our management' s time and attention in order to develop acquired products, drug candidates or technologies; ● incurrence of substantial debt or dilutive issuances of equity securities to pay for acquisitions; ● higher than expected acquisition and integration costs; ● write- downs of assets or impairment charges; ~~35~~ ● increased amortization expenses; ● difficulty and cost in combining the operations and personnel of any acquired businesses with our operations and personnel; ● impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and ● inability to retain key employees of any acquired businesses. ~~Accordingly~~ **37Accordingly** , although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects. We may expand our clinical development, regulatory and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. We expect that if our drug candidates continue to progress in development, we may require significant additional investment in personnel, management systems and resources, particularly in the build out of our commercial capabilities. To date we have hired a core commercial team to plan for potential commercial launches if any of our drug candidates are approved. Over the next several years, we may experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and

sales and marketing. To manage this potential future growth, we may 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 physical 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 may not be able to successfully integrate our existing technology or to modify our technologies to create new immunotherapeutic drugs. If we are able to integrate our acquired assets and licensed assets with our immunotherapy technologies, we believe these assets will give our immunotherapeutic drugs a competitive advantage. However, if we are unable to successfully integrate licensed assets, or other technologies which we have acquired or may acquire in the future, with our existing technologies and potential products currently under development, we may be unable to realize any benefit from our acquisition of these assets, or other technologies which we have acquired or may acquire in the future, and we may face the loss of our investment of financial resources and time in the integration process. We believe that our immunotherapy technology portfolio may offer opportunities to develop immunotherapeutic drugs that treat a variety of cancers and inflammatory and infectious diseases by stimulating a patient' s immune system against those diseases. If our immunotherapy technology portfolio cannot be used to create effective immunotherapeutic drugs against a variety of diseases, we may lose all or portions of our investment in development efforts for new drug candidates. Our internal computer systems, or those of our CROs, CMOs, or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our drug development programs. **Our** ~~Despite the implementation of security measures, our internal~~ computer systems and those of our CROs, CMOs, and other contractors and consultants are vulnerable to damage from cyberattacks, malicious intrusion, computer viruses, unauthorized access, ~~loss of~~ data ~~privacy~~ **breaches, phishing attacks, cybercriminals** , natural disasters, terrorism, war and telecommunication, electrical failures or other significant disruption **even with a cybersecurity risk mitigation program developed by our enterprise. Such information technology systems are additionally vulnerable to security breaches from inadvertent or intentional actions by our employees, third- party vendors, contractors, consultants, business partners, and / or other third parties. The risks of a security breach or disruption, particularly through cyber- attacks or cyber intrusion, including by traditional computer " hackers, " threat actors, personnel (such as through theft, inadvertent mistake or misuse), sophisticated nation- state and nation- state- supported actors, sovereign governments and cyber terrorists, have generally increased over time, including for geopolitical reasons and in conjunction with military conflicts and defense activities, along with the number, intensity and sophistication of attempted attacks and intrusions from around the world. During times of war and other major conflicts, we and the third parties upon which we rely may be vulnerable to a heightened risk of these attacks, including cyber- attacks that could materially disrupt our systems and operations, supply chain and ability to produce and distribute our products and product candidates** . If **any** such ~~an event~~ **events** were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs and commercialization efforts. For example, the loss of clinical study data from completed or ongoing clinical studies for any of our drug candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Further, the risk of cyber- attacks or other privacy or data security incidents may be heightened due to common, external attempts to attack our information technology systems and data using means such as phishing **, other social engineering and vulnerability exploitation** . To the extent that any disruption or security breach were to result in a loss of or damage to our data or ~~applications~~ **38applications** or inappropriate disclosure of confidential ~~36or~~ **or** proprietary information, we could incur liability and the further development or commercialization of our drug candidates could be delayed. While we have not experienced any ~~such event~~ **material disruptions to our business, systems or operations as a result of a cybersecurity incident** to date, if such an event were to occur and cause **material** interruptions in our operations, it could result in a material disruption of our independent drug development programs **and our business overall** . For example, the loss of clinical trial data from ongoing or future clinical trials for any of our product candidates could result in delays in regulatory approval efforts and significantly increase costs to recover or reproduce the data. Our information security systems are also subject to laws and regulations requiring that we take measures to protect the privacy and security of certain information we gather and use in our business. For example, HIPAA and its implementing regulations impose, among other requirements, certain regulatory and contractual requirements regarding the privacy and security of personal health information. In the European Union **,** the General Data Protection Regulation, or GDPR, **further** ~~is even more restrictive~~ **restricts** ~~with respect to~~ all **applicable** personal ~~information~~ **data** , including information masked by a coding system **that is not considered deidentified data under applicable law** . In addition to HIPAA and GDPR, numerous other federal and state laws, including, without limitation, state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use, disclosure **, protection** and storage of personal information. To the extent that any disruption or security breach of our information technology systems were to result in a loss of or damage to data or applications, or inappropriate disclosure of **third- party notifiable** confidential or proprietary information ~~or~~ **,** personal health information **, personal information or personal data** , we could incur substantial liability under laws that protect the privacy of personal information, our reputation would be damaged, and the further development of our product candidates could be delayed, any of which could adversely affect our business **. The costs related to significant security breaches or disruptions could be material and exceed the limits of the cybersecurity insurance we maintain against such risks. We cannot anticipate all possible types of security threats and we cannot guarantee that our data protection efforts and our investments in information technology will prevent significant breakdowns, data leakages, security breaches in our systems, or those of our third- party vendors and other contractors and consultants, or other cyber incidents that could have a material adverse effect upon our reputation, business, operations, or financial condition** . Our business requires us to use hazardous

materials, which increases our exposure to dangerous and costly accidents. Our research and development activities involve the use of biological materials and small amounts of hazardous chemicals. The company has internal policies and procedures for the safe handling and disposal of these materials, in full compliance with applicable laws and regulations, including applicable OSHA, EPA, state and local regulations, and utilizing EPA licensed disposal companies and facilities. Although we believe we have reduced our risk and impacts from these materials through our safety procedures, we cannot completely eliminate the risk of accidental contamination or injury from these materials. The ongoing cost of complying with environmental laws and regulations is significant and may increase in the future. All risks of environmental damage inherent to our operations cannot be mitigated and failure to comply with applicable government regulations could result in the imposition of fines, restrictions, or increased operational costs, which could impact our ability to carry on with our operations. We face the risk of product liability claims, which could exceed our insurance coverage, and product recalls, each of which could deplete our cash resources. As a participant in the pharmaceutical, biotechnology and immunotherapeutic drug industries, we are exposed to the risk of product liability claims alleging that use of our drug candidates caused an injury or harm. These claims can arise at any point in the development, testing, manufacture, marketing or sale of our drug candidates and may be made directly by patients involved in clinical trials of our products, by consumers or health care providers or by individuals, organizations or companies selling our products. Product liability claims can be expensive to defend, even if the drug or drug candidate did not actually cause the alleged injury or harm. Insurance covering product liability claims becomes increasingly expensive as a drug candidate moves through the development pipeline to commercialization. However, there can be no assurance that such insurance coverage is or will continue to be adequate or available to us at a cost acceptable to us or at all. We may choose or find it necessary under our collaborative agreements to increase our insurance coverage in the future. We may not be able to secure greater or broader product liability insurance coverage on acceptable terms or at reasonable costs when needed. Any liability for damages resulting from a product liability claim could exceed the amount of our coverage, require us to pay a substantial monetary award from our own cash resources and have a material adverse effect on our business, financial condition and results of operations. Moreover, a product recall, if required, could generate substantial ~~negative~~ **39negative** publicity about our products and business and inhibit or prevent development of our drug candidates and, if approval is obtained, commercialization of our future drugs ~~. Disruptions in the global economy and supply chains may have a material adverse effect on our business, financial condition and results of operations. The disruptions to the global economy since 2020 have impeded global supply chains, resulting in longer lead times and also increased critical component costs and freight expenses. We have taken steps to minimize the impact of these increased costs by working closely with our suppliers. Despite the actions we have undertaken to minimize the impacts from disruptions to the global 37economy, there can be no assurances that unforeseen future events in the global supply chain, and inflationary pressures, will not have a material adverse effect on our business, financial condition and results of operations~~ . Risks Related to Intellectual PropertyWe license technology from other companies to develop products, and those companies could influence research and development or restrict our use of it. In addition, if we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose license rights that are important to our business. Companies that license technologies to us that we use in our research and development programs may require us to achieve milestones or devote minimum amounts of resources to develop products using those technologies. They may also require us to make significant royalty and milestone payments, including a percentage of any sublicensing income, as well as payments to reimburse them for patent costs. The number and variety of our research and development programs require us to establish priorities and to allocate available resources among competing programs. From time to time, we may choose to slow down or cease our efforts on particular products. If in doing so we fail to fully perform our obligations under a license, the licensor can terminate the license or permit our competitors to use the technology. Termination of these licenses or reduction or elimination of our licensed rights may result in our having to negotiate new or reinstated licenses with less favorable terms. Moreover, we may lose our right to market and sell any products based on the licensed technology. The occurrence of such events could materially harm our business. Our ability to successfully develop and, if regulatory approval is obtained, commercialize our drug candidates may be materially adversely affected if we are unable to obtain and maintain effective intellectual property rights for our drug candidates and technologies. Our success depends in part on our ability to obtain and maintain patent protection and other intellectual property protection for our drug candidates and proprietary technology. We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our drug candidates and technology that are important to our business. This process is expensive and time- consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technologies or from developing competing drugs and technologies. We may also be unable to obtain patent term adjustments or extensions (or similar rights, such as Supplementary Protection Certificates, in foreign countries) at the relevant times, or the duration of any such adjustments, extensions or the like may be less than requested. Biotechnology patents involve complex legal, scientific and factual questions and are highly uncertain and may also result in different outcomes in different territories. To date, there is no consistent policy regarding the breadth of claims allowed in biotechnology patents, particularly in regard to patents for technologies for human uses like those we use in our business. We cannot predict whether the patents we or our licensors seek will issue. If such patents are issued, a competitor may challenge them and may potentially have them revoked or limit their scope, for example based on existing or newly identified prior art or other issues of validity. Moreover, our patents may not afford effective protection against competitors with similar technology. A successful challenge to any one of our patents could result in a third party' s ability to use the technology covered by the patent. We also face the risk that others will infringe, avoid or circumvent our patents. Technology that we license from others is subject to similar risks and this could harm our ability to use that technology. If we, or a company that licenses technology to us, were not the first creator of an invention that we use,

and / or if inventorship were to be decided against us (or our licensor) in any relevant litigation, our use of the underlying product or technology will face restrictions, including elimination, and our ability to defend and / or enforce any affected patent rights could also be materially harmed. If we must defend against suits brought against us or prosecute suits against others involving intellectual property rights, we will incur substantial costs. In addition to any potential liability for significant monetary damages, a decision against us may require us to obtain licenses to patents or other intellectual property rights of others on potentially unfavorable terms. If those licenses from third parties are necessary but we cannot acquire them, we would attempt to design around the relevant technology, which would cause higher development costs and delays and may ultimately prove impracticable. ~~38We~~ **40We** may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms. A third party may hold intellectual property, including patent rights, that are important or necessary to the development of our drug candidates. It may be necessary for us to use the patented or proprietary technology of a third party to commercialize our own technology or drug candidates, in which case we would be required to obtain a license from such third party. A license to such intellectual property may not be available or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition. We may be unable to protect the confidentiality of our trade secrets, thus harming our business and competitive position. We rely upon trade secrets, including unpatented know- how, technology and other proprietary information to develop and maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. We also have agreements with our employees that obligate them to assign their inventions to us. However, it is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees, consultants or collaborators that are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets through such breaches or violations. Further, our trade secrets could be disclosed, misappropriated or otherwise become known or be independently discovered by our competitors. In addition, intellectual property laws in foreign countries may not protect our intellectual property to the same extent as the laws of the United States. If our trade secrets are disclosed or misappropriated, it would harm our ability to protect our rights and have a material adverse effect on our business. We may become involved in lawsuits to protect or enforce our patents, which could be expensive, time- consuming and unsuccessful. Competitors may infringe our patents. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time- consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business. Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our drug candidates and use our proprietary technologies without infringing, misappropriating or otherwise violating the proprietary rights or intellectual property of third parties. We may become party to, or be threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our drug candidates and technology. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. If we are found to infringe a third- party' s intellectual property rights, we could be required to obtain a license from such third- party to continue developing our drug candidates and technology. 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. We could be forced, including by court order, to cease developing the infringing technology or product. In addition, we could be found liable for monetary damages. Claims that we have misappropriated the confidential information or trade secrets of third parties can have a similar negative impact on our business. Third parties may assert that our employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets. We employ individuals who were previously employed at universities or other diagnostic or biopharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees and consultants do not use the proprietary information or know- how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other ~~39proprietary~~ **41proprietary** information, of a former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. 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. Regulatory RisksWe may not be able to obtain or maintain orphan drug designation or exclusivity for our product candidates. We may seek orphan drug designation for some of our product candidates in the United States. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200, 000 individuals in the United States. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same indication for that drug during that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable

so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or the EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. We cannot assure you that any future application for orphan drug designation with respect to any product candidate will be granted. If we are unable to obtain orphan drug designation in the United States, we will not be eligible to obtain the period of market exclusivity that could result from orphan drug designation or be afforded the financial incentives associated with orphan drug designation. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Any fast track designation or grant of priority review status by the FDA may not actually lead to a faster development or regulatory review or approval process, nor will it assure FDA approval of our product candidates. Additionally, our product candidates may treat indications that do not qualify for priority review vouchers. We may seek fast track designation for some of our product candidates or priority review of applications for approval of our product candidates. If a drug is intended for the treatment of a serious or life- threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA fast track designation. If a product candidate offers major advances in treatment, the FDA may designate it eligible for priority review. The FDA has broad discretion whether or not to grant these designations, so even if we believe a particular product candidate is eligible for these designations, we cannot assure you that the FDA would decide to grant them. Even if we do receive fast track designation or priority review, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program. Any breakthrough therapy designation granted by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval. We may seek a breakthrough therapy designation for some of our product candidates. A breakthrough therapy is defined as a drug 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 drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs and biologics 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. Drugs designated as breakthrough therapies by the FDA may also be eligible for accelerated approval if the relevant criteria are met. ~~40Designation~~ **42Designation** as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to drugs considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. If our processes and systems are not compliant with regulatory requirements, we could be subject to delays in submitting BLAs, NDAs or restrictions on marketing of drugs after they have been approved. We currently are developing drug candidates for regulatory approval and are in the process of implementing regulated processes and systems required to obtain and maintain regulatory approval for our drug candidates. Certain of these processes and systems for conducting clinical trials and manufacturing material must be compliant with regulatory requirements before we can apply for regulatory approval for our drug candidates. These processes and systems will be subject to continual review and periodic inspection by the FDA and other regulatory bodies. If we are unable to achieve compliance in a timely fashion or if compliance issues are identified at any point in the development and approval process, we may experience delays in filing for regulatory approval for our drug candidates or delays in obtaining regulatory approval after filing. In addition, any later discovery of previously unknown problems or safety issues with approved drugs or manufacturing processes, or failure to comply with regulatory requirements may result in restrictions on such drugs or manufacturing processes, withdrawal of drugs from the market, the imposition of civil or criminal penalties or a refusal by the FDA and / or other regulatory bodies to approve pending applications for marketing approval of new drugs or supplements to approved applications, any of which could have a material adverse effect on our business. In addition, we are a party to agreements that transfer responsibility for complying with specified regulatory requirements, such as filing and maintenance of marketing authorizations and safety reporting or compliance with manufacturing requirements, to our collaborators and third- party manufacturers. If our collaborators or third- party manufacturers do not fulfill these regulatory obligations, any drugs for which we or they obtain approval may be subject to later restrictions on manufacturing or sale or may even risk withdrawal, which could have a material adverse effect on our business. We have conducted and are conducting clinical trials outside the United States and anticipate conducting additional clinical trials outside the United States, and the FDA may not accept data from such trials. We are currently conducting clinical trials for our product candidates in countries outside of the United States and we anticipate that we will conduct additional clinical trials in countries outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of such study data by the FDA is subject to certain conditions. For example, the clinical trial must be conducted in accordance with GCP requirements and the FDA must be able to validate the data from the clinical trial through an onsite inspection if it deems such inspection necessary. Where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the United States, the FDA will not approve the application on the basis of foreign data alone unless those data are considered applicable to the U. S. patient

population and U. S. medical practice, the clinical trials were performed by clinical investigators of recognized competence, and the data is considered valid without the need for an on- site inspection by the FDA or, if the FDA considers such an inspection to be necessary, the FDA is able to validate the data through an on- site inspection or other appropriate means. In addition, such clinical trials would be subject to the applicable local laws of the foreign jurisdictions where the clinical trials are conducted. A description of any studies related to overdosage is also required, including information on dialysis, antidotes, or other treatments, if known. There can be no assurance the FDA will accept data from clinical trials conducted outside of the United States. If the FDA does not accept any such data, it would likely result in the need for additional clinical trials, which would be costly and time- consuming and delay aspects of our development plan. Risks inherent in conducting international clinical trials include, but are not limited to: ● foreign regulatory requirements that could burden or limit our ability to conduct our clinical trials; ● administrative burdens of conducting clinical trials under multiple foreign regulatory schema; ● foreign currency fluctuations which could negatively impact our financial condition since certain payments are paid in local currencies; ~~41~~ **43** ● manufacturing, customs, shipment and storage requirements; ● cultural differences in medical practice and clinical research; and ● diminished protection of intellectual property in some countries. Changes in product candidate manufacturing or formulation may result in additional costs or delay. As product candidates are developed through preclinical studies to late- 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. During the course of a development program, sponsors may also change the contract manufacturers used to produce the product candidates. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause our product candidates to perform differently and affect the results of clinical trials. Such changes may also require additional testing, notification or approval by the FDA, EMA or other regulatory authorities. This could delay completion of clinical trials; require the conduct of bridging clinical trials or studies, or the repetition of one or more clinical trials; increase clinical trial costs; delay **or prevent** approval of our product candidates and jeopardize our ability to commence product sales and generate revenue. Even if we receive regulatory approval for a drug candidate, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense and subject us to penalties if we fail to comply with applicable regulatory requirements. Once regulatory approval has been granted, the approved product and its manufacturer are subject to continual review by the FDA and / or non- U. S. regulatory authorities. Any regulatory approval that we or our collaboration partners receive for our drug candidates may be subject to limitations on the indicated uses for which the product may be marketed or contain requirements for potentially costly post- marketing follow- up studies to monitor the safety and efficacy of the product. In addition, if the FDA and / or non- U. S. regulatory authorities approve any of our drug candidates, we will be subject to extensive and ongoing regulatory requirements by the FDA and other regulatory authorities with regard to the labeling, packaging, adverse event reporting, storage, advertising, promotion and recordkeeping for our products. In addition, manufacturers of our drug products are required to comply with cGMP regulations, which include requirements related to quality control and quality assurance as well as the corresponding maintenance of records and documentation. Further, regulatory authorities must inspect and approve these manufacturing facilities before they can be used to manufacture our drug products, and these facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations. If we or a third party discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency or problems with the facility where the product is manufactured, a regulatory authority may impose restrictions on that product, the manufacturer or us, including requiring withdrawal of the product from the market or suspension of manufacturing. If we, our drug candidates or the manufacturing facilities for our drug candidates fail to comply with regulatory requirements of the FDA and / or other non- U. S. regulatory authorities, we could be subject to administrative or judicially imposed sanctions, including the following: ● warning letters; ● civil or criminal penalties and fines; ● injunctions; ● consent decrees; ● suspension or withdrawal of regulatory approval; ● suspension of any ongoing clinical studies; ● voluntary or mandatory product recalls and publicity requirements; ● refusal to accept or approve applications for marketing approval of new drugs; ~~42~~ **44** ● restrictions on operations, including costly new manufacturing requirements; or ● seizure or detention of drugs or import bans. The regulatory requirements and policies may change and additional government regulations may be enacted with which we may also be required to comply. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or in other countries. If we are not able to maintain regulatory compliance, we may not be permitted to market our future products, and our business may suffer. We may be subject, directly or indirectly, to federal and state health care fraud and abuse laws, false claims laws, transparency and pricing laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties. If we obtain FDA approval for any of our drug candidates and begin commercializing those products in the United States, our operations will be directly, or indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti- Kickback Statute and the federal False Claims Act. These laws may affect, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include: ● the federal Anti- Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal health care program, such as the Medicare and Medicaid programs; ● federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other third- party payors that are false or fraudulent; ● the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, which

impose certain requirements relating to the privacy, security and transmission of individually identifiable health information; ● the federal transparency requirements under the Patient Protection and Affordable Care Act of 2010 (" ACA ") requires manufacturers of drugs, devices, biologics and medical supplies to report to the Department of Health and Human Services information related to physician payments and other transfers of value and physician ownership and investment interests; ● state law and foreign law equivalents of each of the above federal laws, such as anti- kickback and false claims laws which may apply to items or services reimbursed by any third- party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts; and ● state and federal laws, such as the Physician Sunshine Act, directed at generating transparency on financial issues, including drug prices and payments made by drug companies to various entities and individuals involved in healthcare. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including exclusion from payment by federal health care programs, civil and criminal penalties, damages, fines and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly. ~~43Compliance~~ **45Compliance** with laws and regulations pertaining to the privacy and security of health information may be time consuming, difficult and costly, particularly in light of increased focus on privacy issues in countries around the world, including the U. S. and the EU. We are subject to various domestic and international privacy and security regulations related to personal information, including health information, that are appliable to our business and associated data processing activities. The confidentiality, collection, use and disclosure of personal data, including clinical trial patient- specific information, are subject to governmental regulation generally in the country that the personal data were collected or used. In the United States, we are subject to various state and federal privacy and data security regulations, including but not limited to HIPAA and as amended by the HITECH Act. HIPAA imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information, and mandates, among other things, the adoption of uniform standards for the electronic exchange of information in common health care transactions, as well as standards relating to the privacy and security of individually identifiable health information, which require the adoption of administrative, physical and technical safeguards to protect such information. We may also be subject to state security breach notification laws, state laws protecting the privacy and security of health and personal information, and federal and state consumer protections laws which regulate the collection, use, disclosure and transmission of personal information. These laws may overlap and conflict with each other, and each of these laws is subject to varying interpretations by courts and government agencies, creating complex compliance issues for us. In the EU, personal data includes any information that relates to an identified or identifiable natural person with health information carrying additional obligations, including obtaining the explicit consent from the individual for collection, use or disclosure of the information. We are also subject to the EU General Data Protection Regulation 2016 / 679 (" GDPR "). Violations of the GDPR can carry hefty fines. In addition, we may be subject to additional national laws and regulations that govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts. If we fail to comply with applicable data protection laws and regulations, we could be subject to penalties or sanctions, including criminal penalties. Furthermore, the legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing amount of focus on privacy and data protection issues. Compliance with these laws may be time- consuming, difficult and costly. If we fail to comply with applicable laws, regulations or duties relating to the use, privacy or security of personal data we could be subject to the imposition of significant civil and criminal penalties, be forced to alter our business practices and suffer reputational harm. Changes in health care law and implementing regulations, including government restrictions on pricing and reimbursement, as well as health care policy and other health care payor cost- containment initiatives, may have a material adverse effect on us. In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the regulatory system, health care system and efforts to control health care costs, including drug prices, that could have a significant negative impact on our business, including preventing, limiting or delay regulatory approval of our drug candidates and reducing the sales and profits derived from our products once they are approved. For example, in the United States, the ACA substantially changed the way health care is financed by both governmental and private insurers and significantly affects the pharmaceutical industry. Many provisions of ACA impact the biopharmaceutical industry, including that in order for a biopharmaceutical product to receive federal reimbursement under the Medicare Part B and Medicaid programs or to be sold directly to U. S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the drug pricing program under the Public Health Services Act, or PHS. Since its enactment, there have been judicial and Congressional challenges and amendments to certain aspects of ACA. There is continued uncertainty about the implementation of ACA, including the potential for further amendments to the ACA and legal challenges to or efforts to repeal the ACA. In addition, the Inflation Reduction Act of 2022, enacted in August 2022, empowers the Centers for Medicare and Medicaid Services to negotiate directly with pharmaceutical companies to set the prices for a limited set of high- cost drugs covered by Medicare, and puts penalties in place for drug manufacturers who increase their Medicare prices by more than the rate of inflation. Other examples of proposed changes include, but are not limited to, expanding post- approval requirements, changing the Orphan Drug Act, and restricting sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether government regulations, guidance or interpretations will be changed, or what the impact of such changes would be on the marketing approvals, sales, pricing, or reimbursement of our drug candidates or products, if any, may be. ~~44Risks~~ **46Risks** Related to Our Capital StockOur history of losses and uncertainty of future profitability make our common stock a highly

speculative investment. We have had no commercial revenue to date from sales of our drug candidates. We had an accumulated deficit of $ 1. ~~3~~ **4** billion as of December 31, ~~2022~~ **2023** . We expect to spend substantial funds to continue the research and development testing of our drug candidates. In anticipation of FDA approval of these products, we will need to make substantial investments to establish sales, marketing, quality control, regulatory compliance capabilities and commercial manufacturing alliances. These investments will increase if and when any of these drug candidates receive FDA approval. We cannot predict how quickly our lead drug candidates will progress through the regulatory approval process. As a result, we may continue to lose money for several years. We cannot be certain that we will achieve or sustain profitability in the future. Failure to achieve profitability could diminish our ability to sustain operations, pay dividends on our common stock, obtain additional required funds and make required payments on our present or future indebtedness. Our share price has been and could remain volatile. The market price of our common stock has historically experienced and may continue to experience significant volatility. From January ~~2021~~ **2022** through December ~~2022~~ **2023** , the market price of our common stock has fluctuated from a high of $ ~~57~~ **48** . ~~20~~ **40** per share in the ~~fourth~~ **first** quarter of ~~2021~~ **2023** , to a low of $ ~~15~~ **19** . ~~37~~ **85** per share in the ~~first~~ **second** quarter of ~~2021~~ **2022** . Our progress in developing and commercializing our products, the impact of government regulations on our products and industry, the potential sale of a large volume of our common stock by stockholders, our quarterly operating results, changes in general conditions in the economy or the financial markets and other developments affecting us or our competitors could cause the market price of our common stock to fluctuate substantially with significant market losses. If our stockholders sell a substantial number of shares of common stock, especially if those sales are made during a short period of time, those sales could adversely affect the market price of our common stock and could impair our ability to raise capital. In addition, in recent years, the stock market has experienced significant price and volume fluctuations. This volatility has affected the market prices of securities issued by many companies for reasons unrelated to their operating performance and may adversely affect the price of our common stock. In addition, we could be subject to a securities class action litigation as a result of volatility in the price of our stock, which could result in substantial costs and diversion of management' s attention and resources and could harm our stock price, business, prospects, results of operations and financial condition. Our ability to use our net operating loss carryforwards will be subject to limitation and, under certain circumstances, may be eliminated. As of December 31, ~~2022~~ **2023** , we had net operating loss carryforwards, or NOLs, of approximately $ ~~623~~ **618** . ~~1~~ **4** million for federal income tax purposes, and $ ~~879~~ **1** . ~~9~~ **0** ~~million~~ **billion** for state income tax purposes. Utilization of these NOLs depends on many factors, including our future income, which cannot be assured. In addition, utilization of our net operating loss and research and development credit carryforwards may be subject to substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future provided by Section 382 of the Internal Revenue Code of 1986, or Section 382, as well as similar state provisions. In general, an ownership change, as defined by Section 382, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50 percentage points over a three- year period. In October 2007, June 2009, December 2009 and December 2013, we experienced a change in ownership as defined by Section 382. Historically, we have raised capital through the issuance of capital stock on several occasions which, combined with shareholders' subsequent disposition of those shares, has resulted in three changes of control, as defined by Section 382. As a result of these ownership changes, utilization of at least some of our federal NOL carryforwards is subject to an annual limitation. We have not undertaken a study to assess whether an ownership change or multiple ownership changes have occurred for (i) acquired businesses with NOLs prior to being acquired by the Company, (ii) the Company on the state level, (iii) the Company since March 2015 or (iv) research and development credits. If, based on such a study, we were to determine that there has been an ownership change at any time, utilization of net operating loss or tax credit carryforwards would be subject to an annual limitation under Section 382 (or similar state provisions). Any unused annual limitation may be carried over to later years, and the amount of the limitation may, under certain circumstances, be subject to adjustment if the fair value of our net assets is determined to be below or in excess of the tax basis of such ~~45assets~~ **47assets** at the time of the ownership change, and such unrealized loss or gain is recognized during the five- year period after the ownership change. Subsequent ownership changes, as defined in Section 382, could further limit the amount of net operating loss carryforwards and research and development credits that can be utilized annually to offset future taxable income. Additionally, the Tax Cuts and Jobs Act limited the deduction for net operating losses to 80 % of taxable income while providing that net operating loss carryovers for years after 2017 will not expire. The CARES Act provides relief to corporate taxpayers by permitting a five year carryback of 2018 – 2020 NOLs, removing the 80 % limitation on the carryback of those NOLs, and accelerates refunds for minimum tax credit carryforwards, along with a few other provisions. During the twelve months ended December 31, ~~2022~~ **2023** , no material adjustments were made to provision amounts recorded as a result of the enactment of the CARES Act. Refer to Note 15, " Income Taxes, " in the accompanying notes to the financial statements for additional discussion on income taxes. General Risk FactorsIf we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock. Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. We have designed, implemented and tested the internal control over financial reporting required to comply with this obligation, which was and is time consuming, costly, and complicated. 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. Any testing by us conducted in connection with Section 404 of the Sarbanes- Oxley Act of 2002, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal

controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock. We have many competitors in our field, and they may develop technologies that make ours obsolete. Biotechnology, pharmaceuticals and therapeutics are rapidly evolving fields in which scientific and technological developments are expected to continue at a rapid pace. We have many competitors in the U. S. and abroad. The competitors of which we are aware that have initiated a Phase 3 study or have obtained marketing approval for a potentially competitive drug to barzolvolimab for treatment of CSU, CIndU, PN and EoE include: Allakos (lirentelimab for EoE), ~~AstraZeneca~~ **Celltrion** (~~Fasenra~~ **CT- P39; omalizumab biosimilar** for CSU), Galderma / Chugai (nemolizumab for PN), ~~Genentech~~ **Novartis** (~~fenebrutinib~~ **remibrutinib** for CSU), ~~Leo Pharma (Adbry for AD), Novartis (ligelizumab for CSU, CIndU~~ and ~~food allergy; remibrutinib for CSU),~~ Regeneron / Sanofi (Dupixent for CSU, CIndU, PN and EoE ~~), and Trevi Therapeutics (nalbuphine for PN~~). Our success depends upon our ability to develop and maintain a competitive position in the product categories and technologies on which we focus. Many of our competitors have greater capabilities, experience and financial resources than we do. Competition is intense and is expected to increase as new products enter the market and new technologies become available. Our competitors may: ● develop technologies and products that are more effective than ours, making ours obsolete or otherwise noncompetitive; ● obtain regulatory approval for products more rapidly or effectively than us; and ● obtain patent protection or other intellectual property rights that would block our ability to develop competitive products. We **or the third parties** upon whom we depend may be adversely affected by natural disasters **or other unforeseen events** and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.Any unplanned event,such as flood,fire,explosion,earthquake,extreme weather condition ~~,medical epidemic,including the COVID- 19 pandemic~~ ,power shortage,telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities,or the manufacturing facilities of our third- party CMOs,could severely disrupt our operations and have a material adverse effect on our business,results of operations,financial condition and prospects.For example,our operations are located primarily on the east coast ~~of~~ **48of** the United States,and any adverse weather event or natural disaster,such as a hurricane or heavy snowstorm,could have a material adverse effect on a substantial portion of our operations.If any event occurred that prevented us from using all or a significant portion of our manufacturing and lab facilities, ~~that~~ damaged critical infrastructure,such as third- party manufacturing facilities,or ~~that~~ otherwise disrupted operations and travel,it may be difficult or,in certain cases,impossible for us to continue our business for a substantial period of time.The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event.We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans,which could have a material adverse effect on **our business.We** face risks related to health epidemics and outbreaks, including COVID- 19, which could significantly disrupt our preclinical studies and clinical trials. **Disease outbreaks, epidemics and pandemics, including COVID- 19, in regions where we have concentrations of clinical trial sites and other business operations, could adversely affect our business, including by causing significant disruptions in our operations and / or in the operations of manufacturers and CROs upon whom we rely. Disease outbreaks, epidemics and pandemics may have negative impacts on our ability to initiate new clinical trial sites, enroll new patients and maintain existing patients who are participating in clinical trials, which may result in increased clinical trial costs, longer timelines and delay in our ability to obtain regulatory approvals of our product candidates, if at all. For example, patient enrollment and recruitment could be delayed due to local clinical trial site protocols designed to protect staff and patients from certain outbreaks, which could delay the expected timelines for data readouts of our preclinical studies and clinical trials. Additionally, general supply chain issues may be exacerbated during disease outbreaks, epidemics or pandemics and may also impact the ability of our clinical trial sites to obtain basic medical supplies used in our trials in a timely fashion, if at all. Moreover, the extent to which disease outbreaks, epidemics and pandemics may impact our business, results of operations and financial position will depend on future developments, which are highly uncertain and cannot be predicted with confidence. New health epidemics or pandemics may emerge that result in similar or more severe disruptions to our business. A future disease outbreak, epidemic or pandemic adversely affects our business, financial condition, results of operations and growth prospects.** The future progression of **the COVID- 19 epidemic and its effects on our business and operations are uncertain. The impacts of a potential resurgence of COVID- 19 could pose the risk that we or our employees, suppliers, customers and others may be restricted or prevented from conducting business activities for indefinite or intermittent periods of time, including as a result of employee health and safety concerns, shutdowns, shelter in place orders, travel restrictions and other actions and restrictions that may be prudent or required by governmental authorities. This could disrupt our ability to operate our business, including producing drug product and administering our preclinical and clinical studies. In addition, fluctuations in demand and other implications associated with** the COVID- 19 pandemic **have resulted in,** and ~~its~~ **could continue resulting in, certain supply chain constraints and challenges. Disruptions in the global economy and supply chains may have a material adverse** ~~effects~~ **effect** on our business **, financial condition** and **results of** operations ~~are uncertain~~ . The ~~duration and~~ **disruptions to** the ~~geographic~~ **global economy due to geopolitical events have impeded, and may continue to impede in the future, global supply chains, resulting in longer lead times and also increased critical component costs and freight expenses. We have taken steps to minimize the** impact of ~~the~~ **these increased costs by working closely with our suppliers. Despite the actions we have undertaken to minimize the impacts from disruptions to the global economy, there can be no assurances that unforeseen future events in the global supply chain, and inflationary pressures, will not have a material adverse effect on our** business **,** ~~disruption and related~~ financial **condition** ~~impact resulting from the COVID- 19 pandemic cannot be 46reasonably estimated at this time and our business could be adversely impacted by its effects. In an~~ **and results** ~~effort to halt or slow the outbreak~~ of ~~COVID- 19, many governments~~

have, at times, placed significant restrictions on travel and many businesses have, at times, announced closures for extended periods which could adversely impact our operations . Enrollment of patients in our clinical trials and our planned and ongoing preclinical and clinical trials may be delayed due to COVID- 19. The impact of the COVID- 19 pandemic on the operations of the FDA and other health authorities may delay potential approvals of our clinical trial protocols. In addition, we rely on independent clinical investigators, contract research organizations and other third- party service providers to assist us in managing, monitoring and otherwise carrying out our preclinical studies and clinical trials, and the pandemic may affect their ability to devote sufficient time and resources to our programs. We also rely on third party suppliers and contract manufacturers to produce the drug product we utilize in our clinical trials, and the pandemic may cause delays in the delivery of active pharmaceutical ingredients (" APIs ") and drug product. Temporary closure of our facilities, or facilities at which our clinical or preclinical trials are conducted, or restrictions on the ability of our employees, clinicians or patients enrolled in our trials to travel could adversely affect our operations and our ability to conduct and complete our preclinical and clinical trials. In addition, the COVID- 19 pandemic, including insufficient vaccination of the general population and the emergence of COVID- 19 variants, could affect the health and availability of our workforce as well as those of the third parties on whom we rely. If new, more infectious or severe variants emerge, it is possible that the impact of the pandemic on our business may increase or lengthen in duration. As a result of the foregoing factors, the expected timeline for data readouts of our preclinical studies and clinical trials and certain regulatory filings may be negatively impacted, which would adversely affect our business . We depend greatly on the intellectual capabilities and experience of our key executives and scientists, and the loss of any of them could affect our ability to develop our products. The loss of any of our executive officers could harm us. We entered into employment agreements with each of our executive officers, although an employment agreement as a practical matter does not guarantee retention of an employee. We also depend on our scientific and clinical collaborators and advisors, all of whom have outside commitments that may limit their availability to us. In addition, we believe that our future success will depend in large part upon our ability to attract and retain highly skilled scientific, managerial and marketing personnel, particularly as we expand our activities in clinical trials, the regulatory approval process and sales and manufacturing. We routinely enter into consulting agreements with our scientific and clinical collaborators and advisors, key opinion leaders and heads of academic departments in the ordinary course of our business. We also enter into contractual agreements with physicians and institutions who recruit patients into our clinical trials on our behalf in the ordinary course of our business. **49** Notwithstanding these arrangements, we face significant competition for this type of personnel from other companies, research and academic institutions, government entities and other organizations. We cannot predict our success in hiring or retaining the personnel we require for continued growth. Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business. We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with applicable privacy laws, comply with manufacturing standards we have established, comply with federal and state health care fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self- dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Business Conduct and Ethics and launched a Health Care Compliance program, but it is not always possible to identify and deter employee misconduct. The precautions we take and the investments we make 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 be in compliance with such laws or regulations. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant effect on our business and results of operations, including the imposition of significant fines or other sanctions. 47